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BIOLOGICAL EFFECTS AND THERAPEUTIC POSSIBILITIES OF NEUTRONS

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IT IS now possible to obtain neutrons in sufficiently abundant intensities to make worth while the consideration of their biological and therapeutic possibilities. Enough knowledge of the remarkable behavior of neutrons has been accumulated through physical research to enable the prediction of certain biological effects, and to see, in a general way at least, certain therapeutic potentialities of this new kind of corpuscular radiation. The facility with which neutrons pass through matter, and penetrate and disrupt atomic nuclei, of which they are now believed to be fundamental constituents, gives them an importance in some fields of atomic physics which is not equalled by alpha, beta, or gamma rays. This naturally reflects on the various fields of biological application of corpuscular and quantum radiations.

I. NATURE AND BEHAVIOR OF NEUTRONS

Neutrons are electrically uncharged elementary particles which have very nearly the same mass as hydrogen atoms. They were discovered in 1932 by Dr. J. Chadwick, of Cavendish Laboratory, Cambridge University, who has very appropriately been awarded the Nobel Prize for the discovery. Neutrons are usually produced by bombarding beryllium metal with alpha particles from radium or radon, or by bombarding some element with deuterons (charged atoms of heavy hydrogen) which have been electrically accelerated to very high speeds. Although they are particles, neutrons pass through ordinary matter with facility resembling that of very hard gamma radiation. Their collisions, and other interactions, are with atomic nuclei, not with extra-nuclear electrons; hence they do not produce trails of ionization along their paths through matter, but collide, at intervals, with atomic nuclei. A nucleus struck by a neutron is either driven away as an (ionizing) recoil nucleus, or it captures the neutron, thereby being transmuted temporarily or permanently into another nucleus.

Since neutrons have no electric charge, they are not acted upon by the electronic fields of extra-nuclear electrons, nor are they stopped at nuclear boundaries, like other impinging particles; they may pass directly into atomic nuclei with little resistance.[1] Once a neutron has penetrated an atomic nucleus, it has considerable chance of disturbing the previous nuclear equilibrium. The particular kind of "disturbance" depends on the kind of nucleus and

[1] More exactly, the field of the neutron interacts with other atomic fields only through very short distances. Its "radius" is estimated to be of the order of 10^{-12} cm., as compared with atomic radii of 5 to 19×10^{-9} cm., and nuclear radii of about 1 to 10×10^{-12} cm.

on the velocity of the impinging neutron. Slow neutrons are most effective. If the velocity is very high, the neutron may simply pass through the nucleus and leave it unaltered. If the neutron stops, however, the nucleus may be disintegrated immediately, or it may be transmuted to another kind of nucleus. In the latter case, if the new nucleus is stable, the transmutation only results in the formation of a heavier nucleus from a lighter one, usually accompanied by the emission of a quantum of gamma radiation; but if it is unstable, it will disintegrate: hence the neutron has brought about induced radioactivity. The answer to the question of which of these processes will result from the penetration of the nucleus by a neutron depends on the kind of nucleus and the speed of the neutron.

To date, more than 40 elements have been made artificially radioactive by neutron bombardment; in some cases, two or more radioactive elements are created from a single bombarded element. The half-lives of the radioactivities vary from a few seconds to about fourteen days: the decay products are beta and gamma rays of singular energies, depending on the element. Whereas natural radioactivity is confined to three heavy elements, uranium, thorium, and actinium, and their descendants (except for the very feeble radioactivity of rubidium, potassium, and samarium), artificial radioactivity has been induced in elements throughout most of the atomic scale.

The possibility of applying artificially radioactive elements to biological research and radiation therapy has already aroused much interest; this field will doubtless be explored as fast as experimental facilities can be established and experiments performed. Indeed, it now seems very possible that artificially radioactive elements may eventually replace radium and radon for certain types of therapy. Their chief advantages would seem to lie in the homogeneity of their radiations, the suitability of their half-lives for therapeutic uses, and the non-toxicity of their decay products. But the production of these elements by neutron bombardment (directly or indirectly) is an extremely inefficient process: the average number of bombarding neutrons required to produce one atom of a radioactive element must be reckoned in powers of ten. Accordingly, the potential biological effects, useful or otherwise, of a given neutron source are necessarily larger than those, useful or otherwise, from any artificially radioactive material created by the same neutron source.

II. Biological Effects Expected from Neutron Irradiation

It is the purpose of this paper to call attention to some biological effects and possible uses of neutrons. I believe that very valuable applications may develop, particularly because of the peculiar absorption characteristics of different elements for neutrons. Thus, if a beam of slow neutrons traverses a heterogeneous mass of matter, the absorption does not follow the laws of absorption and scattering either of corpuscular or of quantum radiation. On the contrary, *certain elements absorb neutrons very strongly, and others, very little.* Moreover, the criterion for strong or weak absorption of neutrons of a given velocity is not the atomic number of the element (as with gamma or roentgen rays), but its particular nuclear structure. Thus boron (at. wt. 10.82) absorbs slow neutrons about 90 times as strongly as an equal amount of carbon (at. wt. 12); cadmium (112.41) absorbs about 825 times as strongly as tin (118.7), while tin has about the same absorption, per atom, as carbon.[2] From this contingency arises one of the most promising types of application of neutrons to biological processes. This will be discussed further on.

a. *Effects Due to Elastic Collisions.* For purposes of comparison, let us consider what would happen if two identical organisms are exposed, respectively, to a beam

[2] Taken from data of Dunning, Pegram, Fink, and Mitchell. Interactions of neutrons with matter, *Phys. Rev.*, 1935, *48*, 256.

of gamma radiation and to a beam of neutrons of heterogeneous energies. In the former case, the absorption is directly proportional to the number of electrons per atom, hence to the atomic number of the element, approximately. Consequently, the heavier elements absorb more strongly than the lighter ones. The energy goes into the ejection of electrons, and ultimately disappears as heat.

In the case of the organism exposed to heterogeneous neutrons, the absorption of energy is by a very different process. It is largely due to *hydrogen atoms*, except in regions where there are appreciable concentrations of atoms which absorb neutrons very strongly. The "absorption" by hydrogen atoms is mostly a scattering process: the neutrons undergo elastic collisions (i.e., non-capture collisions, or "billiard-ball collisions") with hydrogen nuclei, which recoil along short but highly ionizing paths, as compared with those of electrons ejected by gamma rays. A single neutron may be scattered many times before coming to rest. The large absorption of neutrons by hydrogen arises from two circumstances: the great abundance of hydrogen in organic matter, and the relatively large collision cross-section of hydrogen atoms, as compared with other atoms. (The nuclear cross-sections of carbon, nitrogen, and oxygen, for slow neutrons are, respectively 0.12, 0.32, and 0.09 times that of hydrogen.) A point of special interest, in this connection, in that the wide and rather uniform distribution of hydrogen throughout the organism tends to make the distribution of energy, absorbed by this recoil process, *uniform*, whereas the heavier elements, which absorb gamma rays and roentgen rays strongly, are localized to a considerable extent in bones and other special tissue.

It is only feasible to consider here the biological effects of neutrons as compared with effects of alpha rays, beta rays and electrons ejected by gamma type radiation. The major effects of fast neutrons should arise from the ejection of H-particles *within the tissue*. The ionization of an H-particle, per unit path-length, is about one-fourth that of an alpha particle, and the range is about four times that of an alpha particle of the same energy. Similarly, the ionization per unit path-length of an H-particle is of the order of 100 times that of an electron, and its range is, roughly, 1 per cent of the range of an electron of similar energy, ejected by a quantum of gamma radiation.

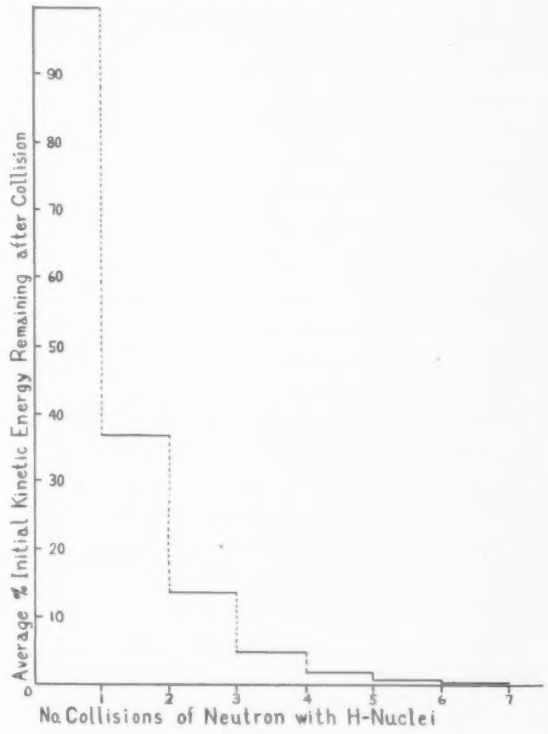

FIG. 1

Unfortunately, there are probably no experimental data on the biological effects of alpha particles (or H-particles) acting *within tissue* of appreciable thickness. Such experiments are made extremely difficult by the fact that, unless neutrons are used to generate them, heavy particles are only obtainable from certain radioactive chemical substances whose dissemination throughout animal or plant tissue would be attended with great difficulty.

When a neutron collides with a hydrogen nucleus, it imparts to the H-particle approximately 63 per cent of its kinetic energy, on the average. So the decline of kinetic energy of the neutron, with suc-

cessive H-collisions, is very rapid, as shown in Figure 1. Since the average distance between successive collisions of fast neutrons is relatively large (a matter of centi meters), the number of collisions of the particle will be rather few, in an organism of ordinary thickness; indeed, for a thickness of less than 1 cm., the number of cases in which a fast neutron makes more than one collision may be neglected, for a first-order approximation. With these facts available, one may calculate with reasonable accuracy the amount of energy dissipated within a given layer of matter, due to collisions with hydrogen atoms, if he knows the amount of hydrogen present, the number of kinetic energy of the incident neutrons, and the absorption (scattering) coefficient of hydrogen. Such a calculation is analogous to the calculation of roentgen- or gamma-ray absorption, where the nature of the absorber and wave lengths of the incident radiation are known, although the actual absorption processes are very different ones. Unfortunately, most practical sources of neutrons emit these particles with very heterogeneous energies. The problem of getting a homogeneous beam from such a source is, again, analogous to the problem of getting a beam of monochromatic roentgen rays from a roentgen tube: the beam can be filtered, to remove or diminish the less penetrating components, or a beam of homogeneous radiation can be selected by means of a spectrometer, for roentgen rays, or a velocity-selector, for neutrons. But the latter methods are of such low efficiency that their use cannot be considered unless the output required is very low, or the input very high.

Table I

Element	Atomic Number	Atomic Weight	Collison Cross-Section for Slow Neutrons, cm.^{2} $\times 10^{24}$	Relative Absorption, per Atom, Compared with Hydrogen	Relative Absorption, per Atom, Compared with Carbon	Relative Absorption *per Gram;* Based on Carbon = 1.00
Hydrogen	1	1.008	35.0	(1.00)	8.5	101.6
Carbon	6	12.00	4.1	0.12	(1.00)	(1.00)
Nitrogen	7	14.01	11.3	0.32	2.76	2.36
Oxygen	8	16.00	3.3	0.09	0.8	0.65
Sodium	11	23.00	4.2	0.12	1.0	0.53
Magnesium	12	24.32	3.5	0.10	0.85	0.42
Phosphorus	15	31.03	14.7	0.42	3.68	1.39
Chlorine	17	35.46	39.0	1.11	9.52	3.22
Calcium	20	40.07	11.0	0.31	2.68	0.80
Lithium	3	6.94	45.	1.3	11.	19.0
Boron	5	10.82	360.	10.3	88.	97.5
Yttrium	39	88.9	800.	22.9	195.	26.4
Cadmium	48	112.41	3300.	94.3	815.	86.0
Barium	56	137.37	140.	4.0	34.	3.
Samarium	62	150.43	4700.	134.3	1144.	92.
Europium	63	152.0	est. <1000.	<28.6	<244.	<19.
Gadolinium	64	157.6	30000.	857.0	7320.	557.
Terbium	65	159.2	est. <1000.	<28.6	<244.	<19.
Dysprosium	66	162.5	700.	20.0	171.	13.
Iridium	77	193.1	285.	8.1	69.	4.
Mercury	80	200.61	380.	11.0	93.	5.6
Lead	82	207.20	8.6	0.25	2.	0.1
Thorium	90	232.15	32.0	0.9	8.	0.4

b. *Effects Due to Selective Absorption.*

Leaving, now, the elastic collisions of neutrons, we shall consider their absorption by a few particular elements whose absorption is very much higher than that of hydrogen. As previously mentioned, these elements evidently owe their strong absorption to their particular nuclear structures, which make them particularly susceptible to nuclear transformation (transmutation) due to bombardment by slow neutrons. Among these may be mentioned lithium, boron, yttrium, cadmium, barium, iridium, mercury, and some of the rare-earth elements, samarium, europium, gadolinium, terbium, and dysprosium. Table 1, prepared from data of Dunning, Pegram, Fink, and Mitchell,[3] gives the relative absorptions of slow neutrons by various elements with which we are here concerned. The upper part of the table includes the elements that constitute most organic tissue; the lower part is for some elements whose absorption is particularly high. The data for lead are included, for comparison.

Now it is immediately evident that if there is, in any particular part of the organic tissue which is irradiated with slow neutrons, an appreciable concentration of elements that absorb them strongly, there will be a greater dissipation of neutron energy in these regions than in the surrounding tissue. Even extremely small concentrations of some of these elements suffice to give strong absorption. On the other hand, the amounts of *any* of the elements listed in the lower part of the table are probably negligibly small, even in terms of their neutron absorption, in most organic matter. There exists, however, this important possibility: *a high absorber of neutrons may be introduced*, by injection or some other means, *into the regions of the organism wherein it is desired to dissipate a great deal of energy in the form of ionization*. The element chosen for the purpose must, obviously, be in the form of a nontoxic compound. The type of compound used is irrelevant, as far as the neutron absorption is concerned, since this absorption is purely an atomic phenomenon. An analogous procedure can be used for selective absorption of roentgen rays and gamma rays; but the elements of strong absorption are necessarily the *heavy* elements, whereas strong neutron absorbers include elements of *very low* atomic number, as shown in Table 1.

High selective absorption of slow neutrons seems, in all cases, to be connected with nuclear transformations in the absorbing element, brought about by neutron bombardment. In this connection, special attention should be called to the fact that *the energy released by the absorption of neutrons in matter is not the energy of the incident neutrons, except in cases of elastic collisions, such as those with hydrogen. Otherwise, the energy released is nuclear energy of the bombarded atoms. The neutrons serve, essentially, as trigger mechanisms which only start the nuclear transformations that release energy*. They differ from trigger mechanisms, in the ordinary sense of the expression, in that they become parts of the atomic nuclei in which they are absorbed. Since capture of the neutron is a fundamental part of the transformation, it is evident why slow neutrons are more efficacious than fast ones in bringing them about. The nuclear absorption of neutrons is a distinct phenomenon which has no counterpart in the absorption of gamma rays or roentgen rays.

The form in which energy is released by nuclear absorption of neutrons depends on the absorber. In the case of light elements, particularly lithium and boron, low-range alpha particles are emitted; in the case of heavy elements, the products are (so far as we now know) beta rays and gamma rays. In some cases, the emission is simultaneous with the absorption of the neutron; in others, namely those elements in which artificial radioactivity is induced, the emission will succeed the absorption, according to the laws of radioactive decay of the element concerned. The *amount* of energy released in any element, due to neutron absorption, is the product of the number of

[3] Dunning, Pegram, Fink, and Mitchell, *loc. cit.*

neutrons absorbed, N, and the energy released by the absorption of a single neutron, e. Approximate relative values of e are known for a few light elements;[4] others will doubtless be measured soon. The energy released, e, may be either positive or negative, depending on the element and transformation involved. The release of energy by naturally or artificially radioactive elements is, of course, a release of nuclear energy without external stimulus. Instantaneous disintegrations of elements by neutrons (if they are ever truly "instantaneous") may be regarded as "induced radioactivity of zero half-life," without departing from the truth in any way.

c. *Summary of the Effects to be Expected from Neutron Irradiation.* The biological effects to be expected from the action of neutrons are of two kinds: (*a*) those produced in the bulk of tissue, due to elastic collisions of neutrons, especially those with hydrogen nuclei, and (*b*) those produced in specific regions where (even small) concentrations of highly absorbing atoms are present. In either case, the ionizing action which arises from neutron bombardment, like that from gamma and roentgen irradiation, will probably be chiefly *destructive*, hence applicable to problems such as the production of mutations in animals and plants, and to the destruction of malignant cells, such as those of cancerous tissue. Any constructive stimulation will probably be, as in the case of other radiations, at best an open question. The action of neutrons differs conspicuously from those of other radiations in that the effects are, broadly speaking, greatest in *light elements*, particularly hydrogen, as contrasted with the heavy element absorption of gamma type radiation. The scattering of neutrons by hydrogen results in the production of short-range, but highly ionizing particles, as compared with the long-range, low-ionizing paths of electrons ejected by gamma rays. Finally, slow neutrons can be subjected to strong selective absorption by certain elements; this absorption may result in the spontaneous release of atomic energy from the atoms in which absorption occurs, and is not furnished by the neutrons themselves.[5]

III. SOME PHYSICAL PROBLEMS THAT SHOULD BE SOLVED

Much remains to be done in the way of purely physical research before it will be possible to calculate the exact amount, form, and distribution in which energy will be liberated in any given mass of material irradiated with a neutron beam from a (practical) source of neutrons. Several types of such physical problems may be cited:

(1) The development of simple and reasonably accurate means of measuring the number of neutrons, per second, in any beam, and the distribution of their velocities.

(2) The neutron "absorption," in any absorber, is divided into two parts: nuclear absorption (true absorption), and scattering. The ratios of these, for different elements and for neutrons of various energies, must be determined. Some data on this subject are already available;[6] others will doubtless appear soon.

(3) The scattering of neutrons of various velocities by various substances must be further examined for the purpose of finding the mean free paths between successive collisions, under various conditions. This information would be very desirable for determining the amount and distribution of energy released by scattering, in any absorber, and for designing appropriate scatterers and filters to surround neutron sources.

(4) The processes and energy relations in nuclear transformations must be further

[4] Thus H. J. Taylor (*Proc. Roy. Soc. A 47*, 1935, 873) has shown that boron, when disintegrated by slow neutrons, emits alpha rays whose energy is about 2×10^6 electron volts; this corresponds to a range of about 1.1 cm. in air, or about 7.6 microns in the gelatine of a photographic plate.

[5] Neutrons, like alpha particles, never exist free in nature. Alpha particles eventually capture electrons and become helium atoms; neutrons eventually enter, and attach themselves to atomic nuclei, thereby producing nuclear transformations.

[6] Mitchell, A. C. G., and Murphy, E. J., *Phys. Rev.*, 1935, *48*, 653; also *Bull. Amer. Phys. Soc.*, 1935, *11*, 13.

investigated. In some cases, artificial radioactivity is induced; in others, instantaneous nuclear transformations occur, accompanied by the emission of alpha rays or beta and gamma rays; in other cases, both artificial radioactivity and instantaneous transformations are produced.[7] The problems are to determine, for each element, what processes occur, what isotope is involved in each process, the kinds and energies of the particles and quanta emitted by the elements so disintegrated, and the influence of the velocities of the neutrons on these processes.

IV. SOME FIELDS OF APPLICATION OF NEUTRONS TO BIOLOGICAL AND MEDICAL RESEARCH

Some likely fields for biological and therapeutic research, involving the direct application of neutrons (apart from applications of neutron-induced artificially radioactive elements) have occurred to me, and may be mentioned here. Two general divisions of these applications may be conveniently set up, namely, "bulk-effects" produced by elastic collisions of neutrons with hydrogen and other nuclei in the irradiated matter, and "specific local effects," arising from the selective absorption of neutrons by atoms of high neutron-absorbing power, which process is followed by the liberation of nuclear energy by nuclear transformations. Within the latter of these divisions are included the interesting possibilities of introducing and localizing small concentrations of strong neutron absorbers in specific regions of the organism under investigation, followed by neutron irradiation, as pointed out earlier in this paper.

In the field of experimental biology there may be mentioned: (1) investigation of the bulk effects of neutrons in living tissue (animal and plant), as shown, for example, by their effects on the speeds of mitosis; (2) the destruction or enfeeblement of living bacteria by neutrons; (3) search for specific effects in organs or other special tissues of higher animals subjected to slow neutron bombardment; (4) investigation of the efficacy of neutrons in producing mutations in animals and plants. I regard (4) as one of the most interesting applications of neutrons to pure biology.

In the field of medical research there may be cited: (1) the possibility of destroying or weakening cancerous cells, by the general or selective absorption of neutrons by these cells. In particular, there exist the possibilities of introducing small quantities of strong neutron absorbers into the regions where it is desired to liberate ionization energy (a simple illustration would be the injection of a soluble, non-toxic compound of boron, lithium, gadolinium, or gold into a superficial cancer, followed by bombardment with slow neutrons); (2) the possibility of obtaining specific destructive action of slow neutrons on disease-producing bacteria. This seems to merit careful investigation, both from a medical and a purely biological standpoint. However unlikely, it is not inconceivable that, in some instances, a non-toxic compound of an element that absorbs neutrons strongly might be concentrated in infected regions and used to destroy the bacteria by subsequent neutron irradiation.

Researches covering these fields might well be expected to occupy the entire time of many workers for many years. Yet, if they led to the eradication of a single disease, or to a better understanding of biological processes involved in disease, so that the way to cure was made clearer, the effort would be justified.

V. PRODUCTION OF NEUTRON BEAMS

By "production of neutrons" is meant their liberation (ejection) from atomic nuclei. Like alpha particles, neutrons exist only in nuclei, and must be removed from them if they are to be used. The removal of a neutron from a nucleus involves nuclear disintegration, just as the spontaneous

[7] Artificial radioactivity produced by neutron bombardment.
Part I: Fermi, E., Amaldi, E., D'Agostino, O., Rasetti, F., and Segrè, E. *Proc. Roy. Soc. A 146*, 1934, 483.
Part II: Amaldi, E., D'Agostino, O., Fermi, E., Pontecorvo, B., Rasetti, F., and Segrè, E. *Ibid., 149*, 1935, 522.

emission of an alpha particle does. But, unlike alpha particles, which are spontaneously emitted by 23 radioactive elements and isotopes, neutrons are not spontaneously emitted by any known element,[8] and must be liberated by bombarding elements with particles or quanta of high energy. This fact makes the production of dense neutron beams difficult or expensive, by any method yet developed.

Neutrons have been obtained by disrupting nuclei with alpha particles (helium nuclei), protons (hydrogen nuclei), deuterons (nuclei of heavy hydrogen, or deuterium), and gamma rays. In each case, the disrupting agent must have sufficient energy to enter the nucleus and to overcome the binding energy which normally retains the neutron in the nucleus. In the case of gamma rays, no energy is required to penetrate the nucleus; hence only the binding energy is concerned.

The original method of obtaining neutrons, namely by bombarding beryllium with alpha particles from polonium, will not be considered here because of the low yield of neutrons, as compared with other sources, and because of the difficulty of getting large quantities of polonium. Three methods that are feasible for obtaining neutrons, at rates exceeding a million per second, will be considered, in probable inverse order of their potential neutron yields.

(1) *Bombardment of Beryllium with Alpha Particles from Radium or Radon.* This method consists in intimately mixing powdered beryllium metal with radium or radon, in a sealed container. A Ra-Be source is, of course, constant, whereas a Rn-Be source decays at the same rate as the Rn gas. The introduction of beryllium into radon or radium in no wise injures the use of the gamma rays in the customary manners, since the neutrons are produced by the alpha particles which are otherwise unused, and the gamma-ray absorption of beryllium (at. wt. 9.02) is very small, indeed ($\mu = 0.074$ per cm. Be). The emission of neutrons is merely added to the emission of gamma rays by the source.

According to Fermi, Amaldi, D'Agostino, Rasetti and Segrè,[9] 1 curie of radon, mixed with beryllium gives, roughly, one million neutrons per second. On this basis, 1 gram of radium, mixed with beryllium, would give about 1.3 millions per second. The efficiency of this process is accordingly about 1 neutron per 100,000 alpha particles.[10] More recent estimates indicate a much higher yield of neutrons from Rn-Be. Jaeckel[11] estimates the yield to be 10 million neutrons per second per curie Rn; Paneth and Loleit[12] estimate the yield to be 3 million neutrons per second per curie; the corresponding efficiencies are: 1 neutron per 10,000 to 30,000 alpha-particles.

If desired, the gamma rays from a Ra-Be source of neutrons can be greatly reduced in intensity by filtering through a few centimeters of lead, without proportionate loss of neutron intensity, since the lead is quite transparent to neutrons (see Table 1). Conversely, the neutron intensity can be greatly reduced, without proportionate loss of gamma rays, by successive filtering through a few centimeters of paraffin (to slow down the neutrons) and a thin filter of boron or cadmium (to absorb the slow neutrons). Unless a paraffin filter is used (or some other material rich in hydrogen), the neutrons will not be appreciably absorbed; their initial velocities are very high, so they pass through matter with absorption that is less than that of the hardest gamma rays known. A Ra-Be or Rn-Be source may accordingly be used for the gamma rays without the necessity of filtering out the neutrons.

The strongest source of this type reported thus far is that of Paneth and Lo-

[8] If neutron-emitting radioactive elements ever existed in the earth's crust, they must have decayed, and had no long-lived progenitors.

[9] *Loc. cit.*

[10] For comparison 1 gram of radium emits about 7.26×10^{10} gamma rays per second, of which about 5.56×10^{10} are "hard" rays. See: Rutherford, Chadwick, and Ellis, "Radiations from Radioactive Substances," Cambridge University Press, 1930, p. 501.

[11] Jaeckel, R. *Ztschr. f. Phys.*, 1934, *91*, 493.

[12] Paneth, F. A., and Loleit, H. *Nature*, 1935, *136*, 950.

leit, who used 2,200 millicuries of Rn mixed with beryllium.[13]

(2) *Irradiation of Beryllium with Hard Gamma Rays.* Szilard and Chalmers[14] discovered, in 1934, that hard gamma rays from radium or radon disintegrated beryllium, accompanied by the emission of neutrons, as suggested by Chadwick and Goldhaber. Recently, Chadwick and Goldhaber[15] have further investigated this process; from their measurements it is possible to make an approximate calculation of the number of neutrons emitted per second by several kinds of sources. Taking the area of the beryllium nucleus as 10^{-28} cm.^{2}, for this "photo-disintegration" process, and the number of gamma rays from 1.0 gm. Ra, or 1.0 curie Rn, whose energies exceed 1.7×10^6 volts, as 1.14×10^{10} per sec., it is calculated that 1 gm. Ra or 1 curie Rn, surrounded by 10 cm. thickness of solid beryllium (7.8 kg. Be), would emit about 900,000 neutrons per second. This is of the same order as the strength of the source described under (1) above. Through the courtesy of the staff of the American Oncologic Hospital, Philadelphia, Dr. L. H. Rumbaugh and I are conducting a series of experiments with a neutron source of about 200,000 photoneutrons per second, obtained by allowing part of the gamma radiation from 4 grams of radium to pass through 500 grams of beryllium metal. Obviously, methods (1) and (2) can be combined.

The production of neutrons by photo-disintegration of beryllium and deuterium with hard gamma rays is of special interest because of a known but undeveloped possibility, namely, the production of intense beams of high energy gamma rays by high voltage machines. Thus a current of 1 microampere, in a tube operated at 1.7 to 3.5 millions of volts would, if converted into gamma rays (roentgen rays), be capable of producing some 500 millions of neutrons per second, by photo-disintegration of beryllium. This neutron flux would equal that from at least 200 grams of radium. Gamma rays used for generating photo-neutrons must be very hard rays; the binding energy of the neutron in beryllium, which is the most easily disintegrated element, is believed to be between 1.3 and 2.0 millions of volts. Consequently, only about 16 per cent of the gamma rays from radium or radon are hard enough to effect the disintegration.

(3) *Bombardment of Various Elements with High Velocity Deuterons Generated in High Voltage Machines.* The development of apparatus for generating high voltages, by means of which charged nuclear particles can be accelerated to great velocities, holds out the greatest promise for the production of intense neutron beams. There is every reason to believe that these machines will presently be able to generate neutrons more rapidly than the combined output of all the Ra-Be and Rn-Be sources that could be prepared from all the radium that has ever been mined. At present, high voltage machines are in an experimental and developmental stage. But they have already made possible the performance of many valuable physical experiments that involve neutrons, directly or indirectly, and have shown the lines along which future developments of high voltage apparatus may be expected to proceed.

Neutrons have been generated in high voltage machines by bombarding various elements with ions of hydrogen, helium, and deuterium; by far the greatest efficiency is obtained with deuterium ions (deuterons) so only this method will be considered here.

For the generation of neutrons, voltages exceeding 2 million are very desirable, because the efficiency of neutron production rises rapidly with the voltage of the ions. The considerable difficulties attendant on the generation of such voltages are being overcome by various means. Six types of generators will be listed here. The potentialities of none of these have been exhausted, so it is impossible to describe one

[13] Paneth and Loleit, *loc. cit.*

[14] Szilard and Chalmers. *Nature*, 1934, *134*, 494.

[15] Chadwick, J., and Goldhaber, M. *Proc. Roy. Soc. A 151*, 1935, 479.

method as "best." Some of the methods have been further developed than others, as regards the magnitude of the voltages and ion currents attained, and some are better than others in regard to constancy and homogeneity of output.

For convenience, high voltage generators may be divided into two classes: (A) those which generate the full voltage in a single step, and (B) those in which the "output voltage," used in accelerating the ions, is reached by recurrent application of lower accelerating voltages along the paths of the ions. In the first group there may be listed:

(1) Electrostatic generators, particularly those invented by Van de Graaff, and used by Van de Graaff and Bramhall, by Tuve, Dahl, and Hafstad, and others.

(2) High voltage transformers, particularly arrangements using a group of transformers in cascade, as used by Crane and Lauritsen.

(3) Series-parallel condenser generators, developed by Cockroft and Walton, in which a set of high voltage condensers are charged in parallel and discharged in series. (This was the first method by which ions were artifically accelerated to sufficiently high velocities to produce nuclear disintegrations in the laboratory.)

The second group includes:

(4) Successive acceleration of ions through hollow cylinders connected to a high frequency vacuum tube oscillator. This method, developed by Lawrence and Sloan, gives "output voltages" which are, roughly, the products of the peak voltages of the numbers of pairs of accelerating tubes.

(5) The "cyclotron," invented by E. O. Lawrence. This ingenious and singularly successful apparatus employs only two electrodes and a strong magnetic field at right angles to the electric field. As in (4), the electrodes are connected to a high frequency oscillator. With a peak voltage of only 25,000 volts, deuterons of energies exceeding 6 million volts have been produced. This machine has probably yielded more information about nuclear transformations and has been used for inducing artificial radioactivity in more elements than has any other high voltage machine, at the present time.

(6) Beams' apparatus for successive accelerations. This machine is similar in principle to that mentioned in (4), but employs the transmission of an electric pulse along "trolleys," instead of an oscillating circuit. The apparatus is of more recent design than the others, and is still in an experimental state.

Space does not permit a detailed discussion of these apparatus. The advantage of high voltage machine generation of neutrons, over generation by radium or mesothorium sources, lies in the great output that is potentially available. This is because deuterons are used instead of alpha particles, because very large numbers of ions can be used, and because the voltages to which they can be artificially accelerated greatly exceed the equivalent voltages accelerating natural alpha particles. The disadvantages of high voltage sources are that the machines are costly to construct, require the most careful design, based on considerations of the intended use, and must be constantly maintained by skilled operators.

VI. THE HANDLING OF NEUTRONS

(a) *Protection.* The protection of personnel against harmful physiological effects of neutrons (which one might call "neutron burns") is analogous to protection against gamma and roentgen-ray burns. As with confined sources of gamma type radiation, the simplest form of protection against neutrons is distance from the source. Protective absorbers of neutrons must necessarily be thicker than those used for the same degree of protection against gamma radiation of radioactive origin, because of the low absorption coefficients of all elements for fast neutrons.

Absorption of neutrons must be in two successive steps: first, diminution of their

velocities by scattering, and second, removal of the slow neutrons by nuclear absorption. The former process is best accomplished by passing the neutrons through hydrogen-bearing materials such as paraffin, water, or oil; for the latter process, boron, cadmium, lithium or their compounds are most efficient and convenient. A good filter that performs both of these functions is a water solution of boric acid, 2 or 3 feet thick.

When the production and filtering of neutrons are accompanied by gamma rays, or other penetrating emissions, protection must be provided against such emissions. For example, in the use of Ra-Be or Rn-Be sources, one must provide the customary protection against the gamma rays of the Ra or Rn. In addition to this, there is a (relatively weak) emission of very penetrating gamma radiation associated with the *production* of the neutrons by these sources. (Its mean energy is estimated to be of the order of 6 million volts, as compared with the maximum energy of 2.19 million, for Ra C.) High voltage machine sources of neutrons usually emit penetrating gamma radiation. Thus Crane, Delsasso, Fowler, and Lauritsen[16] find that gamma rays of 11 wave lengths are emitted by lithium, when bombarded by fast protons of energy less than 1 million volts. The hardest of these gamma-ray lines corresponds to an energy of 16 million volts. The *absorption* of neutrons by some elements is also accompanied by gamma-ray emission. For example, slow neutrons, when absorbed in cadmium, cause the emission of quanta whose energies are estimated to be as high as 10 million volts.[17] The number of absorption-emission quanta is probably exactly the same as the number of neutrons absorbed in the quantum-emitting absorption process involved. Their high energies tend to minimize the danger of physiological effects.

Frequent blood counts of persons exposed to strong neutron sources will serve to detect excessive dosages of gamma rays, and *probably* of neutrons; the latter has not yet been settled by experiment. According to recent reports, persons working in the vicinity of the cyclotron (in California) become very noticeably *radioactive*, as a result of artificial radioactivity produced in their body tissues by absorption of slow neutrons. Measurement of the extent of such radioactivity should provide an immediate and simple means of determining the order of magnitude of the exposure to slow neutrons (but not to fast ones). An obvious variation of this method would be to carry in a pocket an element such as silver, rhodium, vanadium, bromine, or iodine (i.e., an element in which artificial radioactivity is strongly induced by exposure to slow neutrons), and to measure its radioactivity at some definite time after the exposure to slow neutrons. The amount of exposure to fast neutrons is not so easily determinable.

(b) *Measurement and Filtration.* The intrinsic characteristics of a beam of neutrons are: first, the number traversing unit area in unit time; second, the velocities of the neutrons; and third, the directions of their paths. The first and second of these determine the energy flux in the beam; the third is important for calculating effects of the beam when the source is of extended area, or when the beam has been passed through a scatterer of extended area.

Unfortunately, the measurement of these characteristics is not very easy, at the present time. The number of neutrons emitted, per second, by any source is probably not known to better accuracy than a factor of two; the distributions of their velocities are probably even more uncertain than the number emitted; and scattering experiments that are free from errors of performance and interpretation are not easy to devise, especially when the neutrons used are heterogeneous in energy. These difficulties arise mainly from the fact that the efficiencies of detection and measurement of neutrons vary through

[16] Crane, H. R., Delsasso, L. A., Fowler, W. A., and Lauritsen, C. C. *Phys. Rev.*, 1935, *48*, 125.

[17] Herszfinkiel, H., and Wertenstein, L. *Nature*, 1936, *137*, 106.

wide limits with the velocities of the particles being measured, and the limits of these variations are unequal for different means of measurement. In general, it is necessary to use more than one method of measurement to make even an approximate determination of the energy flux in a neutron beam.

Six methods of measuring neutron beams may be listed here:

(*a*) *Paraffin-lined ionization chambers.* Here, the integrated ionization produced of H-particles ejected from the paraffin by neutrons is measured. This method is fairly suitable for neutrons of high energy, but is open to the errors attendant on the measurement of the ionization of any nuclear particles, and the additional uncertainty of how the probability of ejection of an H-particle depends on the velocity of the neutron. The method is not suitable for slow neutrons.

(*b*) *Thin ionization chambers, arranged with very sensitive linear amplifiers.* These record the passage of individual ionizing nuclear particles, and measure the ionization per cm. path of each particle, from which the energy of the particle can be deduced. They have been a very valuable help in the study of neutrons, but are subject to the uncertainty of efficiency for detecting neutrons of various velocities. When the ionization chambers are lined with lithium or boron, they are adaptable for measurement of slow neutrons; when lined with paraffin, they may be used for fast neutrons, but with different efficiencies.

(*c*) *Methods using artificial radioactivity induced by neutrons.* These involve the exposure of suitable "detector" elements to the neutron beam, followed by measurement of the ionization produced by the decay of the radioactivity of the detector, by means of Geiger-Müller counters or ionization chambers. The detector element usually has very selective response to neutrons of different velocities; neutrons of low, or relatively low, energies give the greatest response.

(*d*) *Nuclear disintegrations in photographic plates.* By special technique, the paths of alpha and H-particles emitted by the disintegration of light elements can be recorded in certain photographic plates. This method has the disadvantages of slowness (because of the time required to make microscopic examination of relatively large areas), and of selective response to relatively slow neutrons. The records are, of course, permanent. This method will doubtless be further developed.

(*e*) *Wilson cloud chambers.* With these apparatus, the paths of disintegration products of nuclear disintegrations can be photographed, and the kinds and energies of the particles determined. They must be used with relatively weak sources, and must be protected against (strong) gamma radiation, which renders them inoperative.

(*f*) *Chemical measurement.* Hopwood and Phillips[18] recently reported the results of attempts to measure the integrated effects of neutron irradiation by means of the chemical action on colloids, and by the promotion of simple chemical reactions. They found the effects of neutrons to resemble those of gamma radiation, in both cases. It is expected that this, or a similar method, will be further developed.

A beam of heterogeneous neutrons may be subjected to strong filtration, which removes the low energy particles. A filter consisting of a few millimeters of cadmium, boron, or lithium will remove a very large percentage of the slow neutrons without removing significant percentages of the fast ones. However, much remains to be learned about filtration processes. For example it has been lately found that cadmium, whose absorption of slow neutrons is known to be extremely high, nevertheless transmits a band of slow neutrons which are capable of inducing radioactivity in gold.[19] This, and similar phenomena found in silver and indium, suggest that the neutrons which are strongly absorbed

[18] Hopwood, F. L., and Phillips, J. T. *Nature*, 1935, *136*, 1026.
[19] Frisch, O. R., Hevesy, G., and McKay, H. A. C. *Nature*, 1936, *137*, 149.

in any element have a *minimum* energy of magnitude depending on the element, as well as a maximum energy; in other words, the neutrons may move too slowly to be captured by a nucleus, as well as too fast for capture. More complete information on this subject will probably lead to a modification of filtering technique.

The optimum thickness of paraffin for slowing down neutrons from a Rn-Be source is about 10 cm., where the disintegration of lithium is used for detection of the slow neutrons.[2] For neutrons of lower initial energies, I find that the optimum thickness of paraffin is less than 10 cm.; for neutrons of higher energy, it would doubtless be greater than 10 cm. The most appropriate scatterers for neutron sources of various energy maxima and energy distributions are yet to be determined. The process of slowing down neutrons by hydrogen collisions is somewhat complicated by the fact that hydrogen also *absorbs* part of the slow neutrons, which process is accompanied by the emission of gamma radiation. (The absorption is caused by the direct combination of the neutron with a hydrogen nucleus, forming an atom of deuterium.) The amount of the absorption and the energies at which the neutrons are most apt to be absorbed by hydrogen have not yet been accurately determined.

I am greatly indebted to Dr. L. H. Rumbaugh for his discussions and constructive criticisms of this paper.

Additional Note. Since the foregoing paper was written, two important papers describing experiments on the biological action of fast neutrons have appeared. In one of these, Lawrence and Lawrence[20] compared the action of measured dosages of fast neutrons from the cyclotron (California) on the blood of live rats with the effects of measured dosages of very hard roentgen rays (900,000 volts). The effects were similar in character, as regards the diminution of the number of lymphocytes per cubic centimeter in the blood, but the dosage of neutrons required to produce a given effect was only about one-tenth the roentgen-ray dosage which gave the same effect, indicating that *the fast neutrons were about 10 times as efficacious as hard roentgen rays in producing this action.* The other paper, by Zirkle and Aebersold[21] describes experiments on the relative retardation of the growth of roots of wheat seedlings that had been irradiated with measured dosages of fast neutrons and hard roentgen rays. They find that *one roentgen of fast neutrons is as effective as 20 roentgens of the x-rays* in this action. It is significant that the apparatus and methods of measurement of dosages used by these authors were the same as those of Lawrence and Lawrence, making the results of the two kinds of experiments directly comparable. This fact allows the significant conclusion to be drawn that the biological effects of equal amounts of fast neutron irradiation of different organisms may depend considerably on the nature of the organism and/or the biological process thereby affected.

[20] Lawrence, J. H., and Lawrence, E. O. The biological action of neutron rays. *Proc. Nat. Acad. Sc.*, Feb., 1936, *22*, 124.

[21] Zirkle, R. E., and Aebersold, P. E. Relative effectiveness of x-rays and fast neutrons in retarding growth. *Proc. Nat. Acad. Sc.*, Feb., 1936, *22*, 134.

A ROENTGENOLOGIC CRITERION OF DERMOID CYST*

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A CASE of dermoid cyst of the anterior mediastinum studied in The University of Chicago Clinics has furnished what appears to be a new sign for the roentgenologic diagnosis of this condition.

REPORT OF THE CASE

The patient, a housewife, aged fifty-five, was admitted to the Outpatient Department of The University of Chicago Clinics on November 25, 1935.

History. In 1929 the patient began to experience occasional attacks of palpitation and in 1932, following an attack of diphtheria, there was for a time some difficulty in swallowing described by her as due to "paralysis of the throat." In the past three years increasing palpitation and fatigue had made it impossible for the patient to attend to her housework, dyspnea on climbing stairs had become progressively worse and there were occasional gastrointestinal complaints such as eructation, nausea and emesis. The patient suffered no pain save an occasional "catch" in the left chest, did not cough and had never expectorated hair, teeth or sebaceous material. She did report, however, that every morning on rising she expectorated mucus that seemed to come from the throat.

Abstract of Physical Examination. Temperature, 99.2° F., pulse, 66; respiration, 20; blood pressure, 160/90.

Chest: No difference was noted in the shape or size of the two sides of the chest but there was some limitation of excursion on the right side. Percussion over the anterior wall of the right side of the chest revealed an area of dullness extending from the midline to a point 11 cm. to the right of the sternum and from the second rib above to the sixth rib below. Within this area breath sounds and tactile fremitus were diminished. On the posterior wall there was a similar but smaller area of dullness and diminished breath sounds and tactile fremitus.

Laboratory Examinations: Blood Wassermann and Kahn tests, negative; red blood count, 4,800,000; white blood count, 11,700; hemoglobin, 85 per cent (Dare method); differential count: polymorphonuclears, 85 per cent; lymphocytes, 9 per cent; monocytes, 6 per cent. Urine, negative; Aschheim-Zondek test, negative; sputum negative for acid-fast bacilli and sebaceous material (three examinations). Electrocardiogram, normal mechanism. Stool negative for blood and parasites.

Roentgen Examination. Stereoscopic roentgenograms of the chest made with the patient standing (Fig. 1) demonstrated an oval soft tissue mass 12 cm. long and 8 cm. broad lying in the anteromedial portion of the right lung field. Medially the mass was indistinguishable from the mediastinal shadow but above, below and laterally it contrasted sharply with air-containing lung. On closer inspection it was noted that the upper pole of the mass was less dense than the rest, a sharp line 2 cm. below the upper pole and perpendicular to the long axis of the body marking the boundary between these two zones of density.

In roentgenograms made with the patient lying on the left side, film against anterior chest wall, the axis of the cone of radiation directed parallel with the floor, this line of demarcation was found to have shifted and become parallel with the long axis of the body (Fig. 2). The differences in density were not great enough to show by roentgenoscopy but the roentgenograms left no doubt as to the existence of a "fluid" level within the tumor.

In searching for an explanation of this finding, there was considered first the possibility that the cyst might communicate with a bronchus, in which case the relative translucence of the upper pole might be due to the presence of air. This seemed unlikely because of the rather slight difference of density in the two parts of the cyst. Furthermore, the history did not indicate the presence of a bronchial fistula, and iodized oil introduced into the trachea did not enter the cyst.

A suggestion was made that finely divided calcified material suspended in the cyst fluid might have settled out, leaving a denser fluid below, a less dense fluid above. It seemed most probable, however, that the cyst contained a mixture of aqueous fluid and a fat which at body temperature was fluid and therefore free

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to float on the non-lipoid fluid as a cream. Such an assumption was in keeping with the known fact that dermoids regularly contain fat and it explained also why there was so little difference in opacity above and below the faint but definite "fluid level."

It had been noted that at the upper pole in Figure 1 and the lateral pole in Figure 2 the

Fig. 1. Roentgenogram made with patient standing facing film. It is well recognized that fat is less opaque to roentgen rays than water or water-containing tissues. In this case, liquid fat floating on aqueous fluid makes the upper pole of the dermoid distinctly less dense than the remainder of the tumor. A sharply defined horizontal gravity level 2 cm. below the apex of the upper pole marks the boundary between fat and aqueous fluid. Note that at the upper pole the cyst wall shows silhouetted against air-containing lung without, fat within.

cyst wall itself could be made out. Its outer surface showed, of course, because of contrast with air-filled lung and under the theory expressed above the inner surface showed because of contrast with fat.*

* The physical factors concerned in the roentgen differentiation of fat-containing tissues from non-lipoid tissues have been discussed by F. E. Templeton of this institution in a paper entitled "Roentgen Diagnosis of Lipomata" to appear in a later issue of this Journal.

Preoperative Diagnosis. Dermoid cyst of the right side of the anterior mediastinum.

Operation. On January 15, 1936, the anterior mediastinum was opened through a right-angled incision along the right side of the sternum and extending laterally for 5 inches over the fifth intercostal space. The mesial ends of the third, fourth, fifth and sixth cartilages were sectioned and the fifth intercostal tissues incised. The tumor lay in the anterior mediastinum to the right of the pericardium and compressed the base of the right lung. It was oval in shape and cystic in character and, a cleavage plane having been located, the tumor was dissected out and removed.

Fig. 2. Roentgenogram made with the patient lying on left side, face against film, radiation from behind parallel with floor. The gravity level has now shifted until it is parallel with the long axis of the body and now the inner and outer surfaces of the lateral wall of the cyst are shown. The principle is the same in the case of lung abscess with bronchofistula, except that the differences in opacity between air and aqueous fluid are of course much greater than the differences between fat and aqueous fluid. In large lung abscess with bronchofistula or in hydropneumothorax, air and fluid are easily differentiated on the roentgenoscope. In this case of dermoid cyst, however, even though the roentgenograms had convinced us of the presence of layering between fat and aqueous fluid we could not differentiate the fat and aqueous layers at roentgenoscopic examination.

Roentgen Examination of Excised Tumor. Immediately after the cyst had been removed from the chest and while it was still warm, the specimen was supported in front of a vertical cassette changer and a roentgenogram was made

FIG. 3. Roentgenogram of excised tumor made immediately after operation and while the tumor was still at about body temperature. Under these conditions it is possible to make out structures that did not show in roentgenograms of the chest with the tumor in situ. Note shadow of hair ball floating in aqueous fluid with its upper surface projecting into the fluid fat. Note also patches of calcification at upper and lower pole which were not seen in Figures 1 and 2.

(Fig. 3) with the axis of the cone of radiation directed parallel with the floor. Under these conditions the floating fat, being in the fluid state, showed as a definite layer at the upper pole of the cyst. By the time the tumor was opened for inspection and sectioning it had been chilled to below room temperature, which explains the pathology report of fat collected into clumps floating in aqueous fluid. Later a typical sample of the cyst contents including aqueous fluid, lumps of fat and part of the hair was placed in a thin-walled celluloid cylinder and incubated at 37.5° C. for twenty-four hours. In a roentgenogram of this cylinder and its contents after incubation (Fig. 4) there is seen layering of fat above aqueous fluid similar to that noted in the preoperative examination (Figs. 1 and 2) and the roentgenogram of the freshly excised cyst (Fig. 3).

Gross Pathology. The gross specimen consisted of an ovoid cyst-like structure measuring 12 cm. in its greatest diameter. In some parts the blood-stained, grayish, yellow outer surface was smooth; in others, roughened by old fibrous adhesions. The tumor felt uniformly cystic with a wall of uniform thickness. On being opened the cyst was found to be filled with a yellowish, gray, viscous fluid. Floating, partly submerged in this fluid, were clumps of yellowish fat and a ball composed of blond hair in which additional clumps of fat were caught. All of the hair lay free in the cyst cavity without connection of any sort to the wall.

The wall of the cyst was from 3 mm. to 6 mm. thick and its inner surface had a glistening yellowish color.

Microscopic Examination. A smear from the fluid showed numerous fat globules interspersed with cholesterol crystals. Sections from the wall of the principal cyst showed that it was made up of three layers: an outer layer of areolar tissue, a central layer of dense adult fibrous connective tissue, and a thin inner layer of stratified squamous epithelium showing no hair follicles. Numerous large foci of densely

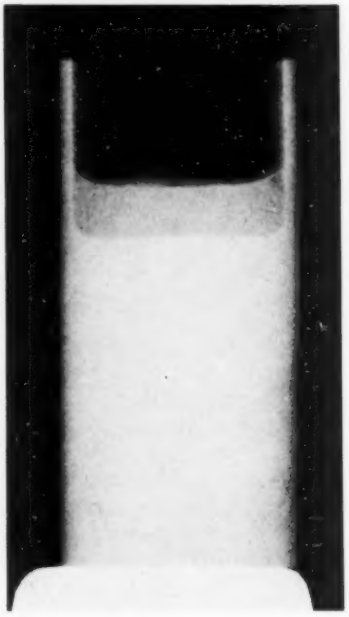

FIG. 4. Roentgenogram showing aqueous fluid, fat and hair removed from cyst and incubated at 37.5° C. for twenty-four hours. Before the tumor was opened for inspection it had been chilled to below room temperature. Under these conditions no fluid fat was found but instead a viscous aqueous fluid in which were floating clumps of hair and yellowish fat resembling butter. Figure 4 demonstrates that at body temperature these lumps of solid fat become fluid and float on the aqueous portion as a cream.

packed lymphocytes were located in the outer layer of areolar tissue, and within these foci were seen Hassall's corpuscles typical of thymic tissue. A section through one of the small locules located at the lower pole of the principal cyst in a region where the epithelial lining was absent showed large foci of fat-filled macrophages, one focus of calcification and numerous cholesterol crystal clefts surrounded by foreign body giant cells.

Analysis of Fat. The fatty material which solidified out of the cyst contents on cooling was butter yellow in color. It melted at a temperature of 34° to 39° C. and solidified at 20° to 25° C. Examined chemically by Miss Jeanne Hudson, it was found to be rich in eikosyl-alcohol. This is the substance which Ameseder found to be present in dermoid cysts.

Pathological Diagnosis. Dermoid of the mediastinum partially surrounded by a small amount of aberrant thymic tissue.

Postoperative Course. The patient recovered and was discharged from the hospital on March 1, 1936. When last seen as an outpatient on April 17, 1936, her general condition was good and the wound was healed.

REVIEW OF LITERATURE

A rather careful search of the literature fails to reveal a single reference to fluid levels in dermoid cysts. Many authors describe the contents of such cysts as mixtures of lipoid and aqueous material, and in 1925 Bobbio and Gamua[4] found that fluid removed from a dermoid cyst separated into layers with the fat floating on top. They did not observe this layering in roentgenograms, however.

With a single exception, previously published roentgenograms of dermoids fail to show fluid levels, except in those instances where for some reason both air and fluid were present. The exception is a 1933 publication by Pasman and Pepe.[16] These authors make no mention of a fluid level but their published preoperative roentgenogram shows layering of fluid very similar to that noted in our case.

In 1933 Hedblom[14] found reports of 185 proved cases of intrathoracic dermoid or teratoma and added 6 cases that had been seen by him. Since his publication there have been published 22 additional cases in which the diagnosis is definitely established, so that, including our case, the total number reported is now 208 of which 162 are dermoids, 46 teratomata.

DISCUSSION

Roentgenologic demonstration of the presence of a large, oval, sharply defined, unilateral mediastinal mass strongly suggests a diagnosis of dermoid cyst. Usually but not invariably solid teratomata are irregularly lobulated rather than oval. In most cases echinococcus cyst, encapsulated effusion, substernal goiter, aneurysm, cold abscess or malignant tumor can be excluded by surface morphology as demonstrated in roentgenograms, but sometimes it has been necessary to resort to diagnostic aspiration.[14]

It appears, therefore, that there is some real need of a roentgenologic sign characteristic of dermoid cyst, and this layering of floating fat and aqueous fluid seems to be such a sign. On the other hand, absence of this sign is probably not dependable negative evidence because presumably some dermoids will not contain a suitable mixture of lipoid and non-lipoid material, and in others even at body temperature a suitably mixed content may be semisolid and therefore not free to separate. Obviously layering cannot be expected to show unless film, patient and roentgen tube are arranged so that the axis of the cone of radiation is directed approximately tangential to the surface between fat and aqueous fluid. Such a condition automatically obtains during routine chest roentgenography of a standing or sitting subject but not during roentgenography of the pelvis of a recumbent patient suspected of having a dermoid cyst of the ovary.

SUMMARY

In a proved case of mediastinal dermoid cyst, preoperative roentgenograms showed within the shadow of the tumor a definite fluid level that shifted with the position of the patient. This was interpreted as due

to a layer of liquid fat floating on aqueous fluid. The assumption was confirmed by roentgenography and dissection of the excised tumor, and the sign is presented as a criterion for the differentiation of dermoids from certain other mediastinal lesions.

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CONGENITAL CYSTS OF THE LUNG FROM THE ROENTGENOLOGIC VIEWPOINT*

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UNTIL 1925, congenital cysts of the lung were considered to be extremely rare, and hence of minor importance in the differential diagnosis of pulmonary lesions. In that year, however, Koontz reported a case and collected 108 other cases. With the interest of diagnosticians thus aroused, further reports began to appear, and during the past decade the literature on the subject has become rather profuse. In 1934 Wood reported 16 cases observed at The Mayo Clinic and found records of 23 other cases in the American and English literature. A year later Pearson estimated the total number recorded at 172 but remarked that this number should be further increased by adding cases reported as acquired bronchiectasis, localized emphysema, and pneumothorax which from the description must have been instances of congenital cyst. One probable reason for the assumption that the affection is extraordinarily rare is the great variety of names applied to lesions which should properly be included under the designation, congenital cysts, such as atelectatic bronchiectasis, bronchiectatic atelectasis, fetal bronchiectasis, agenetic bronchiectasis, saccular degeneration of the lung, congenital cystic malformation of the lung, honeycomb lung, pneumatocele, and other names. At all events, it is evident that the affection occurs sufficiently often to require attentive consideration in the diagnosis of pulmonary diseases.

MORBID ANATOMY

The morbid anatomy of the affection was epitomized clearly by Koontz. He recognized two general types of cavities, namely, bronchial dilatations, as shown by persisting muscle fibers and cartilage in the walls, and "cavities resembling emphysematous blebs lying subpleurally." Between the two extremes are all sorts of gradations and transition types. The cavities may or may not communicate with the bronchi. In most cases the epithelium lining the cysts is columnar and ciliated, but it may be devoid of cilia, or be cuboidal or flat, or the membrana propria may be denuded. Mucous glands are often present and may give rise to retention cysts. Complete lack of pigment in the congenital lesions distinguishes them from the acquired variety. Absence of pigment is also emphasized by Kaufmann and by MacCallum. Among other salient features described by Koontz, or mentioned in more recent reports of cases, are the following: The cysts may be single or multiple, unilocular or multilocular, and vary in size from minute blebs with a diameter of less than 1 cm. to enormous cysts that occupy half or more of the thoracic cavity. They may contain air or fluid only, or both, and when fluid is present it often has a high content of albumin. Individual and solitary cysts are likely to be spherical or ovoid, but air-filled cysts in situ and under pressure of adjacent structures may assume the form of a portion or all of the lobe affected, and multiple closely packed cysts are likely to be polyhedral, thus justifying the appellation "honeycomb lung." Pulmonary alveoli in the vicinity of the cysts may be collapsed and atelectatic or, more often, may have failed to develop. In some instances marked fibrosis about the cysts has been noted. The cysts may occur in any portion of either or both lungs from hilus to periphery. In Koontz's series both lungs were implicated in one-fourth of the cases, the right lung in one-fourth, and the left lung

* Read at the Thirty-sixth Annual Meeting, American Roentgen Ray Society, Atlantic City, N. J., Sept. 24–27, 1935.

in almost one-half. Males and females are affected about equally often, and cysts have been found throughout "the span of human life, extending from premature still-births to extreme old age."

Complications and concurrent affections seem to occur less often than one might expect. Nevertheless, cases are recorded in which the cysts were associated with hydrothorax, pneumothorax, empyema, bronchopneumonia or lobar pneumonia, and, though rarely, with tuberculosis. In at least one reported instance the cysts coexisted with sarcoma. Occasionally fluid in the cysts is purulent from secondary infection.

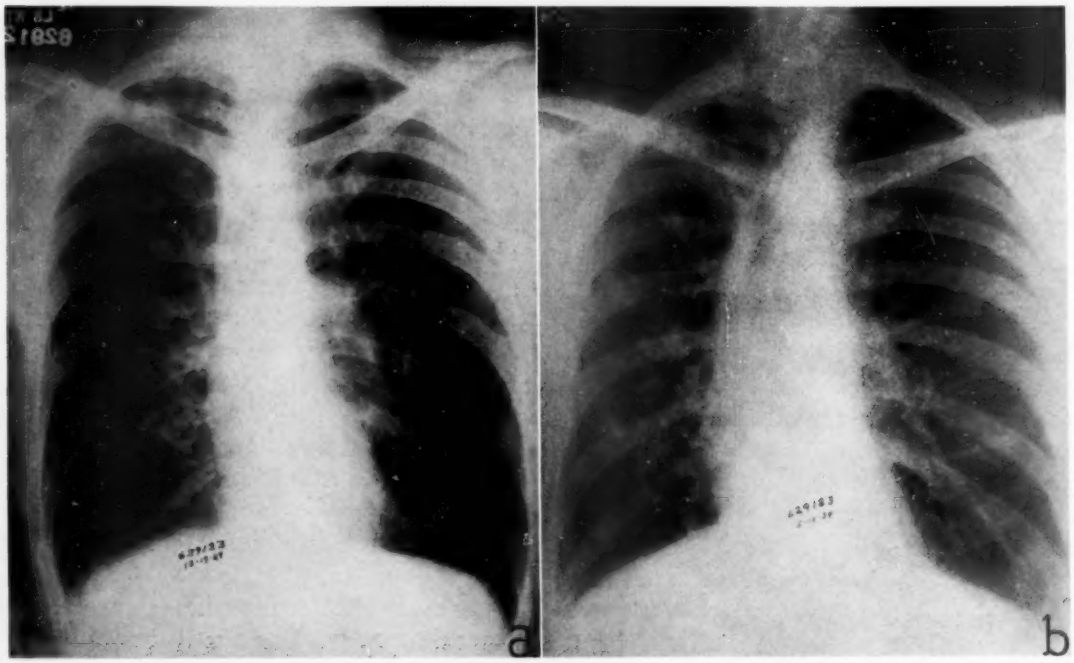

FIG. 1. Case 1. *a*. Roentgenogram made at patient's first visit, in 1927, showing multiple small cysts filled with air in the lower two-thirds of the right lung. These cysts measure from 1 to 2.5 cm. in diameter and are evidenced by fine ring-like shadows. The largest is seen directly under the ninth rib, posteriorly. There is also some evidence of secondary infection and fibrosis, with resulting retraction of the mediastinal structures to the right. *b*. Seven years later. Very little change is seen in the size and distribution of the air-filled cysts. There is, however, slightly more retraction of the mediastinal structures to the right, due no doubt to the old fibrosis.

CLINICAL MANIFESTATIONS

The clinical manifestations as described by many observers include attacks of dyspnea, cyanosis, cough, cardiac palpitation and, though rarely, hemoptysis, all varying in their combinations and degree of severity. Wood has pointed out that the symptoms and signs necessarily vary according to the extent of the lesions, their site, and the presence or absence of increased intrathoracic pressure. In many cases in which the cysts were small or only moderately extensive there were practically no symptoms and the lesions were discovered only accidentally. However, Wood has suggested that the possible presence of cysts should always be considered in infants who have recurring attacks of severe dyspnea with cyanosis, and also in adults who have progressive dyspnea without other known cause. But confident diagnosis of the condition from symptoms and physical signs alone is seldom if ever possible, and roentgenologic examination is essential not only for identification of

the lesions, but often also for their discovery.

Posteroanterior stereoscopic roentgenograms of good quality are usually adequate for revelation of the cysts. Occasionally lateral views are desirable to determine exact relations. When a cyst is in contact with the thoracic wall, the induction of pneumothorax, as employed by Wilson, may make it possible to distinguish the wall of the cyst. Roentgenography after intratracheal injection of iodized oil is often advantageous in determining whether cysts are open or closed and in depicting them more distinctly.

Since the publication of Koontz's paper, reports of 78 cases observed with the roentgen ray and of 6 discovered at necropsy have appeared in the more readily available literature. Among these 84 cases, 35 were verified by histologic examination ofter operation or necropsy. The cysts were, or appeared to be, single in 43 cases, multiple in 41. They contained varying amounts of fluid in 27 cases, and were filled with air only in 57.

To the foregoing may also be added 4 additional cases observed at The Clinic:

REPORT OF CASES

Case I. A man was first seen at The Clinic in 1927 when he was thirty-six years of age. He complained of "lung trouble" for the previous seven years with occasional blood-streaked sputum. He was subject to frequent colds but he did not complain of pain. For many years he had had dyspnea on the slightest exertion. On examination at this time he was found to have an afternoon temperature of approximately 100° F. Repeated examinations of the sputum failed to reveal any tubercle bacilli. Roentgenograms were interpreted as revealing diffuse bronchiectasis on the right (Fig. 1, *a*).

The patient had been examined from time to time in the next seven years, but in spite of the fact that his sputum was negative for tubercle bacilli he had been considered to have tuberculosis and had been treated in a sanatorium for several months without much improvement.

The patient then returned to The Clinic in 1934, seven years after his first examination, with a history of having had several hemorrhages in the past seven years. He still had a slight cough and occasionally blood in his sputum; repeated examinations of the sputum, however, were still negative for tubercle bacilli. His temperature at this time was normal. He still complained of dyspnea on slightest exertion. Roentgen examination revealed a fine network of shadows throughout the right lung, with many ring-like shadows which gave the lung a somewhat honeycombed appearance. A

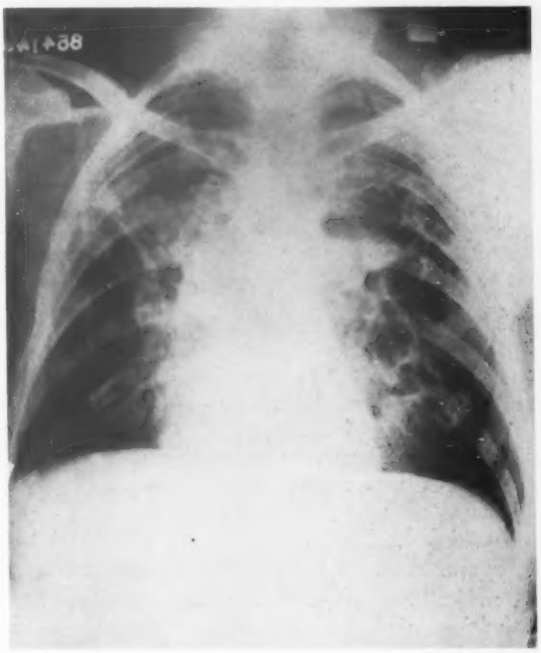

Fig. 2. Case II. Multiple cavities throughout the midportion of the left lung, surrounded by ring-like shadows. There is a small amount of fluid in the lowermost cyst at the left border of the heart. There is also definite disease on the right which, after ruling out primary bronchogenic malignancy, was interpreted as tuberculosis.

roentgenologic diagnosis of congenital polycystic lung with superimposed infection and bronchiectasis was made. On comparing these films with those made seven years previously it was found that there was very little if any change, which further substantiated the diagnosis of polycystic lung (Fig. 1, *b*). The clinicians agreed that tuberculosis could be ruled out and thought that the clinical data substantiated the diagnosis of congenital polycystic lung.

Case II. A man, aged forty-eight, came to The Clinic complaining of cough and foul spu-

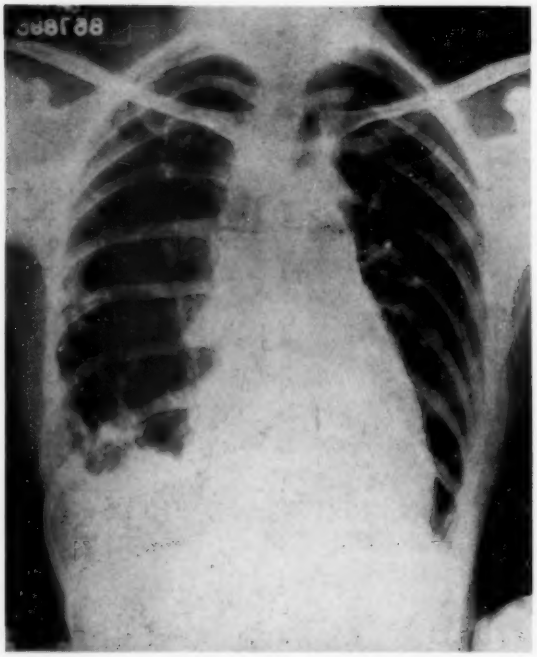

FIG. 3. Case III. Diffuse congenital cystic disease of the right lung, evidenced by the fine network of shadows resembling cobwebs. There is also thickening of the interlobar pleura, and an old infection at the base with a small amount of fluid.

tum which had been present for the previous six years. He had a normal temperature, and the clinical and physical findings were those of bronchiectasis. Roentgen examination disclosed several small cavities in the middle and lower portions of the left lung, some being partially filled with fluid. There was considerable infiltration in the right lung, extending to the infraclavicular region, with calcified hilar nodes. The roentgen diagnosis was congenital polycystic left lung and tuberculosis on the right (Fig. 2). There was no history of foreign body or any very severe respiratory infection The patient was examined bronchoscopically to rule out bronchostenosis or foreign body; the bronchi on both sides were very markedly dilated and very little pus was present. There was a peculiar appearance of the terminal bronchi on the left in that the mucous membrane seemed to be atrophic in character. Repeated examinations of the sputum failed to reveal any tubercle bacilli. A careful review of the roentgenograms, in my opinion, justifies a diagnosis of congenital polycystic lung complicated by infection and concurrent disease in the right lung.

CASE III. A woman, aged forty-two, had always been slightly dyspneic. Five years before coming to The Clinic she had had an attack of pleurisy and a roentgen diagnosis of pleurisy with collapse of the right lung had been made at that time. Roentgenologic examination at The Clinic disclosed lack of normal pulmonary markings and increased radiance throughout the right lung, fine stringy shadows indicative of walls of cysts, thickening of the parietal pleura and apparently a small amount of fluid at the right base, and thickening of the interlobar pleura (Fig. 3). The mediastinal organs were displaced slightly to the left. The roentgenologic and clinical diagnosis was congenital cystic disease of the lung with thickened pleura. The clinical consultant commented that spontaneous pneumothorax may have occurred during the attack of pleurisy five years previously, thus accounting for the roentgenologic report of collapse of the lung; more probably, however, the manifestations of the polycystic lung were mistaken for those of pneumothorax.

CASE IV. A man, aged thirty-eight, came to

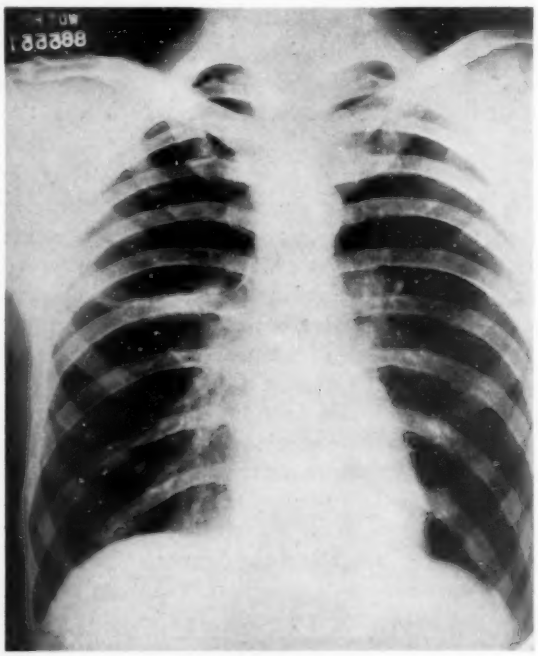

FIG. 4. Case IV. A rather large, single congenital cyst of the upper portion of the right lung, with lack of pulmonary markings at the levels of the first and second ribs anteriorly. The thin wall of the cyst can be seen at the level of the second rib. There is also some interlobar pleurisy.

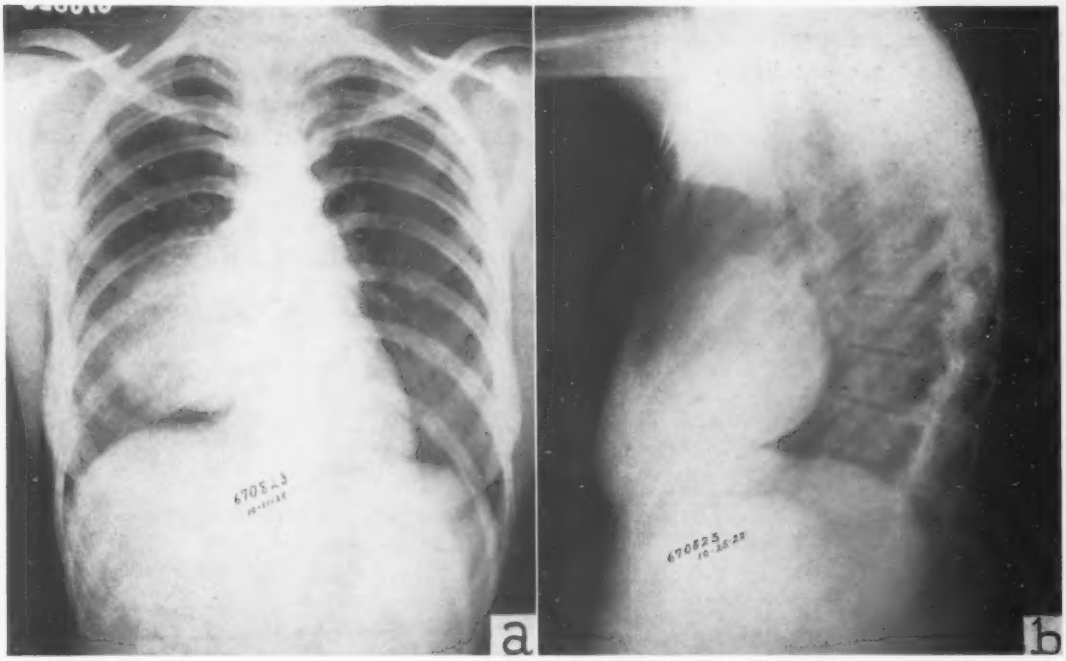

Fig. 5. Congenital pulmonary cyst filled with fluid. The patient was a woman aged nineteen. The cyst was removed transpleurally and the pathologic report was as follows: "Fibrous-walled cyst filled with clotted blood, columnar epithelial-lined ducts and fibrous tubes with lining cells closely resembling bronchial epithelium, and complete absence of pigment." The pathologic report warrants a diagnosis of congenital pulmonary cyst. *a*. Anteroposterior view; *b*, lateral view. (This case has been previously reported by Dr. Harrington.)

The Clinic because of a cough and hemorrhagic sputum of two weeks' duration. A similar episode had occurred fifteen years before. On roentgen examination a definite deficiency of normal pulmonary structures in the upper three-fourths of the right lung was noted (Fig. 4). Instead there were fine curvilinear shadows characteristic of a multilocular cyst. The right apical region was completely transradiant. The mediastinal organs were not displaced. On the basis of these signs the roentgenologic diagnosis was congenital cystic disease of the lung. Bronchoscopy revealed an anomalous opening of the bronchus from the right middle lobe. The consulting clinician concurred in the diagnosis of polycystic pulmonary disease.

ROENTGENOLOGIC FEATURES

From all the material at hand it is evident that the roentgenologic manifestations of congenital pulmonary cysts and the facility with which these cysts can be diagnosed vary according to their content, size, number and situation, and the presence or absence of complications or concurrent disease.

Cysts completely filled with fluid and without any inflammatory zone about them cast round or ovoid, uniformly dense, sharply circumscribed shadows which are easy to discern but not confidently distinguishable from those of many other pulmonary lesions. Usually the fluid-filled cyst is single, relatively large, and resembles a benign neoplasm, primary or metastatic new growth, hydatid cyst, dermoid cyst, or aneurysm. Some of these conditions often have characteristic marks of identification, but after all possible exclusions have been made, the examiner usually is obliged to content himself with the nonspecific diagnosis of tumor of the lung (Fig. 5, *a* and *b*). An infected fluid-filled cyst enveloped by an irregular zone of reactive inflammation will almost inevitably be mistaken for an abscess or pneumonic consolidation.

Cysts containing both air and fluid in varying proportions are depicted so strikingly that they are not likely to be overlooked (Fig. 6, *a* and *b*). The dense shadow of fluid, with its level upper surface surmounted by a transradiant hemispherical bubble of air, is pathognomonic of a cavity containing these elements; but abphenomena. Tuberculous cavities are almost invariably accompanied by tuberculosis elsewhere in the lung; statistics indicate that not more than 5 per cent of congenital cysts are associated with tuberculosis. Echinococcal cysts are rare in this country, and dermoid cysts are likely to exhibit their well-known identifying cri-

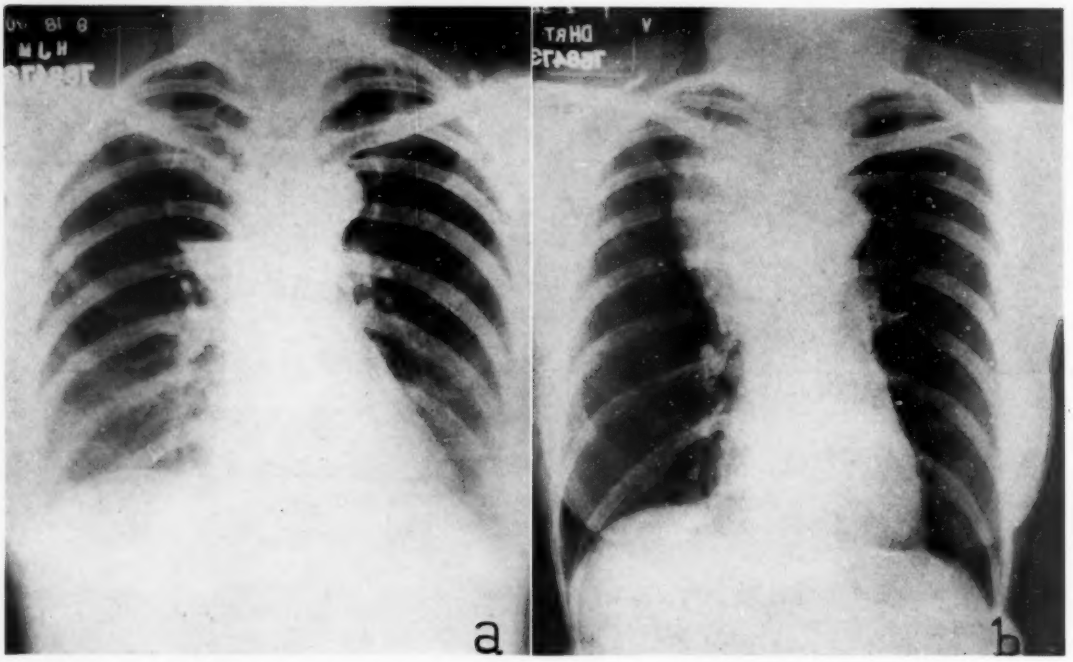

FIG. 6. *a*. Roentgenogram showing large cyst partially filled with fluid corresponding in situation to an azygos lobe. The patient was a woman aged thirty-seven; *b*, a year and a half later the cyst was completely filled with fluid. A roentgen diagnosis of a cystic azygos lobe was made at this time. A large cystic mass containing about 750 c.c. of pus was removed and a bronchial fistula communicating with the cyst was closed. On pathologic examination of the specimen, the wall of the cyst was found to be lined with epithelium and contained all types of pulmonary tissue. Complete absence of pigment was also noted. (This case has been previously reported by Dr. Harrington.)

scess, tuberculous cavitation, and draining hydatid cysts would have to be considered in the differential diagnosis. If the cavity is single, large, and has a sharply delineated wall that is thin or not unduly thick, it probably represents a congenital cyst, although a draining echinococcal cyst would not definitely be excluded. If the cavity is surrounded by a dense, irregular shadow indicative of an inflammatory zone, abscess will rightly have diagnostic preference; although this may be in error, for an infected cyst may give rise to similar teria. Multiple aggregated cysts of moderate size, with thin ring-like walls and small amounts of fluid, present a picture that is virtually pathognomonic.

Large cysts containing only air, which are most often single or not exceeding two or three in number, can usually be identified with a high degree of confidence (Figs. 7, 8, 9, *a* and *b*, and 10, *a* and *b*). The brilliantly transradiant area is devoid of normal pulmonary markings, and that portion of the wall of the cyst in contact with the unaffected part of the lung appears as a

regularly curved line (Fig. 8). Often such cysts affect a large part or all of the lung and may project across the mediastinum into the opposite lung (Fig. 9, *b*). As the outer wall of the cyst is likely to be in contact with the thoracic wall and is thus indistinguishable, the condition is often mistaken for pneumothorax (Figs. 9, *a* and 10, *a*). In pneumothorax, however, the transradiant region is bordered by the dense shadow of compressed lung whereas a cyst rather seldom causes such compression. Further, in doubtful instances the outer wall of a cyst can be demonstrated by Wilson's procedure of inducing slight pneumothorax (Figs. 9, *b* and 10, *b*). Scott and Waltz quote Clairmont to the effect that an interlobar line may be seen crossing a cyst, but not in pneumothorax.

Multiple, grouped, air-filled cysts are not uncommon. In typical instances the affected region is abnormally clear, normal pulmonary and vascular markings are effaced, and the walls of the cyst are depicted as delicate, complete or incomplete rings (Figs. 1 and 11), or as a complex network of shadows resembling cobwebs (Fig. 3). Multiple, relatively small, air-filled cysts tightly compacted together are often polyhedral and the appearance resembles that of a honeycomb (Fig. 1).

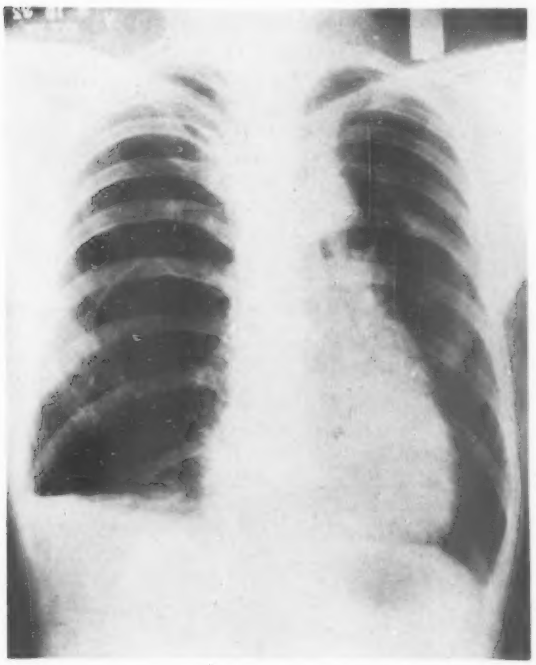

Fig. 7. Large congenital pulmonary cysts filled with air. One cyst extends from the level of the seventh to the eleventh rib posteriorly on the right. There is also a cyst in the left lung at the level of the second to the fifth rib anteriorly. (This case has been previously reported by Dr. Wood.)

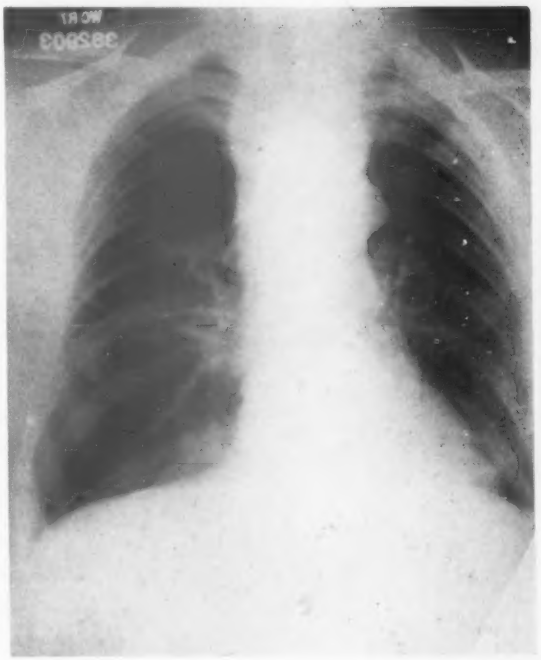

Fig. 8. Showing some displacement of the trachea and mediastinal structures to the left. Roentgenograms made after injection of iodized poppy-seed oil disclosed direct bronchial connection. A large congenital pulmonary cyst involves the upper portion of the right lung and extends across the mediastinum at the level of the eighth rib posteriorly. The wall of the cyst can be seen at the second interspace, anteriorly, as a fine curved line. The patient, a man aged forty-three, complained of cough and dyspnea with moderate expectoration for several years. A review of the roentgenograms taken eleven years previously revealed that cystic change was present at that time. (This case has been previously reported by Dr. Wood.)

Multiple air-filled cysts often require distinction from emphysema, diaphragmatic hernia, and bronchiectasis. Cysts are frequently mistaken for emphysema because the latter is also characterized by increased transradiancy of the lungs and, in extreme forms of the affection, by

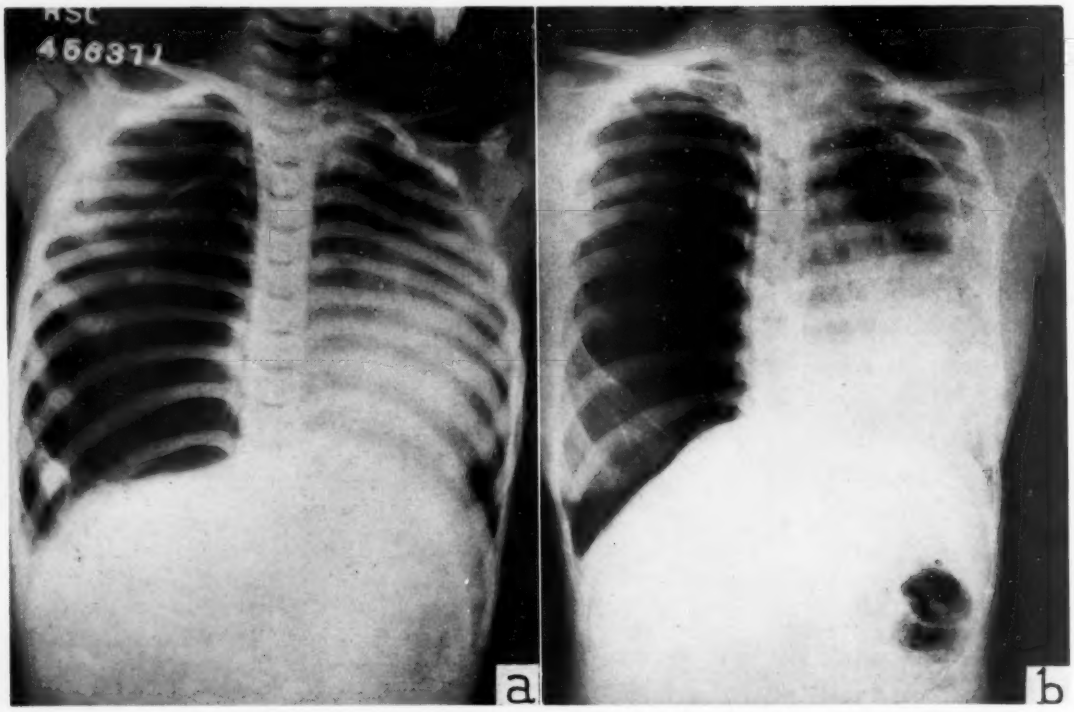

Fig. 9. *a*. Taken in 1924 following thoracotomy. The outline of the wall of the cyst, which has been partially collapsed as a result of induced pneumothorax, is evident on the right; *b*, appearance ten years later: a large cyst filled with air fills the entire right side of the thorax and extends across the mediastinum and into the upper portion of the left side of the thorax. (This case has been previously reported by Dr. Wood.)

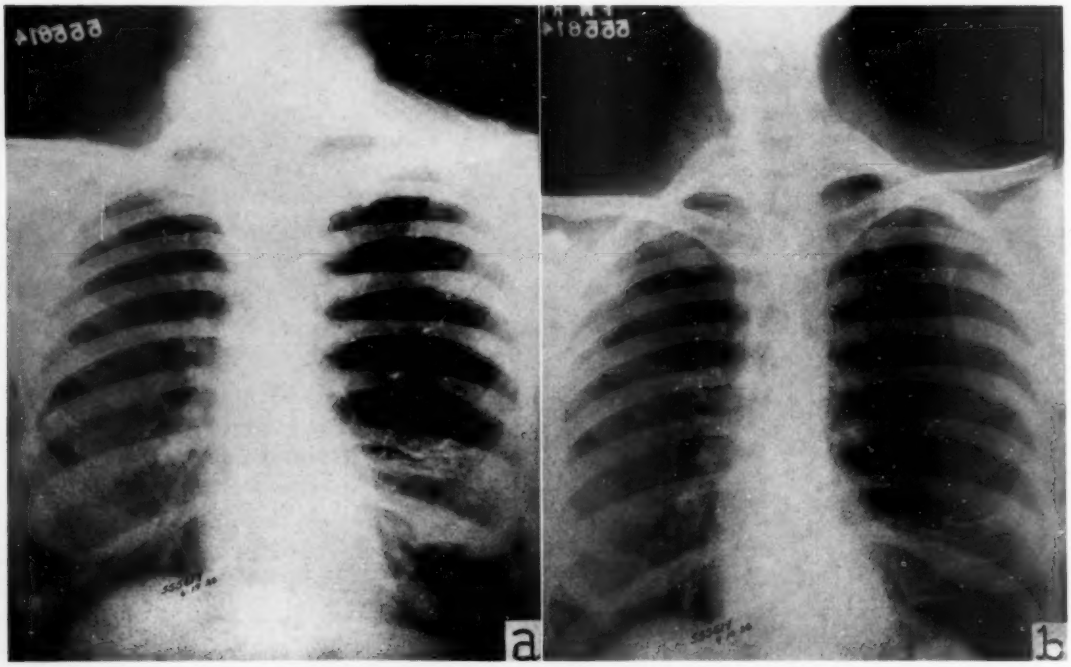

Fig. 10. *a*. This case was reported in 1927 as a case of obstructive emphysema by Col. J. A. Wilson who referred the patient to The Clinic in 1926. The complete lack of pulmonary structure in the entire upper lobe of the left lung gives the appearance of pneumothorax except that there is no evidence of compressed lung at the hilus; *b*, after induced pneumothorax following Wilson's technique. The thin wall of the cyst can be clearly seen at the level of the first and second ribs anteriorly. A diagnosis of congenital pulmonary cyst filled with air was made.

emphysematous blebs or bullae which cast ring-like shadows. However, emphysematous blebs and bullae occur on the surface of the lung, whereas pulmonary cysts occur more often in the substance of the lung, and if stereoscopic films are employed the ring-like shadows should be easily localized and properly interpreted. Generalized emphysema, with its depression of the diaphragm on both sides and vertical position of the heart, should scarcely be a source of error in diagnosis; but the localized, compensatory, and obstructive forms of emphysema may more easily be confounded with cystic disease. However, even in these forms the peripheral bronchovascular markings are likely to be exaggerated instead of being minimized or effaced as in cystic disease. Further, in obstructive emphysema, the cause of obstruction, whether foreign body or tumor, may be evident.

Hernia of the stomach and bowel through the diaphragm may be a deceptive simulant of pulmonary cysts, and vice versa. In thoracic roentgenograms alone, perhaps the most distinctive criterion is the shadow of the diaphragmatic arch, which is broken, deformed, or untraceable in hernia, and normal in cystic disease; examination with an opaque meal, however, will furnish a safer basis for judgment.

Most perplexing among simulants of congenital pulmonary cysts, whatever the content of the latter may be, is acquired bronchiectasis, especially when the dilatations or cysts are multiple, small, and grouped. Although bronchiectasis usually affect lower bronchi, the sacculations are usually surrounded by dense fibrous tissue, the shadow of which is evident, and the bronchovascular markings are accentuated; these are not always convincing differential marks. As acquired bronchiectasis and congenital cysts are both essentially dilatations of bronchi, and as absolute distinction can be made only by histologic examination, it is inevitable that each will occasionally be mistaken by the roentgenologist for the other. As acquired bronchiectasis is by far the more common disease, it should be favored proportionately in diagnosis.

Absence of mediastinal displacement and the unchanging appearance of the roentgenologic picture at successive examinations, even after long intervals, are rather common characteristics of all congenital cysts and thus assist in their recognition.

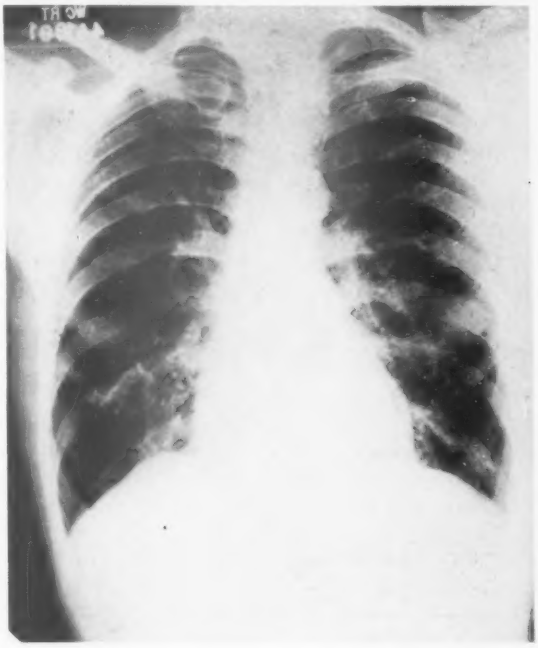

Fig. 11. Multiple air-filled pulmonary cysts at the right base. The outline of one cyst shows at the level of the tenth rib on the right as a ring-like shadow, and another can be seen between it and the heart. A small cyst is present at the same level on the left.

But these factors are not altogether constant, for an enormous cyst may displace the heart and great vessels toward the opposite side (Figs. 7 and 9), or adhesions resulting from secondary inflammatory processes may draw the mediastinal organs toward the affected side (Fig. 1); cases of cystic disease have been reported in which the cysts progressively increased in size (Fig. 9).

All the foregoing considerations of diagnosis and differentiation apply particularly to cysts without complications or

association with other disease. When the cysts are complicated by pneumothorax from rupture of a cyst, or by hydrothorax, empyema, the pneumonias, tuberculosis, or any of the various diseases that may attack the lung, exact diagnosis is almost impossible. Statistics indicate that not more than 5 per cent of cysts are associated with tuberculosis, and notwithstanding the number of complications and associated diseases that may occur they are more often absent than present.

In a large proportion of cases the roentgenologist can identify congenital cysts, especially the larger air-containing cysts, and in most of the others he should contribute data which in correlation with the clinical facts will lead to the diagnosis. That cooperation with the clinician is requisite in all cases scarcely needs to be emphasized. Until ten years ago the roentgenologist undoubtedly failed to recognize many congenital cysts, but now that he has become so keenly conscious of them, he must resist the unavoidable tendency to mistake other lesions for them.

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BRONCHOGRAPHY AS AN AID IN THE INTERPRETATION OF THE ROENTGEN SHADOWS CAUSED BY PLEUROPULMONARY CHANGES IN TUBERCULOSIS*

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IN FORMER publications by Neuhof,[1] Murphy[2] and one of us,[3] a preliminary report presented the findings in bronchographic studies in 65 tuberculous patients. Since then the work has been extended both quantitatively and to include confirmatory studies of post-mortem bronchograms followed in many instances by careful analyses at autopsy. In this paper we wish to emphasize again the value of bronchography in the light of our experience with 180 patients in whom a total of 200 injections of lipiodol was made.

This study is an outgrowth of observations of frequent discrepancies found between autopsy revelations and the conception of the existing pathologic process as interpreted from roentgen shadows. The necessity for pneumograms became still more evident when collapse therapy came up for consideration in any patient: (1) presenting disputed evidence of cavitation, or (2) a mucopurulent expectoration negative for tubercle bacilli persisting after a supposed effective collapse. In other words, the purpose of this investigation has been to solve practical problems by attempting to dissociate roentgen shadows seen in pulmonary tuberculosis.

It is interesting to note that the recent literature amply reflects the justification for supplemental bronchograms. Thus, Sicard and Forestier,[4] in speaking of the indications for lipiodol studies, said (referring to lipiodol) "without it, most radiographs are a meaningless jumble of shadows, blotches and clouds." And very recently Shapiro and Jaches[5] have written:

There is probably no aspect of the disease of the lung upon which bronchography has not thrown considerable light in recent years. In tuberculosis, lung abscess, bronchiectasis, benign and malignant tumor and in obscure diseases of the lung, the application of bronchographic method has greatly clarified our conception of the disease process present, often proving our principal means of establishing an accurate diagnosis.

As the work progressed, it was felt advisable to check the interpretations of the bronchograms in the living with similar studies after death. Since the beginning of 1934, therefore, a plain roentgenogram followed immediately by a film after the injection of barium sulphate into the trachea was taken of every patient who had died. In about 25 per cent of the deaths autopsies were obtained which offered opportunity for careful dissection of the bronchi and investigation of the pulmonary parenchyma and pleura. The post-mortem roentgenograms were at first taken with the lungs removed from the chest cavity, but it was soon found that better correlative information could be obtained by taking films with the lungs intact (Figs 1, 2, 3, 4 and 5).

The type of case in which the bronchographic method is essential will be considered below. At this point it becomes necessary to point out the general contraindications which, if held in mind, will obviate the unpleasant complications stressed in the literature heretofore. The most important of these is that the use of lipiodol (or for that matter any contrast medium) is prohibitive in the exudative lesions. Apparently, as shown by Amberson and Riggins,[6] this holds true not only in tuberculosis but also in the acute stage of non-tubercu-

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lous disease of the lungs. These workers have described complicating bronchopneumonia about the lipiodol shadows, dissemination of the inflammatory process into the same or opposite lung and aggravation of the inflammatory lesion following the use of lipiodol in some of their cases. A careful study of the cases cited leaves one

Fig. 1. Left lung field obscured by a homogeneous density which is interrupted by several small high light shadows situated in the first interspace, heart deflected to the right and right lung diffusely infiltrated.

with the impression that, allowing for technical errors to be discussed later, the paramount cause for the accidents appears to be the use of lipiodol in exudative tuberculous lesions, in the acute stage of lung abscess and in the acute bronchopneumonias which complicate bronchiectasis. The understanding of the mechanism by which aggravation of an existing exudative process occurs is not clear, for apparently it is not in the nature of a lipoid pneumonia since, as has been shown by Pinkerton,[7] the simple neutral vegetable oils, of which iodized poppy-seed oil is one, produce no reaction in the alveoli of animals. It seems, therefore, that the changes noted in the

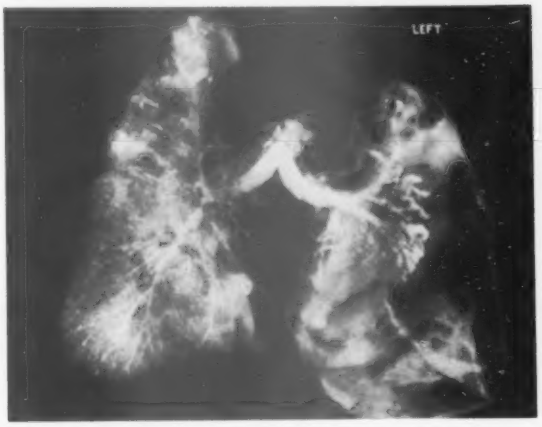

Fig. 2. Same patient as in Figure 1, immediately after death, whose lungs have been removed from thoracic cage and bronchi injected with barium sulphate. Note large empyema sac and collapsed left lung in which the bronchi are dilated. Large cavity in apex not penetrated by the barium because of stenosis of apical branch of upper lobe bronchus.

parenchyma about an acute tuberculous or acute non-tuberculous process are due to foreign body reaction on an inflammatory soil.

Fig. 3. Lower left of right lung field and diaphragm obliterated by dense opacity; upper half replaced by two huge cavities. Bronchopneumonic, soft confluent infiltrate in left mid-lung region.

Fig. 4. Same patient as in Figure 3, immediately after death. Barium is seen to fill the large cavities in the right lung and the widely dilated sacculated radicles of the middle and lower lobe bronchi. Lower lobe partly collapsed by encapsulated empyema. Left mid-lung region shows sacculated bronchiectasis and a filled cavity in the inner and mid zones at the level of the second interspace. (Proved at autopsy.)

Another factor in the production of complications seems to be due to the method of injection of the lipoidol. In our clinic the transnasal, intratracheal route described by Murphy[2] is used. In the past year, the procedure has been modified by spraying with 2 per cent butyn the first part of the trachea through a special cannula devised by one of us (Pagliughi). By this means all coughing is avoided during the instillation of the oil under roentgenoscopic visualization. We surmise that introduction of the oil in this way plays the most important rôle in the prevention of its migration into the gastrointestinal tract and of the use of excessive amounts. We believe that most of the cases of iodism following lipiodol injection result from the rapid absorption and digestion of the oil which so often finds its way into the intestines whenever the supraglottic method is employed. It is obvious too, that, unless the contrast medium is introduced under roentgenoscopic observation, excessive amounts may be used, resulting in flooding and dissemination to parts of the lung not desired in the study. We are impressed with to the fact that flooding, particularly to healthy parts of the lung, may have been responsible for the complications cited in some of the cases of Amberson and Riggins. It seems, therefore, that the accidents referred to above can be avoided by strict attention to selection of cases and by proper technique. In fact we find confirmation of this statement in the paper by Amberson and Riggins wherein they say: "Since our selection of cases and technical procedures have been modified on the basis of this knowledge (referring to the knowledge gained from the cases that showed complications) we have had no more accidents of this kind."

Further proof of the importance of avoiding the introduction of lipiodol in

Fig. 5. Cross section of lung of a patient who presented a far-advanced bilateral fibrocavernous tuberculosis. Note bronchiectasis about cavity.

exudative lesions lies in the fact that, in our series of 180 cases, we have not met with a single instance of aggravation of a previously existing process or of dissemination to other parts of the lung as shown by serial roentgenograms during a period of several months to two years following bronchographic studies. This observation is further corroborated by Mandelbaum[8] who writes: "I, myself, have bronchoscoped and injected over 90 tuberculous patients, having given in all 250 injections without any serious sequela. This was due to the fact that my cases were carefully selected as were yours."

We must not lose sight, however, of the fact that, with all precautions, one is occasionally confronted with after effects of lipiodol injection which apparently are unavoidable. In our own experience these divided themselves into two groups:

(1) Febrility, of slight degree, but which subsided within forty-eight to seventy-two hours was met with in 4 patients, 3 of whom were more or less debilitated. It is believed that the exertion was responsible for the slight fever.

(2) Allergic phenomena. Macular eruption of generalized distribution occurred in one patient, swelling about the face and eyes in two, and swelling about the face and eyes accompanied by bloody urine for forty-eight hours in another. In this last case a restudy of the chart revealed urinary and blood findings indicating a chronic nephritis which was overlooked. Every one of these patients responded favorably to adrenalin.

We are aware that other complications have been mentioned in the literature, but their connection with lipiodol injection is vague and their occurrence unconfirmed by those experienced in bronchography. In summing up it may be stated that, after all is said, one must weigh the possible and probable complications, as one weighs the accidents that may follow any other test, against the advantages derived from the test. This is well illustrated by Amberson and Riggins[6] when they say: "In spite of these disadvantages and dangers, this procedure is still to be regarded as an invaluable aid for the diagnosis of various chest conditions. By attempting as we have done, clearly to visualize the causes and the mechanisms of possible accidents we can with assurance of great success adopt means to avoid these." To this we may add, that, in our opinion, bronchography is just as essential in dissociating the roentgen shadows caused by broncho-pleuro-pulmonary changes in those cases of pulmonary tuberculosis in which the plain roentgenogram fails to reveal a clear picture of the pathologic process that is so necessary for proper therapeutic management of the patient.

The indications for bronchographic studies in pulmonary tuberculosis may best be appreciated by considering specific cases representative of groups of pathologic changes in which the plain roentgenogram leaves one in doubt as to the true nature of the change.

BRONCHIECTASIS IN INFILTRATIVE LESIONS

Case 1. J. H., No. 8518, male, negro, entered the hospital in May, 1932, complaining of productive cough and shortness of breath. His illness dated back to some five months before admission when he began to feel short of breath and developed a cough which continued. A month later he had visited a tuberculosis clinic where he had been advised to enter a hospital for pneumothorax treatment. On admission to the sanatorium physical and roentgenographic examination revealed a mixed, productive cavernous infiltrate confined to the right upper lobe of a pneumothorax pocket overlying the lower lobe. The sputum was positive. We decided to maintain the pneumothorax but this treatment was abandoned in January, 1933. At this time the patient was ambulatory, feeling well except for a slight cough productive of 60 c.c. of mucopurulent sputum daily in which no tubercle bacilli could be found. Figure 6 illustrates a productive infiltrate in the right upper lobe in which there may be discerned many small areas of high light and a small pneumothorax over the lower lobe. There was no convincing evidence of cavitation and it was

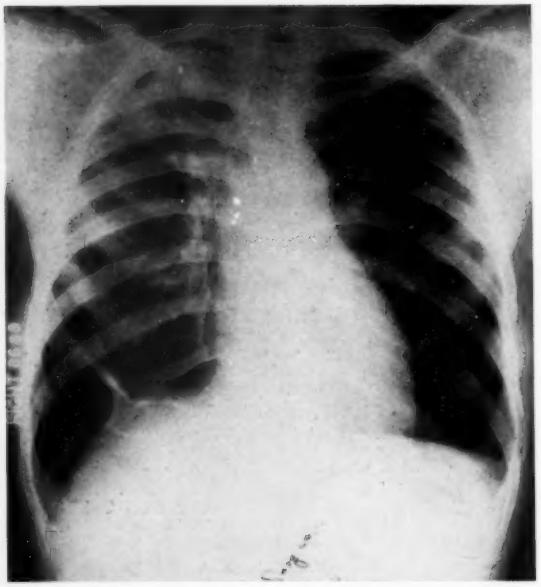

Fig. 6. Case 1. Productive, stringy infiltrate right upper lobe embracing several various sized oval rarefied densities and pneumothorax pocket over lower lobe; 60 c.c. mucopurulent sputum daily, negative for tubercle bacilli.

believed that the high light regions were of bronchiectatic nature and probably the source of the mucopurulent sputum. The bronchogram (Fig. 7) reveals clearly a saccular bronchiectasis of the right upper lobe. The patient has continued to do well and is working.

It is evident that we are dealing with a patient in whom there is bronchial widening in a portion of the lung where previously was present an active tuberculous process. The bronchogram not only makes clear the residual pathology but adequately accounts for the symptoms. Cylindrical to saccular bronchiectasis in productive or fibroid tuberculous infiltrations is present in about 45 per cent of the cases in which bronchographic studies are made. A correct interpretation of the stringy densities which embrace multiple areas of high light as seen in the plain roentgenogram of the above case is very important, for it does away with unnecessary residence in the sanatorium, or surgical collapse.

On the other hand, there are instances where, after months or years of rest treatment, a patient is left with a productive infiltrate so arranged as to include numerous areas of lesser density and an occasional bacillary sputum. These areas of lesser density have been variously interpreted to signify multiple cavitation, bronchiectasis, or inclusions of normal lung tissue. The latter meaning is especially apt to be given when the sputum fails to reveal tubercle bacilli. From a purely academic point of view, dissociation of these probabilities may be interesting but not essential. It becomes very necessary, however, to resolve these shadows with a greater degree of accuracy than can be done from a plain roentgenogram when intelligent further management of the case is considered. The following case is illustrative:

Case II. M. M., No. 8352, white female, aged seventeen, was admitted October, 1931, with all the classical symptoms of tuberculosis, positive sputum and physical and roentgen findings of a bilateral mixed infiltrative cavernous lesion more extensive in the left lung. Pneumothorax was attempted on the left side but no free pleural space could be found. She remained on routine hygienic-bed rest treatment until December, 1932, and then was allowed gradual

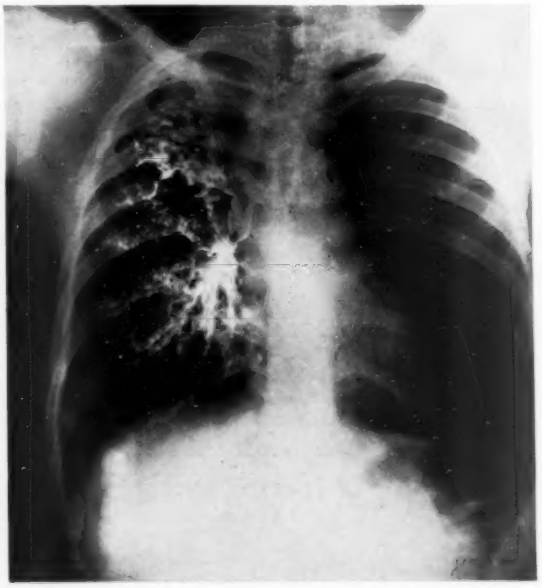

Fig. 7. Case 1. After lipiodol injection. Radicles of upper lobe bronchus show sacculated dilatations, and thus account for the sputum.

exercise. In March, 1933, she was ambulatory, sputum was positive and the roentgenogram showed a remarkable partial resorption of the infiltrate in the right upper lobe leaving residual stringy opacities; the left lung showed further evidence of reduction of volume from that noted on admission and a productive infiltrate embracing many areas of high light as seen in Figure 8. The question of surgical collapse of the left lung arose but the extensiveness of the rib resection could not be agreed upon because one could not be certain of the significance of the numerous rarefied shadows seen on the plain film. The bronchogram (Fig. 9) definitely demonstrated multilocular cavitation and thus the surgeon gained a clearer conception of the type and extensiveness of the surgical procedure indicated.

Fig. 9. Case 11. Bronchogram of same patient showing multiple cavities as demonstrated by the numerous lipiodol levels.

BRONCHIECTASIS IN FIBROCAVERNOUS LESIONS

Bronchial dilatation of some degree is almost a universal finding in the fibrocavernous type of tuberculosis. Since these lesions are practically always attacked by some form of collapse therapy it is essential that one give a more or less correct interpretation of the roentgen densities before surgical collapse is induced, for, if this interpretation is faulty, one may either do too much resulting in an increase in the risk and in the sacrifice of comparatively healthy lung tissue, or one may use accessory surgical procedures unnecessarily. It can readily be seen where the former contention may be true by studying the plain and bronchographic films illustrated by Figures 10 and 11 respectively. In the former are seen 3 large cavities occupying the upper half of the right lung field and numerous small high light areas which can be taken to be small multiple cavities. If this meaning is taken for granted and obliteration of all rarefied shadows be sought, extensive surgery becomes necessary. At times even wide rib resection fails to obliterate these small high light shadows and one must resort to revision of the old thoracoplasty and attempt compression by packing, if productive cough remains and an anatomically effective collapse is the criterion for success. The bronchogram however shows the small rarefied densities within the large cavity to be due to bronchial dilatations the obliteration of which is not essential unless positive sputum

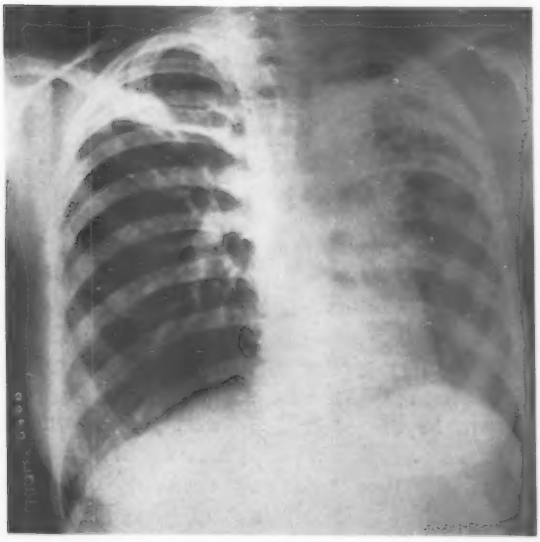

Fig. 8. Case 11. Left diaphragm slightly elevated and mediastinal structures deviated to the same side. Left lung presents a fibrous infiltrate so arranged as to include numerous oval high light areas which may be variously interpreted. Stringy opacities right apex.

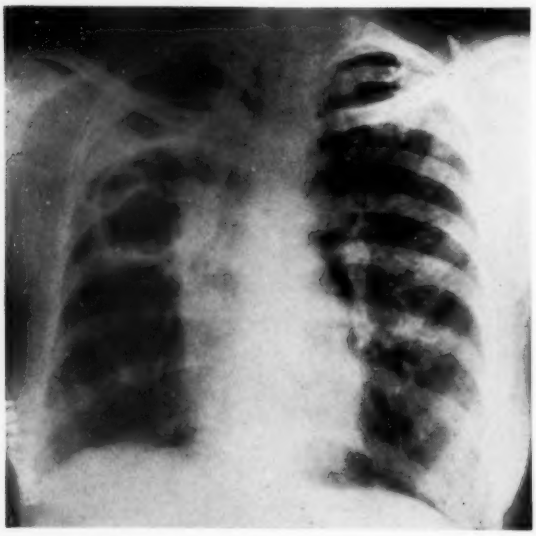

Fig. 10. Mediastinal structures deviated to the right, and within right lung are seen three large cavities. In the lowest cavity can be made out numerous small ring shadows. Left upper lobe discretely infiltrated with dense mottlings.

persists after all cavity bearing areas have been effectively collapsed.

In the same manner the second probability, namely, the use of unnecessary accessory surgery is illustrated in the following case:

Fig. 11. Bronchogram of same patient shown in Figure 10 demonstrating sacculated bronchiectasis of radicles of right upper lobe bronchus.

Case III. A. S., No. 9237, white female, aged twenty-one, admitted December, 1932, with fever, cough productive of positive sputum, and physical and roentgen findings of a fibrocavernous process of the right lung (Fig. 12). Pneumothorax was immediately established and became effective February, 1934, when the sputum failed to reveal tubercle bacilli, the temperature and pulse were within normal limits and the cough had ceased, although a daily quantity of 15 c.c. of mucoid sputum still remained. It will be seen in Figure 13 that there is a partial collapse of the right lung which is held out by stringy adhesions radiating to the chest wall in the first and

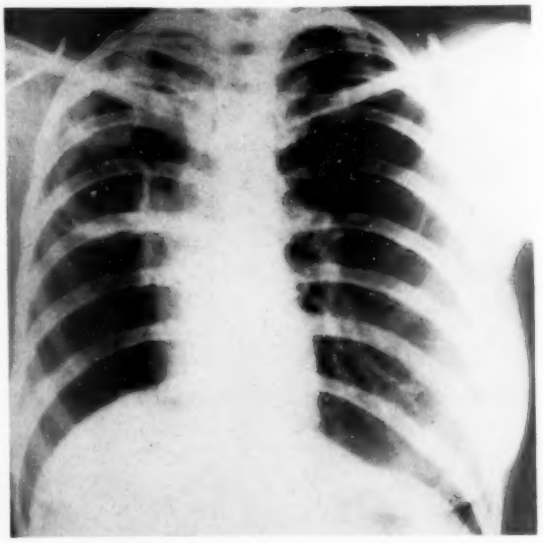

Fig. 12. Case III. Fibrocavernous lesion in upper half of right lung field and deviation of mediastinal structures to the affected side.

second interspaces, and within the partly collapsed upper lobe are many small high light regions. It was contended by some that these represent residual cavities and further collapse should be established by cauterization of the adhesions. In view of a persistently negative sputum and for the sake of the well being of the patient, pneumonolysis was objected to by some and a bronchogram was suggested which proved the rarefied shadows to be due to widening of the radicles of the upper and middle lobe bronchi (Fig. 14). This patient has continued to do well under pneumothorax treatment.

DIFFERENTIATION BETWEEN PLEURAL AND PARENCHYMAL DENSITIES

It is known that pleural thickening may either obscure the lung field entirely or cast bizarre shadows which so confuse the picture as to make impossible a conclusion as to the pathology present. This is still more true when air in the pleural cavity is encountered. In such instances bronchography becomes absolutely requisite. A good example is seen in the following:

Case iv. M. L., No. 9929, white female, admitted February, 1935, after having resided

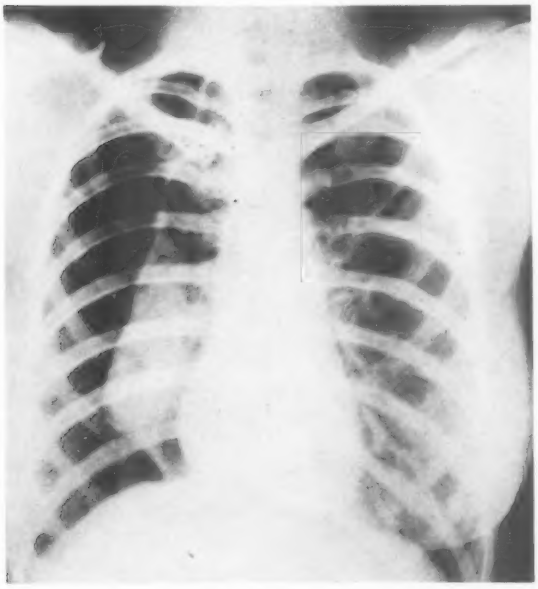

Fig. 13. Case iii. After effective pneumothorax. Note string adhesions radiating into first and second interspaces and partly holding out right upper lobe, within which are numerous small high light regions.

in another sanatorium for two years. She was well preserved, afebrile, ambulatory, complaining of productive cough. The only significant fact in her past history was the presence of a left-sided pyopneumothorax and expectoration of pus several months prior to admission. The sputum contained tubercle bacilli. The roentgenogram (Fig. 15) showed a bilateral partial ineffective pneumothorax and a markedly thickened pleura on the left side where, in addition, the picture was confused by peculiar ap-

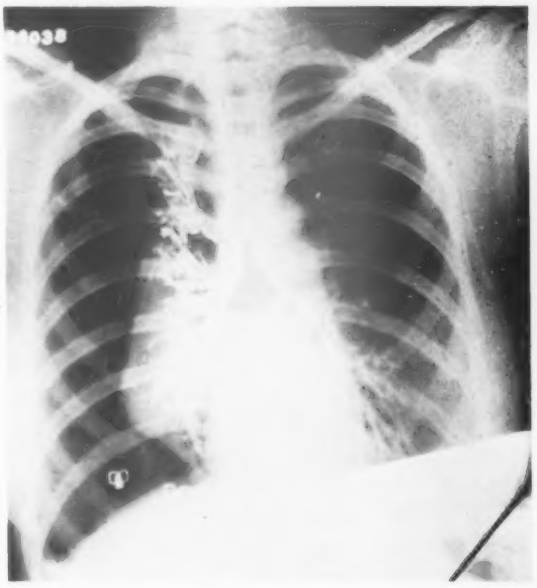

Fig. 14. Case iii. Bronchogram of same patient revealing tubular and saccular bronchiectasis of collapsed upper and middle lobes.

pearing linear shadows. The pneumothorax refills were abandoned for six weeks and at this time it was noted that some re-expansion of the

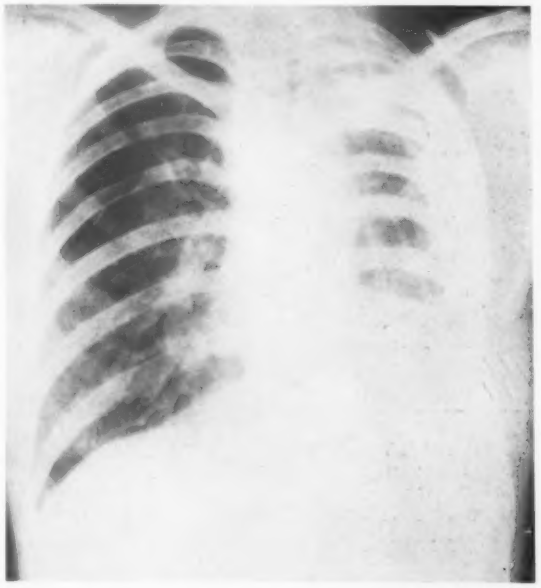

Fig. 15. Case iv. Left diaphragm and outer third of lung field obscured by diffuse density. Lung almost completely collapsed by pneumothorax and stringy densities are seen crossing the pneumothorax cavity. Partial ineffective pneumothorax confined to right upper lobe.

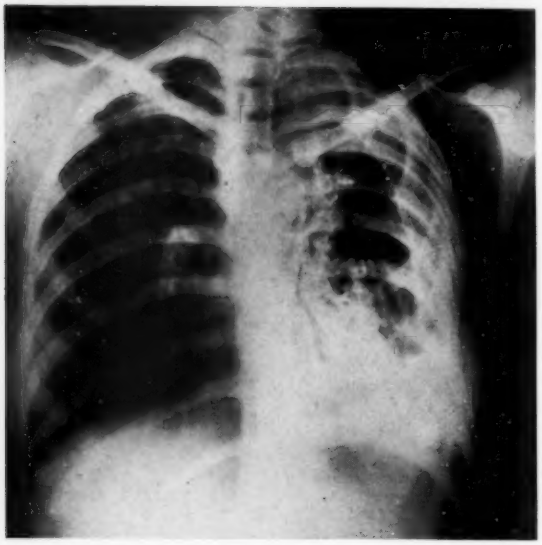

Fig. 16. Case iv. Bronchogram showing lipiodol coating the visceral and parietal layers of the pleura which are represented by dense lines crossing each other just before the bottom of the sinus is reached. Note also slight tubular dilatation of the apical branch of the upper lobe bronchus.

right lung had taken place but none of the left lung. The cause for lack of re-inflation of the left lung was not clear although it was believed to be due to a constant inflow of air into the pleural sac. In other words, a bronchopleural fistula was suspected although no shifting fluid level could be ascertained by roentgenoscopy, nor did the patient expectorate pus at this time. Under ordinary circumstances we inject into the pleural space either gentian violet or methylene blue to convince ourselves of the presence of a bronchopleural connection. In this case, however, we wished to dissociate the various densities and to gain some idea of the bronchopulmonary changes. The bronchogram (Figs. 16 and 17) clearly delineates the lung substance and shows, contrary to expectations, surprisingly little bronchial dilatation. Furthermore, by this means not only is the impression of the presence of a bronchopleural fistula confirmed, but, in addition, a dissociation of the various densities is obtained and the empyema sinus nicely demonstrated.

Fig. 17. Case iv. Bronchogram, lateral view.

Dissociation of Encapsulated Pneumothoraces from Pulmonary Cavities

In a previous article[3] one of us has alluded to the importance of differentiating ring shadows produced by encapsulated pneumothoraces, thin-walled cavities within which there are lung markings of the same density as those surrounding the ring and emphysematous blebs. We wish to stress this importance by presenting the following case:

Case v. H. M., No. 8783, white female, aged thirty-nine, admitted April, 1933, complaining of loss of weight and strength, and productive cough. Examination revealed a fibrocavernous process in the right upper lobe with retraction of the trachea and upper mediastinal structures to the affected side. As seen in Figure 18, the roentgenogram also showed a peculiar linear density which merged at the base with what appeared to be a straight fluid level. The sputum was positive. Pneumothorax was established and resulted in a marked reduction in cough and expectoration and a negative sputum by December of the same year. Figure 19 represents the roentgenogram taken at this time and, while it shows an effective collapse of the upper lobe cavity, it also reveals a large tubular rarefied shadow which aroused discussion. Is it a cavity or an encapsulated pneumothorax? Shall the lung be further collapsed or shall we assume that the compression is effective? The bronchogram (Fig. 20) answers these questions

by convincing one that the large rarefied shadow was a cavity as evidenced by the lipiodol level within it and furthermore brought to light unsuspected superimposed bronchiectasis of the lower lobe. Interestingly enough, a positive sputum was again obtained later on as the pneumothorax was increased. Final obliteration of the cavity was achieved by supplementary phrenicectomy.

A still more striking example is that of the following case:

Case vi. G. K., No. 8778, white male, aged twenty-two, who was admitted from another

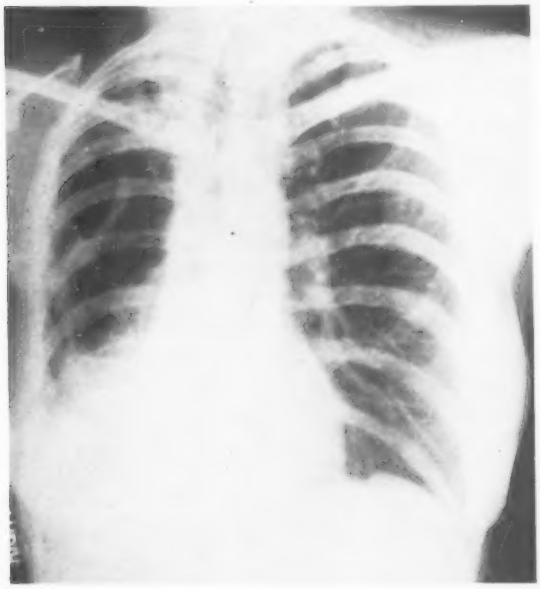

Fig. 18. Case v. Mediastinal structures drawn to the right side and the right lung shows a fibrocavernous process in the upper lobe. A peculiar linear density is seen coursing the lung field from clavicle to ninth posterior rib where it joins with what appears to be a straight fluid level. The base of the lung and the diaphragm are obscured by a homogeneous opacity.

hospital where he had received pneumothorax for fifteen months. He was well nourished, afebrile, and tubercle bacilli were found in the sputum. The roentgenogram (Fig. 21) showed a hydropneumothorax on the right side with the collapse confined to the lower and middle lobes and a moderate-sized cavity below the clavicle in the unaffected upper lobe. At surgical conference it was decided that the cavity was to be attacked by thoracoplasty while the remainder of the lung would be allowed to re-

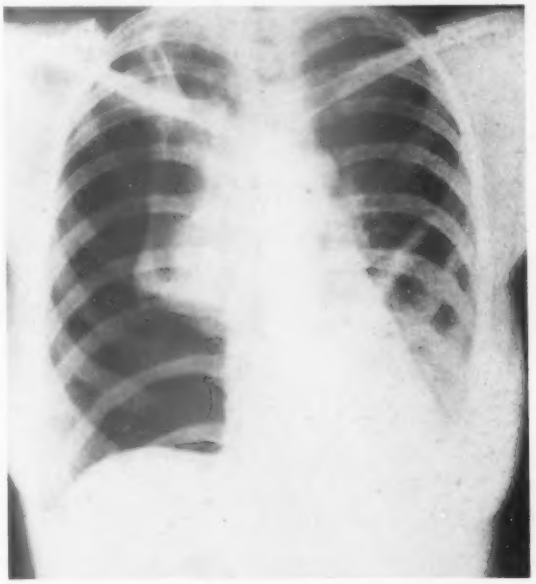

Fig. 19. Case v. After artificial pneumothorax had been initiated. Note that the lung is suspended to the apical pleura by adhesions and presents a tubular rarefied shadow which might be taken for encapsulated pneumothorax.

expand. The question arose, however, as to whether there was only one cavity seen in the first interspace or many as indicated by the

Fig. 20. Case v. Bronchogram reveals a lipiodol level within the tubular density, thus proving cavity. In addition is seen marked tubular and saccular bronchiectasis not suspected in the plain film.

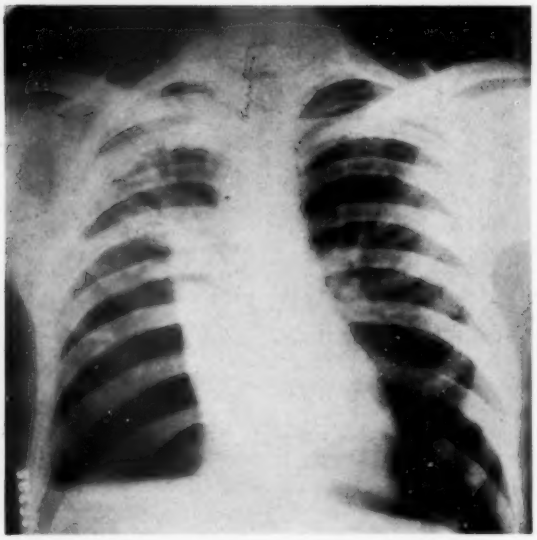

Fig. 21. Case vi. Roentgenogram shows a hydropneumothorax on the right. The right upper half of the lung field is not collapsed because of an obliterative pleurisy. Within the uncollapsed portion of the lung there are numerous very small rarefied areas in the first interspace.

numerous high light shadows about it. The bronchogram (Fig. 22) not only proved the nature of the numerous rarefied densities about the cavity but revealed unsuspected cavity in the second interspace. As a result of this finding the operation was replanned to include more extensive surgery.

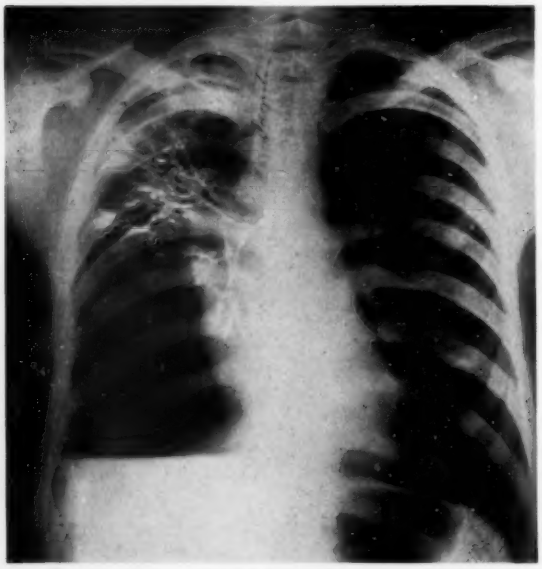

Fig. 22. Case vi. Bronchogram outlines a large annular shadow within which is a lipiodol level situated in the second interspace immediately beneath the pleura. While cavitation was thought to be present in the plain film in the first interspace none was suspected in location outlined by the lipiodol.

following thoracoplasty

It is an accepted observation that inflammatory changes in the pleura and collapse of the lung which follow thoracoplasty may produce roentgen densities over the operative field which either mask the pulmonary markings or make their differentiation from shadows cast by extrapulmonary structures impossible. Tubular to oval shaped rarefied areas may be encountered in the partly collapsed lung; and these, unless defined, may leave one in doubt as to the effectiveness of the thoracoplasty, especially when expectoration, though reduced in quantity, persists. The two case histories which follow may clear the point in question.

Case vii. W. B., No. 7653, colored female, aged sixteen, admitted in 1929 with all the symptoms of tuberculosis, a positive sputum, and roentgen evidence of a bilateral exudative process with cavitation in the right upper lobe. On bed rest she progressed very satisfactorily. In 1932, when we saw her, she was afebrile, on partial exercise, well nourished, and complained merely of a morning cough, productive of sputum in which tubercle bacilli were found. The roentgenogram (Fig. 23) at this time showed a fibrocavernous lesion in the right upper lobe, with pleural thickening over the lower lung field and deviation of the mediastinal structures to the affected side. The left lung was relatively clear except for some fibrous strands in the region of the first and second intercostal branches. A thoracoplasty was performed in December of the same year (Fig. 24) resulting in an effective collapse of the cavity. Although the sputum persistently failed to show tubercle bacilli postoperatively, the plain film did show rarefied shadows in the partly collapsed lung in the region below the operative site and there was a persistence of 30 c.c. of mucopurulent sputum daily. A third stage thoracoplasty was recommended, but because of difference of opinion, a bronchogram was made which revealed extensive saccular bronchiectasis, thus accounting for the

Fig. 23. Case VII. Fibrocavernous lesion right upper lobe and deflection of mediastinal structures to affected side. Diaphragm obliterated by thickened pleura.

Fig. 24. Case VII. Same patient following two stage thoracoplasty. Cavity obliterated and trachea somewhat straightened. High light shadows seen, however, in lower lobe.

roentgen densities and the sputum (Fig. 25). The patient is doing well and sputum still fails to show tubercle bacilli.

The next case exemplifies residual widened bronchial shadows situated directly within the lobe where cavity was present preoperatively.

Case VIII. E. E., No. 9289, white female, aged eighteen, readmitted to the sanatorium in January, 1934, complaining of productive cough and slight loss of weight. Examination revealed an effective pneumothorax collapse of the right upper lobe which had been compressed for several months. In the left lung was found a fibrocavernous infiltrate confined

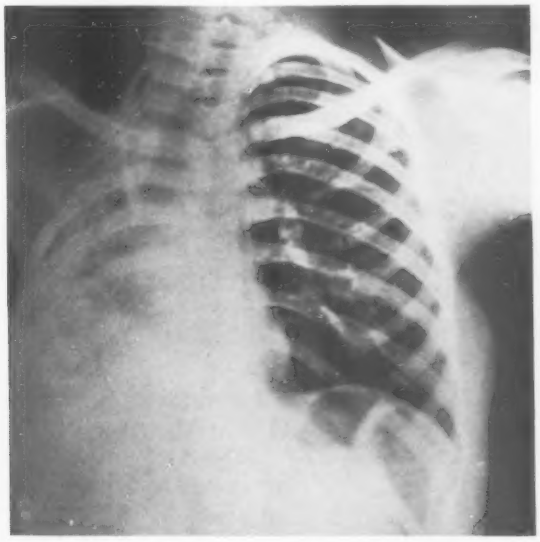

Fig. 25. Case VII. Bronchogram. Note marked saccular bronchiectasis of radicles of upper, middle and lower lobe bronchi, particularly of latter.

Fig. 26. Case VIII. Fibrocavernous infiltrate in left upper lobe and deflection of mediastinal structures to the same side. Also note encapsulated effusion at level of second interspace.

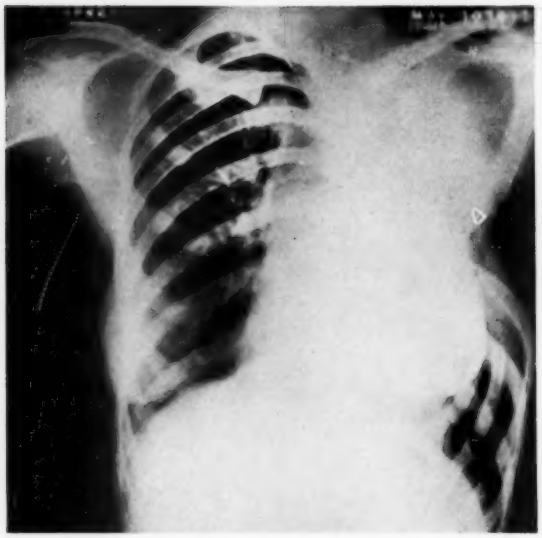

Fig. 27. Case VIII. Same patient following a two stage thoracoplasty. Upper two-thirds of lung field obscured by opacity caused by pleurisy and collapsed lung tissue.

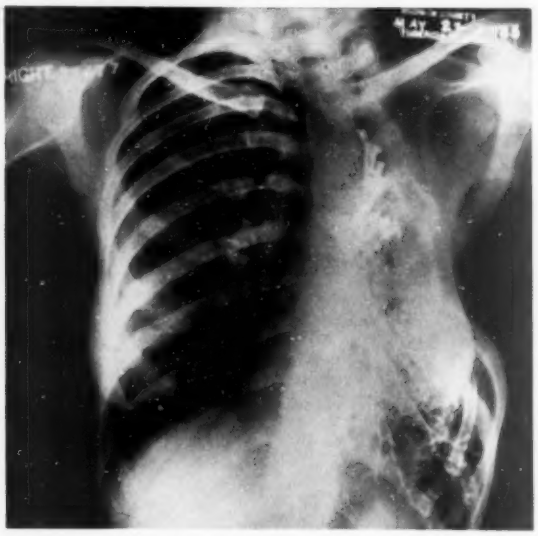

Fig. 28. Case VIII. Bronchogram shows effective collapse of left upper lobe and residual tubular bronchiectasis of radicles of upper lobe bronchus.

to the upper lobe with retraction of the trachea and mediastinal structures to the same side. After a careful review of the history and the roentgenograms on her previous admissions, it was decided to abandon the pneumothorax and later to perform a thoracoplasty on the left. After complete re-expansion of the right lung had taken place (Fig. 26) a two stage thoracoplasty was performed on the left and an effective collapse apparently achieved (Fig. 27). At this time the patient was free of cough but expectorated about 15 c.c. of mucoid sputum daily in which no tubercle bacilli could be found. The plain roentgenogram, as can be seen in Figure 27, showed a dense opacity over the entire upper half of the left lung field obscuring the underlying lung markings. A roentgenogram made using the Potter-Bucky diaphragm still further confused the picture in that it showed tubular rarefied densities in the partly collapsed left upper lobe which were thought by some to be due to residual cavity. The bronchogram (Fig. 28) very clearly shows the degree of collapse and its effectiveness and, in addition, demonstrates residual bronchiectasis which adequately accounts for the sputum.

CONCLUSIONS

Other indications for bronchography in pulmonary tuberculosis have been amply discussed and illustrated in a previous publication.[3] In conclusion, it need merely be stressed that the plain roentgenogram, even when supplemented by Potter-Bucky and stereoscopic films, or films at various angles, fails in many instances to convey a clear picture of the existing pathologic changes. Under such circumstances, the bronchogram serves to add the desired information which, if appreciated, leads to a more intelligent management of the disease.

SUMMARY

1. One hundred and eighty cases of pulmonary tuberculosis in which a total of 200 lipiodol injections was made are reported.

2. The safety of the procedure in inactive patients who present productive lesions is fully discussed and the innocuous complications described.

3. The indications for bronchography are grouped and illustrative cases presented under each group.

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A SURVEY OF BONE AND JOINT TUBERCULOSIS IN DETROIT MUNICIPAL SANATORIA

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DURING the past several years, it has become noticeable that bone and joint tuberculosis has gradually decreased and we became curious to know to what extent this is true in our community, so an attempt has been made to survey the cases of bone tuberculosis of which we have any records, to study, if possible, the incidence as well as the outcome of such lesions.

With tuberculin testing of cows compulsory in Michigan and pasteurization of milk before distribution, our milk supply is excellently controlled and the bovine type of tuberculosis has become a negligible factor to contend with.

TABLE I

Year	No. of Cases Hospitalized for Tuberculosis	No. of Tuberculous Bone Cases	Percentage Bone Tuberculosis
1926	665	9	2
1927	432	7	2
1928	499	11	2
1929	1317	70	6
1930	1449	62	4
1931	1377	55	4
1932	1067	73	6
1933	1029	22	2
1934	1221	18	1.5

In the series of cases which we have studied, over 85 per cent had a healed or active pulmonary lesion, so it is fair to assume that the bone and joint lesion is usually secondary to a primary focus elsewhere in the body.

This study covers the bone lesions recorded in the Herman Kiefer Hospital and the Maybury Sanatorium. These records are quite complete for the past five years, but prior to that period, there was a great deal of shifting about of these patients from one institution to another. Many were operated on at other hospitals and then sent to either Maybury Sanatorium or Herman Kiefer Hospital for further treatment, and sometimes to other hospitals, so that it has been extremely difficult to follow all the cases, as well as to make sure that all cases of bone tuberculosis have been included in this survey.

In 64,000 patients who were examined for tuberculosis in the Out Patient Department, 14,838 were hospitalized for tuberculosis. Among these, there were 445, or 2.9 per cent, who had bone tuberculosis; 337 were white and 108 colored. This indicates that of all cases hospitalized for tuberculosis, 2.9 per cent have bone and joint tuberculosis. To study yearly incidence, admissions at Herman Kiefer Hospital were recorded over a nine year period and in this time, it varied from 6 to 1.5 per cent. Nearly one-half of this number also had pulmonary tuberculosis and would be listed in the hospital as pulmonary lesions with bone and joint involvement as complications. The tuberculous lesions strictly confined to bones and joints would then be about one-half the percentage here recorded.

Since 1929, the great majority of all cases of tuberculosis have been cared for at Herman Kiefer Hospital and Maybury Sanatorium and this concentration brought about an increase in bone lesions which was more apparent than real. That is, many of the bone cases were returned and re-admitted to these city hospitals after surgical procedures elsewhere. They were not new cases, but they were new admissions and that increased the percentage for that particular year, and also the few following years, as will be found in the table showing incidence by years. The percentage of the past year will probably be more accurate in expressing the true incidence of bone and joint tuberculosis.

Why one person should develop pulmonary tuberculosis and another bone and joint disease, we do not know, except that bone and joint disease results from tuberculous nodes, either in the thorax or the abdomen, which spill into the circulation. If this is true, many other tissues in the body must also be simultaneously exposed and the weakest spot must suffer. Such a theory would explain why old surgeons found that in most cases of bone and joint disease, there was usually a history of previous injury to the bone involved which produced weakness. Again, such an injury may only have called attention to a diseased condition already present.

The fact remains that these lesions do occur entirely too often, in spite of all that has been done in tuberculosis prevention, as well as treatment. We have seen spinal lesions develop in hospital patients responding to treatment for pulmonary tuberculosis. The first sign or symptom was a localized tenderness over the area. One child with tuberculosis complained about raising his arm while having a roentgenogram of the chest made and a quite extensive tuberculous process was found in the head of the humerus. If these things are possible, it is more probable that the circulation is invaded more often than we think, and from practically any type or size of a tuberculous lesion. In support of this fact, we have but to recall the cases we have known of tuberculous meningitis, where the source of the infection happened to be a small group of mediastinal lymph nodes, first discovered at post mortem or by the roentgen ray.

Table II shows that the incidence of the disease is greatest at that period in life when physiological activity is greatest. It is in this age period that we find major and minor injuries repaired with ease and abundance, and it requires a very severe injury to incapacitate. The young person has learned to ignore minor injuries and exposes himself to them with reckless abandon. Perhaps many cases of small tuberculous lesions are also conquered or healed in this period, but there are also many who develop definite bone and joint lesions as indicated in Table II. Whatever their capacity, the dosage has been too great to overcome.

The colored population of our tuberculosis hospitals is greater than the percentage of colored population of our city and again, the percentage of bone tuberculosis is far greater than the percentage of pulmonary tuberculosis among our colored hospital patients. The colored population of our city tuberculosis hospitals is from 15 to 17 per cent of the entire number of tuberculous patients, and in this series of bone tuberculosis, we found that nearly 25 per cent of all the patients were colored.

Table II

Decades	White Males	White Females	Colored Males	Colored Females
1st	36	15	8	6
2nd	41	27	17	14
3rd	71	34	22	8
4th	43	16	15	6
5th	23	13	3	4
6th	13	1	3	1
7th	2	2	1	0
Total	229	108	69	39

This can probably be best explained by the dosage of bacilli. We believe, from this and other studies, that the colored people receive much larger doses of tubercle bacilli, through their inferior living conditions, than do the white people, and they are notoriously careless about their physical well being, which may again explain the invasion of their osseous system with tuberculosis. The response of our colored patients to treatment for bone or pulmonary tuberculosis has in no way differed from that of the white race.

The roentgen appearance of bone tuberculosis is rather constant and follows a very definite pattern by which we are able to recognize the disease. Fraser, Allison and Fisher, and Phemister and Hatcher have described the method of attack as well as

the pathology of a tuberculous joint lesion so excellently that little can be added.

We are particularly interested in the early diagnosis of the bone and joint tuberculous lesion by means of the roentgen ray, and we realize that there is a period in the earliest stages of the disease when the soft tissues only are involved and there are no definite or diagnostic roentgen findings.

To illustrate this point, we recall a child of eight years who complained of pain in the right hip joint. Roentgen examination revealed a normal bony pelvis and both femurs were alike. In a few weeks, a tremendous soft tissue swelling and tenderness had developed about the right hip joint and another roentgen examination showed complete dislocation of the femur but no bone abnormality, either in the head of the femur or the acetabulum. On opening the joint, considerable tuberculous granulation tissue was removed but no erosion or necrosis was found in either the bone or the cartilage.

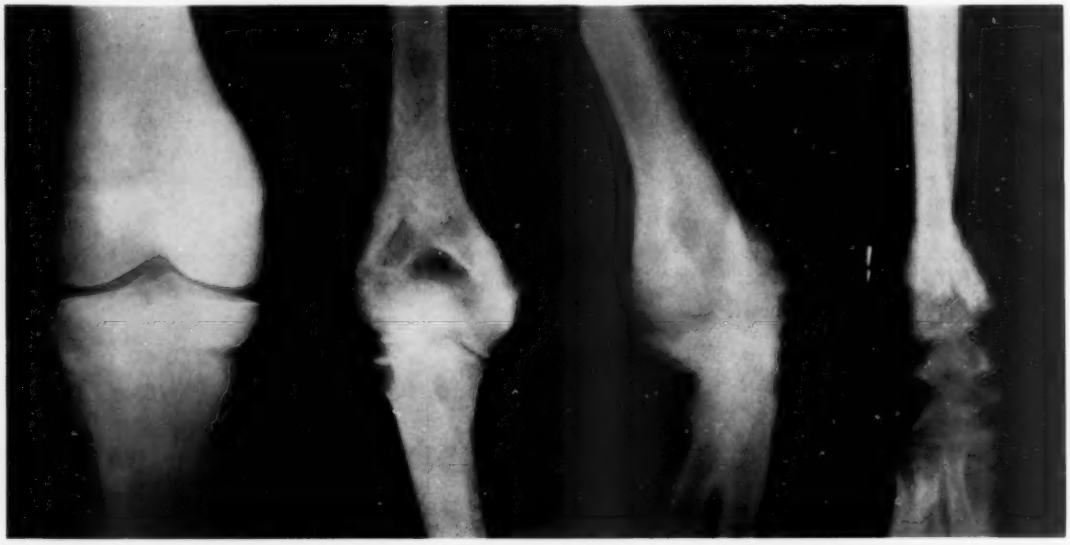

FIG. 1. Tuberculosis of the bone with mixed infection and extensive new bone formation.

If biopsy or culture cannot be obtained, it is necessary to wait until the findings are definite. The most characteristic roentgen appearance is the destructiveness of the process. Bone, cartilage and even periosteum are so completely consumed that there is no walling off or defensive process definitely demonstrable, until a mixed infection sets in. No matter how slow the process may be, the same condition obtains, namely, destruction of bone without bone production. We have observed bone lesions more or less dormant for months or even years, and then they start up with renewed vigor, until the disease has gained sufficient foot-hold to continue uninterruptedly. There may be a change in the speed of the process of invasion, but no change in the method of its attack occurs. The sensitive periosteal tissue, which produces bone with such rapidity and in such abundance in osteomyelitis or syphilis, is so completely destroyed in tuberculosis that it cannot offer any defense or produce any appreciable amount of new bone.

We have seen a number of atypical tuberculous bone lesions appearing in the shaft of the long bones, one at the middle of the radius, another in the humerus, just above the condyles and 3 cases of tuberculosis of the skull, but they all showed the same type of lesion. When a mixed infection sets in, either through a draining sinus or otherwise, the lesion may resemble other types of infection and show an abundance of bone production. We have one case of a

mixed infection of the elbow where an abundance of new bone has been deposited along the upper ulna in layers, perpendicular to the shaft of the bone. The roentgenogram shows the sun-burst type of new bone formation, such as a periosteal sarcoma might produce, but it differs from sarcoma in that it extends directly through the elbow joint to invade the humerus (Fig. 1). Cultures and guinea pig inoculation were positive for tuberculosis. In another instance with mixed infection, we have as nice a case of periosteal elevation of the serated or lace curtain type as was ever found in syphilis of the bone (Fig. 2). Here we have to rely on cultural findings for a definite diagnosis. In the cases here shown,

Fig. 2. Tuberculous lesion in lower femur with definite periosteal elevation. This is not commonly found in tuberculous bone lesions.

Fig. 3. Tuberculous lesion of the skull with typical punched out appearance due to bone destruction.

we have positive laboratory findings to support the diagnosis of tuberculosis (Figs. 3, 4, 5, 6, 7, 8 and 9).

Tuberculosis shows a preference for spongy bone and especially the vertebral column. More than half of our entire series showed spinal involvment. The intervertebral disc is usually attacked first and a narrowing of the joint space is the first roentgen finding. Any other type of infection may destroy the intervertebral disc, but in tuberculosis we have the characteristic absence of lipping or bone deposits. The body of the vertebra is next involved by direct extension from the disc, and coincident with destruction of bone there is always a crushing, with the characteristic tuberculous kyphosis. This again illustrates the thoroughness with which the disease consumes the bony tissues in its path. Metastatic carcinoma of the spine may also destroy a considerable portion of the body of a vertebra, but this process does not involve the intervertebral disc and there is usually enough bony tissue left, even after extensive involvement, to maintain the shape of the body and prevent any collapse or production of kyphosis. Fractures of the vertebral bodies often produce crushing and may be difficult to differentiate. In a fracture, there is always a history of injury and the lines of fracture can usually be demonstrated.

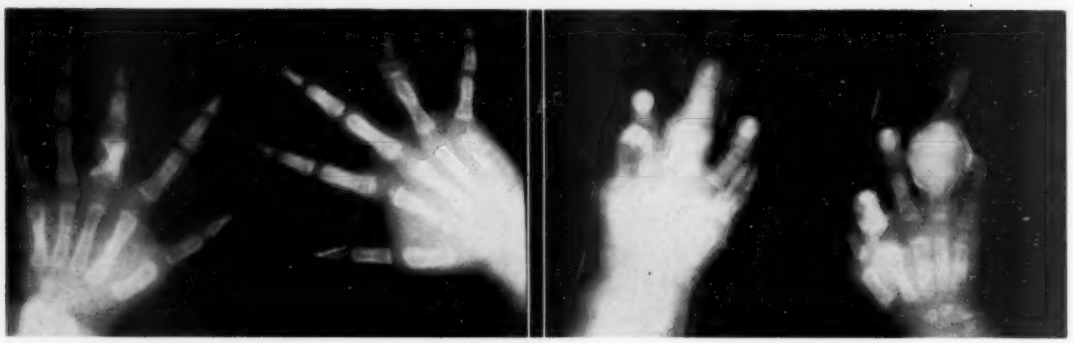

Fig. 4. Tuberculous dactylitis showing the acute stage and the final result after healing.

We have often observed more than one segment of the spine involved simultaneously in the same person, with one or two unaffected vertebral segments intervening, and no other skeletal evidence of tuberculosis, again showing that the spine is indeed a favorite site.

	Cases
Tuberculosis of spine	256
Tuberculosis of hips	108
Tuberculosis of knee	47
Tuberculosis of ribs	27
Tuberculosis of ankles	17
Tuberculosis of fingers	15

Fig. 5. End-result in extensive tuberculosis of the lower jaw. Diagnosis verified by culture.

The location of all the lesions in the order of their frequency is as follows:

Fig. 6. Multiple tuberculous lesions in the spine.

Tuberculosis of elbows	14
Tuberculosis of toes	7
Tuberculosis of wrists	6
Tuberculosis of sternum	6
Tuberculosis of shoulders	6
Tuberculosis of pelvis	6
Tuberculosis of clavicles	4
Tuberculosis of jaws	3
Tuberculosis of skull	3

FIG. 7. Healed tuberculous lesion of the ilium. Diagnosis verified by culture.

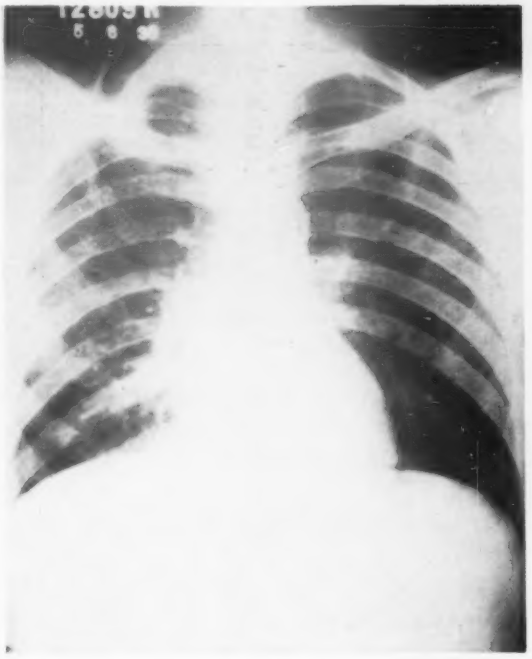

FIG. 9. Tuberculous abscess of second rib on the right, followed by miliary tuberculosis in the lungs. Patient died.

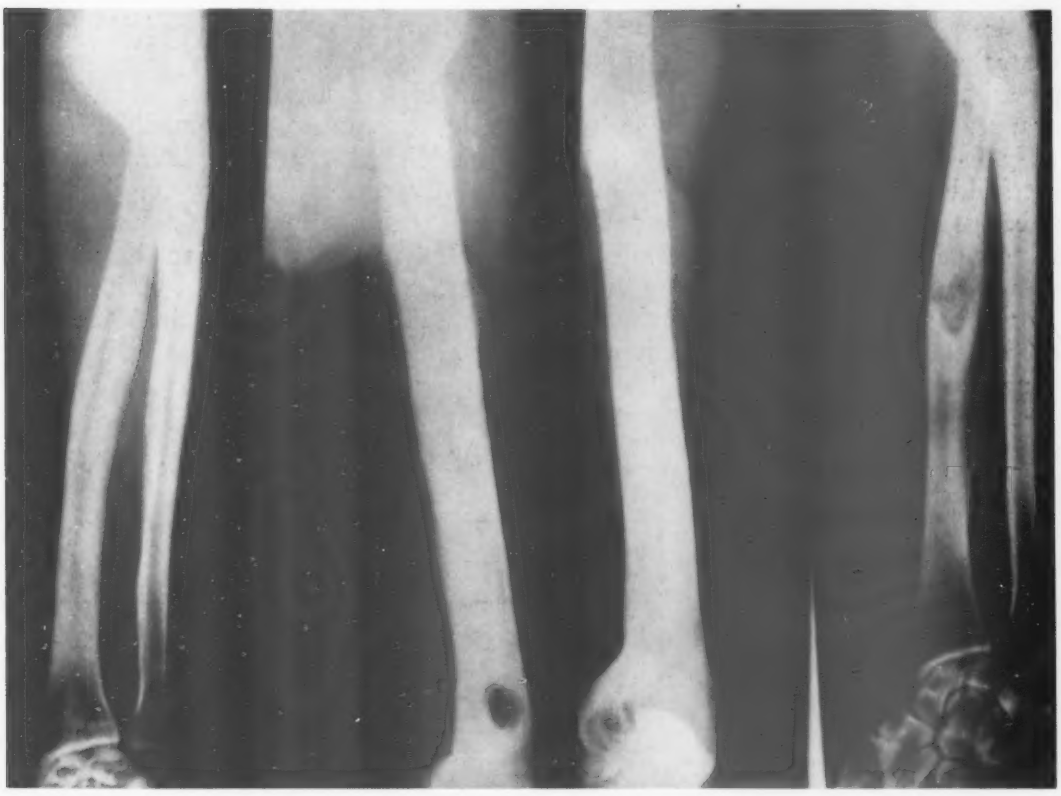

FIG. 8. Cystic type of tuberculous lesion in the long bones. Diagnosis verified by biopsy.

Table III

Location of Lesion	No. of Cases	Operated	Home		Hospital		Dead
			Well	Improved	Improved	Unimproved	
Spine	256	137	120	20	32	6	78
Hips	108	68	77	11	1	6	13
Extremities	84	48	41	2	21	4	16
Flat bones	50	11	16	4	5	3	22
Multiple bone lesions	53	12	9	6	14	1	22

There were 53 cases having multiple bone involvement and nearly all of these had also an active and often far advanced pulmonary lesion, so that no treatment other than the time-honored bed rest could be given.

The tuberculous lesions found in the flat bones, such as the skull and pelvis, were rounded, punched out areas of bone destruction with indistinct or fuzzy outlines, and not in any instance did they occur at or near joints, as in other bones. In the ribs, they appeared anywhere, with a predilection for the costochondral junction.

One colored patient came in with a small rib abscess, near the axillary line, and in a few weeks he developed a miliary pulmonary tuberculosis from which he died. At entrance, he showed clear lungs and the rib abscess was small and solitary, but it must suddenly have spilled a tremendous number of bacilli into the blood stream to produce the extensive generalized infection from which he died.

In the bones of the hands and feet, the shaft is attacked first and if the joints of the metacarpal and metatarsal bones as well as the phalangeal joints are involved, it is usually by direct extension from the shaft. Why this is so, we are unable to say. It is probable that some difference in the vascular supply of these joints protects them, in a measure, from the common frequency with which other joints are involved.

A cystic type of bone tuberculosis has been described but we found only one such case outside of the flat bones and it is easily conceivable how a very slowly progressing bone lesion may assume such an appearance at some period in its progress.

In the treatment of bone tuberculosis, it is well to keep in mind the virulence of the process, and the safest procedure would probably be to excise the lesion, provided its location makes this possible. Rest and immobilization are usually not sufficient but nevertheless perhaps all that can be done as the patient may not tolerate any surgical procedure. Treatment with maggots has lately been used with some success but is often not applicable. We have experimented with superficial roentgen therapy but we are not as yet prepared to

Table IV

Pulmonary Disease	No. of Cases	Home		Hospital		Cases Lost	Deaths
		Well	Unimproved	Improved	Unimproved		
I	48	24	0	12	1	2	9
II	30	9	0	8	2	0	11
III	73	4	3	9	8	2	47
Childhood	26	14	1	4	0	0	6
Pleurisy	33	12	2	4	1	0	14

make any statement as to the results. The plan at present is to give all surgical assistance which the patient can tolerate. Only about half of the patients studied in this series are at present home and well and another 15 or 20 per cent are on the improved list at home and in hospitals, but nearly 30 per cent of the entire series are already dead. Most of them died from generalized tuberculosis, meningitis or pulmonary tuberculosis.

SUMMARY AND CONCLUSIONS

1. The incidence of bone tuberculosis is undoubtedly on the decline due to early recognition of the pulmonary condition and prevention of spread to the bones from the extensive pulmonary disease.

2. A noticeable and almost outstanding fact is the high percentage of colored patients in the group studied and this, we believe, is due to the larger doses of tubercle bacilli received by the colored race because of their inferior living conditions.

3. There is a very high mortality rate in bone and joint tuberculosis which may, in a measure, be explained by the fact that nearly one-half of the entire number studied in this series had an active pulmonary lesion as well as the bone lesion.

The fact remains however, that bone tuberculosis is a serious lesion, and either directly or indirectly brings about a very high mortality rate.

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CHOLECYSTOCOLIC FISTULA*

CASE REPORT

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THE American literature reveals very few references to cholecystocolic fistula. The following case is presented because of the rarity of the condition and because of some interesting features of the case.

CASE REPORT

E. P. L., white female, aged sixty-two, was admitted to the hospital on February 27, 1935,

FIG. 1*a*. Barium-filled colon showing pocket of barium above first portion of transverse colon. The colon is slightly narrowed below and lateral to this small collection.

on the service of Dr. F. A. Erb. She complained of excruciating pain in the right hypochondrium and was vomiting frequently. She was moderately jaundiced and there was generalized abdominal tenderness, more marked in the right upper quadrant where there was also some rigidity. Her temperature was 103°F., pulse 130, and blood pressure 155/60. Her white blood count was 19,700 with polymorphonuclear leukocytes predominating.

The patient had suffered for more than twenty years from attacks which were typical of gallbladder disease. She stated, however, that the present attack was definitely of a different nature than all those preceding. The pain was more intense, of a sharper character, and did not radiate.

Roentgenograms were made of the chest and abdomen on the day of admission. The chest film showed no evidence of abnormality except for a large substernal thyroid. The film of the abdomen showed no abnormality of the urinary

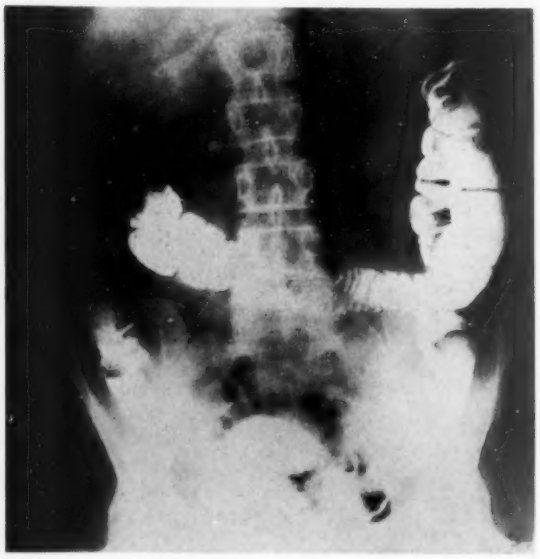

FIG. 1*b*. Same, after evacuation of the enema.

tract. There was no evidence of calcified gallstones and no evidence of intestinal obstruction. There were innumerable, small, calcified densities in the spleen. There were no other pertinent findings in the history or physical examination.

Subsequent Course. On the day after admission, the patient's pain became most marked in the lower abdomen. Her temperature varied from 99°F. in the morning to 102°F. in the evening. During the hospital stay her tempera-

* From the Abbott Hospital, Minneapolis, Minnesota.

ture and abdominal discomfort decreased and the jaundice which was present on admission subsided almost completely. The white blood count gradually fell to 10,200.

On March 9, 1935, roentgen examination of the gallbladder after the administration of dye showed loss of gallbladder function by its failure to concentrate the dye. Gastrointestinal examination four days later revealed a normal stomach and duodenum and a normal distribution of the meal at six hours (ascending colon and lower ileum). A barium enema was administered under roentgenoscopic control and

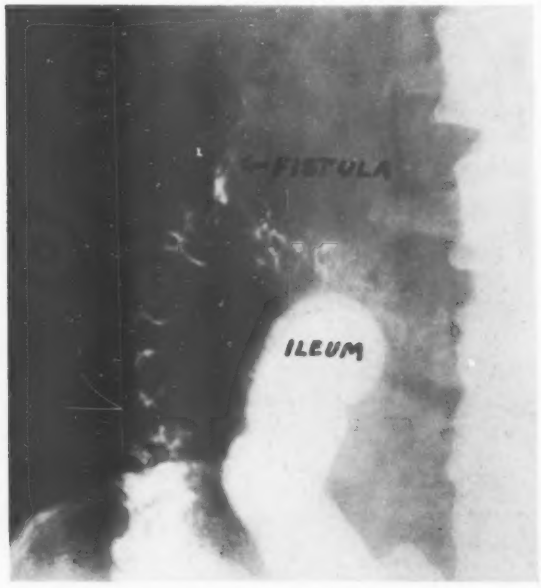

FIG. 2. Second examination showing fistulous tract and change in mucosal topography of the colon.

films were made on March 14, 1935. The only finding of interest was noted just distal to the hepatic flexure. At that point the mucosal pattern of the colon was interrupted and a small pocket of barium collected about an inch above the first portion of the transverse colon. No connection between this pocket and the colon could be traced either roentgenoscopically or on roentgenograms made before and after the evacuation of the enema (Figs. 1*a* and 1*b*). Accordingly, after more careful preparation of the patient, the examination was repeated. At this time a definite fistulous tract, extending upwardly and slightly toward the midline, was demonstrated, although the pocket in the gallbladder region was not filled as it was on the preceding examination. This is best illustrated on the film made after evacuation of the enema on which the alteration of the mucosal relief can also be well seen (Fig. 2). The diagnosis of cholecystocolic fistula was made.

On March 19, 1935, cholecystectomy was performed by Dr. A. E. Benjamin. The gallbladder was small and its walls were markedly thickened. It contained one large cholesterin stone. It was deeply imbedded in dense adhesions which extended to the hepatic flexure and transverse colon. The fistula was closed and a drain was inserted. The patient's fever increased steadily after the operation until 1 A.M., March 21, 1935, when it reached 108°F. and the patient died.

An autopsy was done and the conclusions from the autopsy protocol (Department of Pathology, University of Minnesota) are as follows: (1) chronic cholecystitis and cholelithiasis; (2) fistula between gallbladder and colon; (3) peritonitis; (4) fatty metamorphosis of the liver; (5) obstructive jaundice; (6) substernal thyroid, adenoma; (7) healed miliary tuberculosis of the spleen.

COMMENT

The roentgen diagnosis of cholecystocolic fistula is very rare. Internal biliary fistulae are not very uncommon. They occur most frequently between the gallbladder and duodenum, in which case the diagnosis is made not infrequently after impaction of a gallstone in the gastrointestinal tract. More rarely a fistulous tract may develop between the gallbladder and colon, the stomach, or even a bronchus. Such cases are observed much more frequently by the surgeon and the pathologist than by the roentgenologist. This is because the patient's condition is often so grave that the necessary roentgenologic procedures cannot be carried out and also because the findings which give the diagnosis can easily be overlooked if the possibility of such fistulae is not kept constantly in mind.

In this case the diagnosis was obvious as there was an unusually well-outlined tract and the involvement of the wall of the colon at the fistulous opening was clear cut. In many cases of fistulae between the gallbladder and gastrointestinal tract the bile passages are outlined with air. Indeed, in

some cases air in the bile passages is the only definite sign that the condition exists. Even knowing the diagnosis, close inspection of all films in this case fails to disclose that sign. It seems strange that the barium suspension would flow into the tract which gas did not penetrate, but it is probably a matter of relative pressures.

Judging from this patient's history, it seems likely that the fistula was newly formed. This is suggested very strongly by the history of long-continued attacks of gallbladder disease, with intervening periods of good health ending in an unusually acute attack of pain and fever differing from all the other attacks. It seems reasonable to assume that pain, different in nature from the pain usually associated with gallbladder disease, would be present at the time of formation of a fistulous tract.

Carcinoma sometimes gives rise to biliary fistulae, but here it was ruled out by surgical specimen and post-mortem examination. Infection, alone, could undoubtedly be responsible for a fistula. Here, however, the factors of infection and stone can be blamed for the origin of the condition. It is likely that the stone found at operation or a companion to it, which had perforated the gallbladder and colon walls, was largely responsible.

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TREATMENT OF SUBACROMIAL BURSITIS BY ROENTGEN IRRADIATION*

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CODMAN'S original description[1] of subacromial bursitis was published in 1906. He gives therein the first accurate anatomical description of the subdeltoid and subacromial bursa. The disease, subacromial bursitis, is usually designated by his name. He stated that "It is not too much to assume that this bursa, like any other bursa, in response to the insult of trauma, overuse, unaccustomed uses, following severe treatments or operation in that region, or infection, may become inflamed; may become overdistended with fluids; may be filled with fibrinous exudate; or its contiguous surfaces may become adherent."

Since his original paper Codman has published numerous communications[2,3,4] on this subject, and many others have contributed to its literature. There are those who believe that the symptoms usually ascribed to subacromial bursitis are really due to disease in the sheath of the tendons attached to the greater tuberosity of the humerus rather than to disease of the bursa itself.

ETIOLOGY

Many causes have been attributed to the disease but the etiology is obscure. For many years it was believed that trauma was an important cause but actual experience does not support this view. It may be, however, a contributing factor in some cases. Over-use or unaccustomed uses, irritation due to occupation, focal infection, infection of the bursa proper, endocrine disturbances, particularly the parathyroid, and even metabolic disturbances have been mentioned as causative agents. It is evident, however, that there is no one definite cause of this disease.

PATHOLOGICAL ANATOMY

The disease may be divided arbitrarily into three stages designated by Codman as acute or spastic, subacute or adherent, and chronic. In our opinion, there is no sharp line of demarcation between the subacute and chronic stages—the two stages seem to merge into one another. If the patient has had an acute attack which has subsided and another attack or recurrence with the same symptoms on the same side, occurring within a short period, say, from two to four weeks, this second attack may be called subacute, for while it gives all the symptoms of the acute stage, they are usually not as severe. According to Codman's concept of the pathological condition, it is during this stage that adhesions form in the bursa between the roof and the floor. There is no unanimity of opinion on the pathology of this disease. Many authorities believe the bursa does not even enter into the reaction but rather that the disease is due to a lesion in the supraspinatus tendon and not in the bursa proper.

SYMPTOMS

Symptoms of subacromial bursitis vary with different patients. Whether calcareous deposits are present or not, the clinical picture is much the same. In the main, we may say that the chief symptoms are: (1) severe pain in the shoulder joint of varying degrees of severity, radiating to the neck, arm, forearm and even to the fingertips. The pain suggests brachial plexus distribution, is usually accentuated at night and may even cause nausea; (2) limitation of motion in varying degrees. Posterior and external movement of the arm are markedly restricted; (3) there is usually a point of exquisite tenderness in the region of the

* From the Radiologic Clinic of Drs. Groover, Christie and Merritt.

TABLE I

Name	Sex and Color	Age	Onset and Symptoms	Roentgen Examination	Treatment	Results
N.F.H.	M.W.	34	No history of trauma. Sudden severe pain in left shoulder joint radiating down to the elbow. Marked limitation of motion with a point of tenderness at about the greater tuberosity of the humerus	No evidence of any abnormality of the left shoulder joint	350 r 1 exposure	Increase of pain first twenty-four hours after treatment. Then gradual relief. Well 4 days after treatment. Has been well for past five years. No recurrence
O.G.D.	M.W.	49	No history of trauma. Severe pain in right shoulder joint radiating down to the finger tips. Marked limitation of motion. Point of exquisite tenderness over the acromion process	No evidence of any abnormality of the right shoulder joint	350 r 2 exposures	Increase of pain first twenty-four hours after treatment with gradual diminution of pain. One week later patient still had some pain though markedly decreased. Limitation of motion not so marked. Patient gradually improved after second treatment. Well for last 3 years. No recurrence
J.C.H.	M.W.	72	No history of trauma. Severe pain in left shoulder joint with marked limitation of motion. Point of tenderness over the acromion process	Negative	350 r 1 exposure	No relief one week after treatment. Limitation of motion remained as before treatment. Patient did not return
W.S.S.	M.W.	62	No history of trauma. Severe pain in left shoulder joint. Marked limitation of motion. Pain radiating down to about the midarm and up into the neck. Point of exquisite tenderness over the greater tuberosity of the humerus	Negative	350 r 1 exposure	A great diminution of pain though the pain had not completely stopped. Increased motion of arm
I.F.H.	M.W.	44	No history of trauma. Severe pain over the entire left shoulder girdle radiating to neck and forearm. Marked limitation of motion. Point of exquisite tenderness over greater tuberosity of the humerus	Shows a calcified deposit in the region of the left subdeltoid bursa	350 r 1 exposure	Five days after treatment patient noticed marked decrease in pain and increased motion. Two weeks later patient was entirely well with no recurrence and has been well for the past 22 months
H.B.S.	M.W.	39	No history of trauma. Severe pain in right shoulder joint. Marked limitation of motion. Point of exquisite tenderness at about the acromio-clavicular junction	Shows a calcified deposit in the region of the right subdeltoid bursa	350 r 1 exposure	Increase of symptoms for first forty-eight hours, then gradual diminution of all symptoms. One month later patient was entirely well and has remained well for last 20 months
O.H.J.	M.W.	51	No history of trauma. Severe pain in left shoulder joint. Marked limitation of motion. Point of tenderness over greater tuberosity of humerus	Left shoulder joint shows a a calcified body just a little above the greater tuberosity of the humerus	350 r 1 exposure	One week later patient was entirely free from pain. No evidence of limitation of motion
T.L.	M.W.	60	No history of trauma. Severe pain in right shoulder joint, increasing in severity, radiating down to the forearm. Marked limitation of motion. Point of tenderness over the acromion process	Negative	Patient received some diathermy with little improvement 300 r 3 exposures	Marked improvement one week after treatment. Treatment repeated one week later—still further improvement. Third treatment 5 weeks later with complete relief of symptoms
M.K.H.	M.W.	35	No history of trauma. Severe pain in left shoulder. Marked limitation of motion with point of tenderness at the greater tuberosity of the humerus	Showed a calcified deposit in the region of the subdeltoid bursa	350 r 1 exposure	Pain increased slightly for the first twenty-four hours. Then began to subside. One week later pain was completely gone and motion was restored though not entirely. Complete motion was not regained until 3 weeks after treatment. Patient has been well now for the past year

Table I (*Continued*)

Name	Sex and Color	Age	Onset and Symptoms	Roentgen Examination	Treatment	Results
G.C.	M.W.	44	No history of trauma. Acute pain in right shoulder joint radiating down to the finger tips and into the neck, with marked limitation of motion. Point of tenderness over the acromion process	No examination made	350 r 1 exposure	One week later patient was well and has remained well for eleven months
L.W.	F.W.	35	No history of trauma. Severe pain in right shoulder joint radiating into the neck and arm. Marked limitation of motion	None	350 r 3 exposures	No improvement until third treatment. Then gradual improvement for about two months when condition became worse and all symptoms returned
W.L.G.	F.W.	56	No history of trauma. Severe pain in right shoulder joint radiating down the arm. Marked limitation of motion. Point of tenderness over the acromion process	None	350 r 1 exposure	No relief after one treatment. Did not return
M.M.	F.W.	40	History of injury—fell on left shoulder. Severe pain in left shoulder with marked limitation of motion following injury. Tenderness over greater tuberosity of the humerus	None	350 r 1 exposure	Marked improvement one week after treatment. One month after treatment patient was well. Has been well for two years
J.M.	F.W.	40	No history of injury. Severe pain in right shoulder joint radiating to the neck and down the arm. Marked limitation of motion. Point of tenderness over the acromion process	None	350 r 1 exposure	Gradual improvement until three weeks later patient was completely well and has remained well for 18 months. No recurrence
G.M.	F.W.	38	No history of injury. Severe pain in left shoulder joint radiating down the forearm. Marked limitation of motion. Point of tenderness over the acromio-clavicular junction	Shows a calcified deposit in the region of the left subdeltoid bursa	350 r 1 exposure	Increase of pain for twenty-four hours after treatment, then gradual improvement until two weeks later patient was completely well and has remained well for 17 months
J.M.	F.W.	64	No history of injury. Severe pain in right shoulder joint. Marked limitation of motion. No definite point of tenderness could be determined	Negative	350 r 1 exposure	Was not relieved at all and did not return for more treatments. Received only one treatment
R.A.	F.W.	31	No history of trauma. Severe pain in right shoulder joint. Marked limitation of motion. Point of tenderness over acromion process	None	350 r 2 exposures	Marked improvement two weeks after treatment though there was still considerable pain and limitation of motion. One more treatment was given and a month later symptoms began to decrease rapidly until patient was completely well and has been well for past 12 months. No recurrence
M.S.	F.W.	25	Patient fell down on right shoulder. Has had pain for about six months. Then had severe pain with marked limitation of motion and point of tenderness over greater tuberosity of the humerus	No evidence of abnormality	350 r 2 exposures	No relief. Two weeks later another treatment was given and patient had no relief
A.J.	F.W.	44	No history of trauma. Severe pain in right shoulder joint radiating to the arm. Limitation of motion. Point of exquisite tenderness over greater tuberosity of the humerus	Negative	350 r 2 exposures	Marked improvement. One week later another treatment was given and a week later patient was completely free of pain. Restoration of full motion. Has been well for a year
M.E.	F.W.	64	No history of trauma. Severe pain in right shoulder. Marked limitation of motion. No tenderness	Negative	350 r 1 exposure	Marked improvement one week after treatment and complete relief within one month

greater tuberosity of the humerus which may extend downward to the fingertips or upward to the edge of the acromion process.

The chronic stage gives much the same symptoms as the acute and subacute stages but they are much milder and respond much less favorably to any form of treatment. Also, they are usually of much longer duration when the patient consults the physician. The subacute and chronic stages may occur as such without a primary acute attack. In the subacute and chronic stages, the arm can be abducted to a certain degree to about where the arm forms a right angle with the body. It is at this point that the patient usually experiences the most severe pain. After that point is passed, the arm can be abducted, rotated backward and raised without such acute distress. The greatest degree of pain is again experienced when the arm, descending, returns to a position at right angles to the body. This point of most exquisite pain, at right angles to the body, is probably due to the fact that, at this angle the bursa, being thickened, is pinched between the greater tuberosity of the humerus and the acromion process of the scapula.

DIFFERENTIAL DIAGNOSIS

Subacromial bursitis is the most common ailment of the shoulder but it must be differentiated from several other diseases. If there is a history of trauma, it must be differentiated from fracture or dislocation which can be done by careful history, physical examination and roentgenography. It must be differentiated from tuberculosis, lues, cystic bone lesion, giant cell tumor, osteomyelitis, and malignancy. This also can be done by a careful history, physical examination and roentgenography. In taking a roentgenogram to locate a calcified bursa, it is advisable to take the shoulder joint in two positions: one, with internal rotation of the humerus and the other with external rotation. It is also advisable to take roentgenograms of both shoulders for the purpose of comparison.

TREATMENT

Almost every known form of therapy has been used with more or less success. The truth of the matter is that rest or mere abduction of the arm in a splint and some of the analgesics, or opiates, if necessary, to carry the patient over the acute stage, will bring about a cure in a large number of cases in from six to eight weeks. A very small percentage go into the subacute or chronic stage and the symptoms may subside and recur over and over again. We know of one case refusing treatment of any kind to have had recurrent attacks for the past twelve years.

Most surgeons and orthopedists agree that non-calcifying bursitis requires no operation (although that is not true of Codman, who believes in operation even in the second stage to break up adhesions. He has many cases to prove his point). Many surgeons and orthopedists who have written on the subject recommend the non-operative treatment in this disease even in the cases where calcareous deposits are found. Operations are resorted to only in cases where other forms of therapy have been tried for a period of months and have failed, and where the symptoms, particularly pain and limitation of motion, persist and the patient is incapacitated.

Physiotherapy has long been used in many forms[7] including convective and conductive heat, diathermy, galvanic current, sinusoidal current, ionization needle (chlorine), manipulations, all forms of massage and passive and active motion.

It must be admitted that there is no specific form of treatment. We report here cases treated by roentgen irradiation because anything that will completely stop the pain in a short time and restore the patient to his usual routine is worth considering. The economic factor in this disabling disease is of great importance. It is our experience that roentgen therapy to the affected joint relieves the pain, restores the

normal function and permits the patient to resume his normal routine more quickly than can be accomplished by any other form of treatment.

Among the many characteristic results of roentgen therapy may be mentioned its analgesic effect and its favorable influence upon inflammatory diseases whether acute or chronic. With this in mind we cautiously treated several patients affected with bursitis. As early as 1924, my associate, Dr. E. A. Merritt, treated such cases, with beneficial results. Since that time we have had sufficient experience to establish the value of this method. We also have had the opportunity to treat a series of cases with physical therapeutic measures such as conductive and convective heat, diathermy, massage, manipulation, active and passive motion, as well as a series with roentgen therapy, and we find that the latter method is by far the method of choice.

The treatment customarily given is 350 roentgens with the following factors: 200 kv., 0.25 mm. Cu filter, 50 cm. distance, 15×15 cm. field, to the anterior or posterior shoulder. (In the cases treated prior to 1929 we used 140 kv., 5 ma., 5 mm. Al filter, 15×15 cm. field and 16 cm. distance, 20 min. We find that this was practically the equivalent of 350 r.)

During the first twenty-four hours following treatment, the symptoms are somewhat aggravated and the patient feels as if the treatment had done him harm rather than good, but within the next twenty-four hours there is a marked diminution of pain and a greater ability to move the arm. In most of our cases only one treatment was necessary to completely relieve the patient of pain and restore freedom of motion. In some cases, however, two treatments were required, but in only one case were three treatments necessary.

The average age in the group of patients we are reporting is 46.3 years, the youngest being twenty-five and the oldest seventy-two. Fifty per cent were male and 50 per cent female. In all of the male cases we have no history of severe trauma. Among the females, 2 give a history of trauma. This series does not bear out the belief that sudden trauma is one of the most usual causes of this disease, but conclusions cannot be drawn from such a limited series.

In reviewing our results, we find that 3 patients were not relieved one week after the first treatment and none of these returned for further treatment. One patient was not relieved after two treatments. Another patient improved after three treatments and four months later all the symptoms recurred. The remaining 15 patients were relieved of pain in from twenty-four to forty-eight hours after treatment, and there was marked increased motion of the arm in each case. In most of the acute cases it is necessary to keep the patient quiet and some analgesics should be given to control the pain but this usually becomes unnecessary forty-eight hours after treatment.

Roentgenograms were made in 15 of the 20 cases here reported. Of these, 5, or 33 per cent, showed calcified deposits in the region of the subdeltoid bursa. One of these deposits was just a little above the greater tuberosity of the humerus. The patients with the calcified deposits were re-examined two months after treatment and in 3 cases the calcified bodies had disappeared. This, of course, may occur without treatment of any kind.

CONCLUSION

Twenty cases of subacromial bursitis (Codman's shoulder) are presented in which roentgen therapy has been employed. The results justify the belief that roentgen therapy will relieve pain and restore function more rapidly than other methods of treatment. We have treated many other cases with equally good results but only in the twenty reported here have we been able to follow up the patients for a period ranging from one to five years.

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LUNG CHANGES SUBSEQUENT TO IRRADIATION IN CANCER OF THE BREAST*

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SINCE there has been a difference in opinion among radiologists concerning the importance of changes in the normal lungs following irradiation, and since there are those who hesitate to deliver adequate irradiation to their breast cases fearing secondary lung changes, our review of 70 necropsies on cases of cancer of the breast was undertaken and the deductions from this study are reported briefly in this paper.

Of this group of 70 cases, 53 had received irradiation in some form to the chest, 11 had been treated by both roentgen rays and radium, 32 by roentgen rays alone and 6 by radium alone. Thirty-seven of these cases had radical mastectomies.

FIG. 1. Case 1. Aged sixty-eight. The only case in which fibrosis was found in an otherwise normal lung. Radium had been implanted in axilla at time of operation. No roentgen therapy.

Four had subtotal operations. A large number in this series had been operated upon and had received various types of irradiation before admission to the Jeanes Hospital. In all, nineteen different roentgen laboratories had contributed to the treatment of patients in this group. This is mentioned to justify the assumption that these cases represent a fair cross section of the irradiated breasts in this locality. A few of the patients had been treated by roentgen rays infrequently for a period of eighteen to thirty months. Others had received intensive irradiation over short periods. The filtration varied from 4 mm. of aluminum to 2 mm. of copper and 1 mm. of aluminum. Six were treated with interstitial radium in platinum needles in amounts between 10,010 and 22,680 mg-hr. At least 7 of the patients received an amount approximating 7,000 r; 4 others received more than 10,000 r to the chest wall.

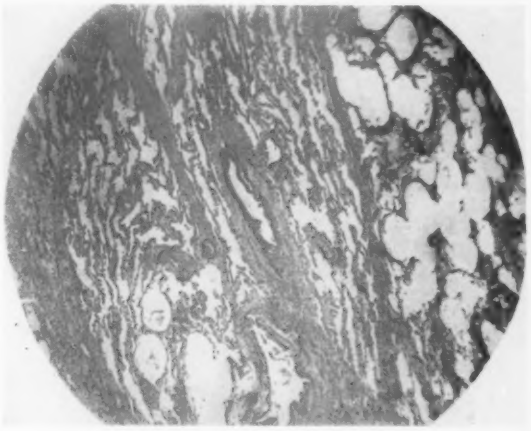

FIG. 2. Case 1. Diffuse fibrosis, involving both the peribronchial tissue and the alveolar walls. No inflammatory infiltration. ×27.

The study of roentgenograms together with the macroscopic report and microscopic sections has proved to our satisfaction that there are two distinct processes found in the irradiated chests of breast cancer patients which at times are confused: (1) transient lung changes, and (2) permanent lung changes.

(1) *Transient Lung Changes.* Groover, Christie, Merritt and Coe[1] have described

* Read before the Philadelphia Roentgen Ray Society, May, 1935.

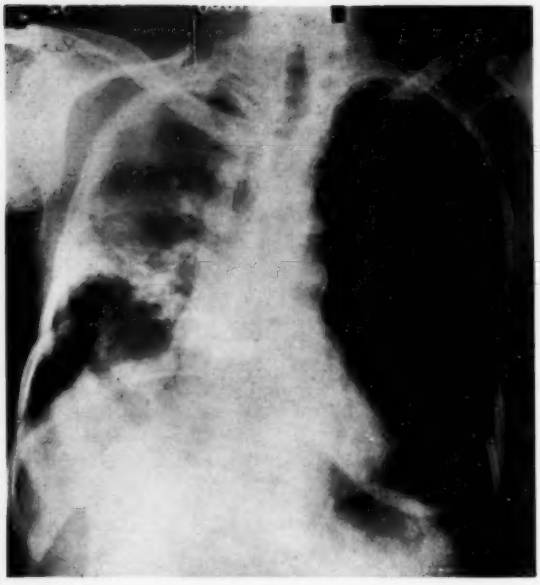

FIG. 3. Case II. Aged seventy-one. During the previous nine months 11,850 r had been delivered to the right side of chest. At autopsy no definite metastatic areas could be found. Numerous small metastases were seen microscopically.

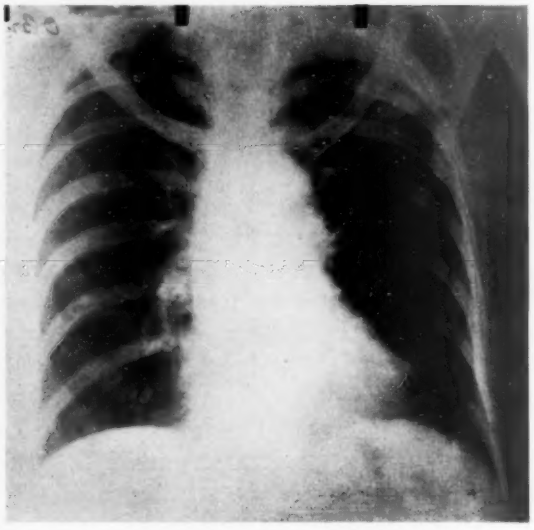

FIG. 4. Case III. Aged fifty-three. Fibrosis reported in left upper lobe. Case microscopically illustrates the Sampson-Handley theory of lymph permeation. The tumor could be traced through muscle, chest wall, parietal and visceral pleura and for a short distance into the lung parenchyma. Both roentgen and radium radiation used in this case.

in detail an acute pleuropulmonitis following heavy doses of roentgen rays to the chest. Our attention was further called to this condition by Desjardins,[2] who differentiated it from a true fibrosis. A number of authors have adequately discussed this acute pneumonic reaction. There are those, however, who continue to confuse it with a fibrosis. In this reaction, a foggy density is seen on the film, which usually extends from the hilus to the periphery of the lung. At times it is patchy in appearance and there may be distinct evidence of pleural involvement. This change

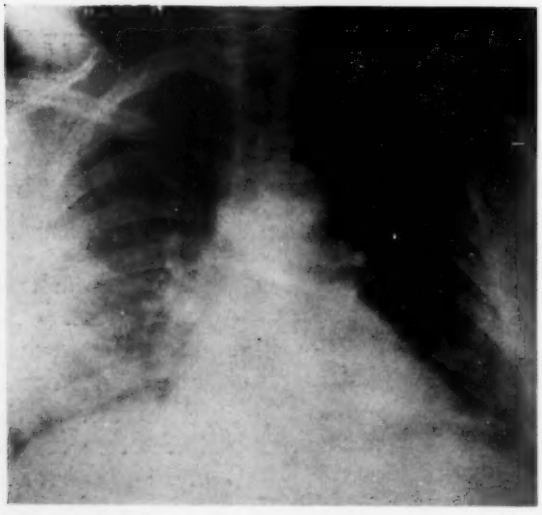

FIG. 5. Case IV. Aged fifty-six. Changes reported as fibrosis. Twenty-one monthly roentgen treatments of unknown intensity plus 3,870 mg-hr. of radium had been employed. It was only after a most careful search that cancer cells were found in a lymph space.

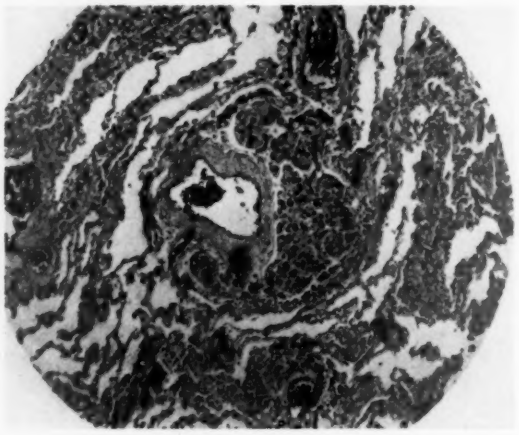

FIG. 6. Case IV. A mass of tumor cells within a perivascular lymphatic vessel. The compression atelectasis shown was due to a terminal pleural effusion. ×100.

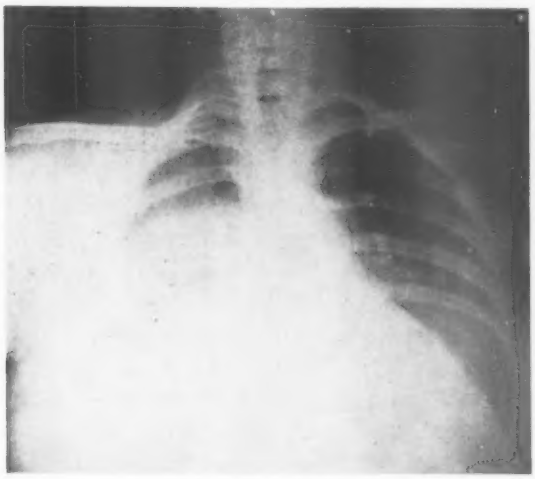

Fig. 7. Case v. Aged forty-seven. A total of 5,400 r plus 20,680 mg-hr. radium interstitially was used in five months. The carcinoma cells in this case were found in the blood vessels in contrast to the previous case. Density due largely to lymphedema.

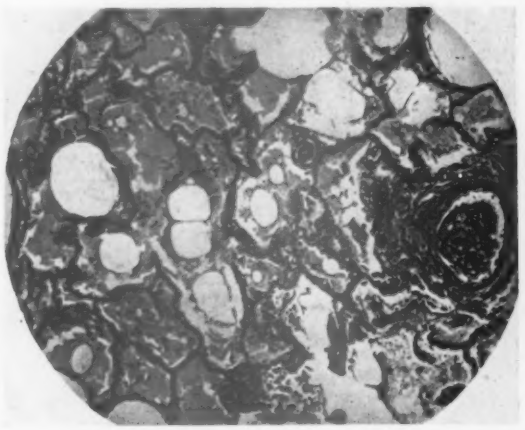

Fig. 8. Case v. Edema in lung tissue in which there were intravascular tumor masses. An artery and four small veins in this one field contain tumor tissue. At autopsy there were numerous discrete tumor nodules in both lungs. ×110.

may occur in two to eight weeks after the completion of a series of intensive treatments, but it is more often seen following a second or third series of less intensity. These findings usually begin to fade in three or four months and at the end of a year have entirely disappeared. Permanent secondary fibrosis rarely follows unless the lungs were vulnerable at the time therapy was instituted.

We have no cases which at the time of death showed a non-complicated pleuropulmonitis attributable to irradiation. An edema was found in lungs filled with metastases and with terminal pneumonia. It is reasonable to believe that the transient changes are produced by an edema in the lungs similar to that recognized in the subcutaneous tissues of the neck subsequent to massive irradiation.

(2) *Permanent Lung Changes. In only*

Fig. 9. Case vi. Aged forty-seven. The fibrosis which appeared after 10,460 r was found microscopically to be of tuberculous origin.

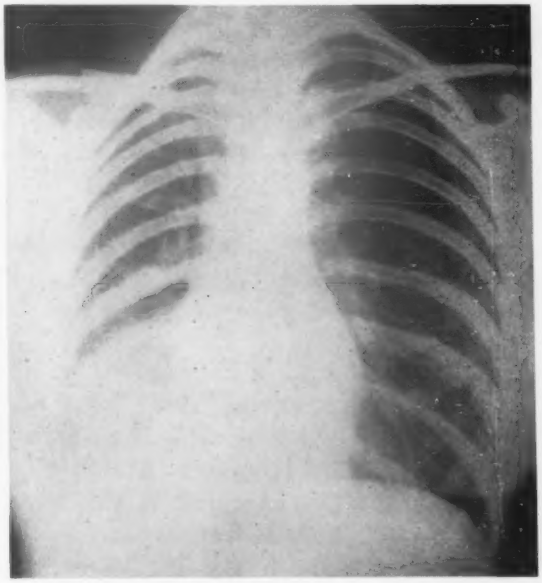

Fig. 10. Case vii. Aged thirty-one. Lymphedema following 11,200 r delivered through nine portals.

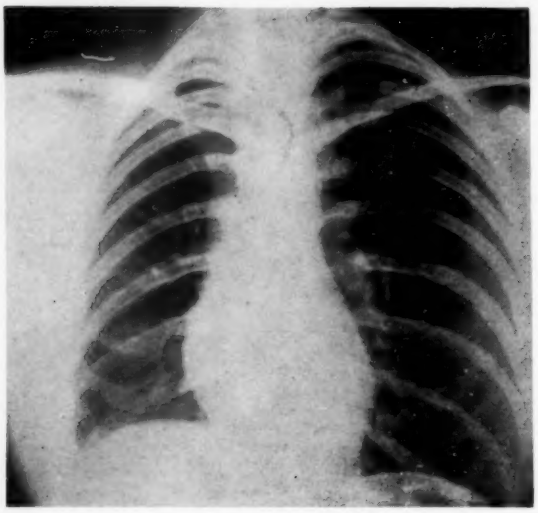

Fig. 11. Case VII. Five months later. (I am indebted to Dr. Eugene P. Pendergrass for this case.)

one case did we find a fibrosis which we believed to be attributable directly to irradiation. This case was a female, aged sixty-eight. Radium had been implanted deeply in the axilla at the time of breast amputation. There was a necrosis of the ribs, thickening of the pleura and a peripheral fibrosis of the lung which was adherent to the chest wall. No roentgen therapy had been given.

There were numerous cases in which fibrosis was found associated with metastases or with tuberculosis. Some of these were reported from the roentgenograms to be irradiation fibrosis and were not proved otherwise until careful histological studies including many sections were made of the autopsied lungs. The cause of the fibrosis was not evident macroscopically. The fibrosis seen in the metastases is so similar in some instances to that found in tuberculosis that differentiation is only possible by microscopic study.

The explanation of this similarity in appearance is found in the identity of the mechanism of invasion. Fitzwilliams and others have shown that after the axillary lymphatics have been blocked either by cancer or by surgery, the deeper lymphatic channels may convey the neoplastic cells to the anterior mediastinum or to the glands at the roots of the lungs by way of the internal mammary vessels or by way of the intercostal lymphatic vessels to the glands along the spine and posterior mediastinum. Tumor cells, therefore, permeating from these glands along the peribronchial and perivascular lymphatics may extend outward into the lung fields in the same manner that tubercle bacilli accomplish their invasion in adult tuberculosis. If irradiation is administered during this process of permeation, fibrosis results, with permanent lung change. This type of fibrosis from irradiation in tuberculosis was described in detail by Desjardins.[3]

It is likewise reasonable to assume that constitutional disease, such as arteriosclerosis, chronic infections or repeated acute infections will leave the lymphatics in a vulnerable condition in which fibrosis may result if the lungs are irradiated.

That certain patients are more susceptible to roentgen therapy than others is an accepted fact, but if an individual has an idiosyncrasy to irradiation, have we any reason to assume that the sensitivity would be specific for lung tissue and would not be manifested on the skin? If this reaction, therefore, is co-existent in the skin and if unnecessary crossfiring is avoided, the changes in the skin should parallel and be an index to the changes in the lungs.

CONCLUSIONS

The infrequency of permanent fibrotic changes in normal lungs subsequent to irradiation has been shown by this study and two distinct reactions are described:

1. A pleuropulmonitis, an edematous reaction, which is transient, usually disappearing within a year, if the lungs are otherwise normal.

2. A fibrosis, which is permanent but rarely occurs unless the lungs are previously made vulnerable by metastasis, chronic disease or infection.

I wish to thank Dr. Willard S. Hastings, Pathologist at Jeanes Hospital for his study and report on the pathological tissue.

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STERILIZATION IN CARCINOMA OF THE BREAST*†

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IT IS a well-known fact that there is a definite relationship between the activity of the ovary and the histology and physiology of the breast. It is equally well known that the parenchyma of the breast may undergo rapid growth and transformation under certain physiological conditions of ovarian activity. Taylor, in an analysis of the evidence bearing on the ovarian origin of the neoplasms of the breast, concluded that there was strong support for the theory that ovarian hormonal influences may play a large part in producing hypertrophy, hyperplasia and neoplasms in the breast.

The idea of indirectly influencing carcinoma of the breast through endocrine channels is not new. It was first brought into focus by Schinzinger at the Surgical Congress in Germany in 1889 when he suggested bilateral oöphorectomy as an auxiliary method of treatment in this disease. The same suggestion was advanced independently of Schinzinger in 1896 by Beatson in England. Believing the hormonal action of the thyroid gland on the mammary gland to be contrary to that of the ovaries, Beatson also prescribed thyroid medication in the hope of augmenting the effect of castration. Schinzinger, noting that carcinoma of the breast was more rapid and more fatal in younger than in older women, decided on castration as a means of hastening old age. Beatson, on the other hand, thought that the occurrence of carcinoma in the breast was due wholly or in part to an abnormal function of the ovaries and that the removal of these organs would therefore, at least in some cases, simply eliminate the cause of the disease. Within the next few years Beatson's results were encouraging. He noted marked improvement in some cases as shown by the shrinkage of the primary tumor and reduction or disappearance of the skin and glandular metastases. In 1902, after considerable experience, Beatson stated that oöphorectomy was justified only in cases of menstruating women over forty years of age. He furthermore specifically stated that no beneficial effect was to be expected in cases with metastatic lesions in the bones or viscera. Numerous other English surgeons followed Beatson's footsteps. Among them were Boyd, Thomson and Lett. Boyd reported a series of 54 cases, 19 of which showed improvement. Twenty-nine of a series of 80 cases collected by Thomson showed improvement. Of the 99 cases gathered by Lett improvement was evidenced in 23 per cent. When patients over fifty years of age were excluded this percentage rose to 41. Similar series of cases have been reported by Michels, Herman, Reynès and others.

Roentgen-ray castration was first tried by Foveau de Courmelles in 1904 and his first report on cases treated in this manner was published in 1909. In 1922 a summary of his 8 cases showed considerable improvement and a more rapid regression of mammary tumors in those cases which received ovarian irradiation in addition to irradiation of the tumor itself. In Germany, Meyer was the first to suggest ovarian irradiation in cases of carcinoma of the breast, and Wintz has been using it regularly as a part of the treatment of carcinoma mammae. The latter author is of the opinion that this additional procedure is of great importance. Additional work on this phase of mammary cancer has been done by Lapeyre, Frangenheim and Kaplan. The prevention of pregnancy in such cases is in itself a very important consideration, as has been pointed out by Wachsmuth, Portmann and others. It is a generally accepted fact that the course of mammary cancer in pregnant women is more rapidly fatal than in non-pregnant patients.

* From the Radiological Clinic of Dr. George W. Holmes, Massachusetts General Hospital, Boston, Mass.
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Trout, studying the effect of pregnancy after operation for carcinoma of the breast, obtained the records of 15 patients with subsequent pregnancies, during which 13 developed cancer in the remaining breast. Of the latter, 12 died very promptly. In view of such facts it is even more important that every measure which may be of definite benefit to the patient be employed.

That sterilization by roentgen irradiation should have displaced bilateral oöphorectomy in these cases is not surprising since the mortality of operation in Lett's series was 6 per cent. We are inclined to believe that there may be a distinct difference in the physiological effect of these two methods of sterilization, although we have no proof of this. The exact effects and the many phases of sterilization are as yet not well understood. Ahlbom, in a study of 163 patients who were sterilized, was unable to note any beneficial effect on the duration of life, nor has any other author been able to do this as far as we know. He did show, however, that in patients in good general condition who were sterilized by means of roentgen rays in addition to receiving direct irradiation of the tumor, there appeared to be a somewhat more rapid improvement than in those treated only by direct irradiation of the tumor. Our own experience parallels that of Ahlbom.

The position of radiation therapy in the treatment of malignancy is an important one. Often it is the only means of bringing relief to the patient and this is particularly true in those cases where metastases are widespread. Hoffman recently reported the case of a white, single female, aged forty-five, with numerous metastatic lesions in the sacrum, left ilium and pubis and also several 1 to 3 cm. painful nodules in the scalp. The pelvis was irradiated and ten months later the patient appeared much improved in health and with no evidence of disease in the breast, chest, neck or scalp. The headaches, diplopia and dimness of vision, of which the patient had complained, had also completely cleared up. Prior to irradiation of the pelvis the patient stated that her menstrual periods had been normal and regular in amount and duration. Hoffman believes this regression of the metastatic lesions may have been due to elimination of the ovarian hormone which normally produces hyperplasia of the breast tissue and which may play a part in the acceleration of carcinomatous lesions of the breast.

To attempt irradiation of each lesion in cases with widespread metastases is obviously unsound. It is not only unfeasible economically but, what is more important, the tremendous total radiation necessary to affect the metastases would seriously impair the natural defense mechanisms of the body. Our experience in such cases leads us to believe that, although some cases do not respond favorably to sterilization, a great many may be expected to show a definite improvement in some way or other. Daland recently reported a patient with multiple bone metastases whose symptoms were completely relieved by the production of an artificial menopause. Curiously enough the bone lesions began to recalcify following this procedure. Martin reports similar results in 2 of his patients. Some of our own patients have shown such results and also marked improvement in the general health, freedom from pain and a better blood picture after sterilization.

CASE REPORTS

The factors used in the treatment of these cases were: 200 kv. (peak), 4 to 20 ma.; filter 0.5 mm. Cu plus 4 mm. of celluloid; skin target distance 50 cm. The dose was measured in air. The treatments were administered in daily doses of 200 to 300 r given at one sitting. Sterilization was brought about in these cases by giving 600 to 1,200 r anteriorly and also posteriorly to the pelvis through 20×20 cm. or 15×15 cm. fields.

Case 1 (MG12555). Female, aged thirty-five. In March, 1930, simple left mastectomy for lump in breast noted six months previously.

In December, 1932, the patient began to have pain in her back. Roentgenograms showed no metastases. On February 24, 1933, cough and bloody sputum. Chest film showed lower half of the lung field dull, interpreted as collapsed lower left lobe, probably from metastases. Back pain was becoming severe. Films of the dorsal and lumbar spine showed metastatic lesions throughout the vertebrae and in the ribs. She was seen in this clinic March 4, 1933. Blood studies: red blood count 4,330,000; Hb. 75 per cent (Tallqvist); white blood count 15,800. Treatment: On account of the wide distribution of the disease it was felt that the possible good effect of any treatment would be of extremely short duration and no attempt was made to irradiate all the areas involved. Anterior pelvis 1,000 r, posterior pelvis 1,000 r, lateral left chest 1,800 r, 15×15 cm. field. Treatment was carried out with extreme difficulty because the slightest movement from bed to stretcher caused the patient excrutiating pain throughout the spine and other bones. Her weight at this time was 110 pounds. At the completion of treatment on April 3, 1933, the patient left the hospital practically free from pain. March 19, 1934—Observation: The patient appeared in excellent health and had gained 35 pounds in weight. She had no complaints whatsoever and there were no palpable masses anywhere. Films of the spine and pelvis showed a very remarkable change from the destructive to the proliferative type of lesion. White blood count 6,300, red blood count 6,100,000 Hb. 85 per cent (Tallqvist). June 21,1934—Observation: The patient was still gaining weight and had an excellent color. No palpable masses. Complains of slight weakness of the back. Little change in the spine except slight extension of metastases. September 18, 1934—Observation: Symptom-free until two weeks ago. The lesion in the left chest which had shown no change for one year, had increased in size and there was some fluid. The patient complained of slight pain in the lumbar spine. Treatment: 300 r to posterior lumbar spine over 10×20 cm. field. Complete relief of pain in forty-eight hours.

Comment. The improvement in this case is remarkable. When first seen the patient suffered intense pain and to the members of the staff who saw her appeared to be in the last stages of the disease. She improved almost immediately after treatment. There are several noteworthy things about the case. One is the change of the bone metastases throughout the entire skeleton from the osteolytic to the osteosclerotic type. Another feature is the gain in weight and improved blood picture. The patient moreover was entirely free from pain for a period of about sixteen months. We are unable to account for such marked improvement except to attribute it to the irradiation of the ovaries.

Case II (PH11535). Female, aged thirty-eight. Referred for postoperative treatment. She had had roentgen therapy (200 kv., peak) in Pasadena, California. (Feb. 8, 1933, posterior left breast 720 r, anterior left axilla 800 r, lateral left axilla 1,470 r. Further treatment: April 4, 1933, lateral left axilla 370 r, posterior left axilla 1000 r, anterior left breast 1,150 r. Further treatment: May 23, 1933, anterior left supraclavicular area 800 r, left lateral axilla 700 r, left anterior breast 900 r, left posterior breast 960 r.) Patient was seen in this clinic on September 25, 1933. Palpable supraclavicular gland. Films of the chest showed mottled area of dullness beneath the second left rib extending outward toward the axillary line, question of metastatic process. Treatment: 900 r anterior left chest, 900 r posterior left chest 20×20 cm. fields. November 1, 1934—Observation: Supraclavicular gland smaller, chest film shows no change. Patient feeling well. March 29, 1934—Observation: Films of the pelvis show localized areas of diminished density about the left acetabulum and the heads of both femora and ischial tuberosities. May 7, 1934—Observation: Patient complains of pain in both hips. There was induration of the left breast area. Treatment: Anterior pelvis 1,200 r, posterior pelvis, 1,200 r, 20×20 cm. fields; 1,500 r to indurated area left lateral breast, 10×10 cm. field. August 29, 1934—Observation: Patient practically symptom-free, considerable gain in weight. The patient looked entirely well. The gland above the left clavicle had disappeared. The bones showed a very remarkable change from the destructive to the proliferative type of metastatic lesion.

Comment. Up to the time of sterilization this patient's course was distinctly downward. The improvement after sterilization was almost immediate and quite marked,

as evidenced particularly by the change in the type of metastatic lesions from the osteolytic to the osteosclerotic type. We are unable to offer any explanation for this phenomenon but believe it may be associated with and result from sterilization. The disappearance of the gland may have been due to direct radiation.

CASE III (MG11304). Female, aged thirty. On December, 1930, radical left mastectomy. Pathological report adenocarcinoma grade III. On May 1, 1931, began to have severe pain in back of head and neck. Difference in size of pupils. Ptosis of the left eyelid. Small tender lump in anterior left chest wall with pain radiating toward the right breast, considerable cough and occasional bloody sputum. Seen in this clinic on January 6, 1931. Treatment: 1,600 r left anterior chest, 1,200 r lateral left chest, 20×20 field; anterior pelvis 650 r, posterior pelvis 630 r, 15×15 cm. fields. Lower right lung field showed 1.5 cm. rounded area of increased density which had appearance of metastasis. July 14, 1931—Observation: Patient still has difference in size of pupils. Headaches relieved completely. Slight induration of left supraclavicular region. No palpable glands. Menopause. On August 31, 1931, patient died suddenly at home, presumably from metastatic involvement of brain.

Comment. The neurological signs, course of disease, and the subsequent sudden death of the patient lead us to believe that metastatic lesions were present in the skull. The severe headaches were entirely alleviated. We believe the regression of the symptoms may have been due to the irradiation of the ovaries.

CASE IV (BM5885). Female, aged forty-one. Radical left mastectomy on August 23, 1932. Adenocarcinoma grade II. Seen in this clinic on September 19, 1932. Treatment: 800 r lateral left axilla, 800 r anterior left chest, 20×20 field. March 8, 1933—Observation: Patient feeling well. Small gland in the right axilla. Treatment: 1,200 r anterior left chest, 1,100 r posterior left chest, posterior pelvis 700 r, anterior pelvis 600 r, 20×20 fields. February 7, 1934—Observation: Patient feeling very well. Slight menopausal symptoms. Chest film negative. Has gained weight. June 25, 1934—Observation: Patient has no complaints except pain in epigastrium. Gastrointestinal examination showed duodenal ulcer. No evidence of metastases. Gland in the axilla no longer palpable. October 8, 1934—Observation: Patient has no symptoms of any kind.

Comment. When last heard from, this patient had no symptoms. We believe that the gain in weight and general improvement in her condition may have resulted from sterilization.

CASE V (BM4081). Female, aged thirty-nine. Radical right mastectomy on November 24, 1931. Adenocarcinoma. Seen in this clinic on January 26, 1932. Film of the spine showed moth-eaten lesion in 12th dorsal vertebra. Appearance typical of metastases. Treatment: 1,000 r anterior right chest, 1,000 r posterior chest, 20×20 cm. fields, 1,200 r over 12th dorsal vertebra, 10×20 field, 1,050 r posterior pelvis, 1,050 r anterior pelvis, 20×20 cm. fields. April 4, 1932—Observation: Extension of process to 11th dorsal vertebra. No treatment. Menstruation ceased, no menopausal symptoms. May 1, 1932—Observation: Lesion in the right shoulder suggestive of metastases. Some pain. Treatment: 1,200 r anterior right shoulder, 1,200 r posterior right shoulder. June 1, 1932—Observation: No pain whatsoever. Numerous skin nodules in right axilla and glandular involvement in the left supraclavicular region. Treatment: 1,000 r posterior left supraclavicular region, 900 r anterior left supraclavicular region. June 25, 1932: Patient too ill to continue treatment. July 30, 1932: Patient comatose and moribund. Died shortly thereafter.

Comment. Although the pain was relieved in this case the rapid progress of the disease was not appreciably checked. Some cases of carcinoma of the breast do not appear to respond in any way to sterilization and this is one of that type of case. We have been unable to find any explanation for this.

CASE VI (BM6175). Female, aged fifty-three. Simple left mastectomy on October 14, 1932. Adenocarcinoma grade III. Seen in this clinic on October 17, 1932. Treatment: 1,000 r left lateral chest, 1,000 r anterior left supraclavicular region, 20×20 cm. fields. December 16, 1932—Observation: Right breast appears filled

with small rounded masses. Treatment: 900 r anterior right breast, 300 r lateral right breast, 20×20 cm. fields. April 14, 1933—Observation: No change. Sterilization advised; 600 r posterior pelvis, 600 r anterior pelvis, 20×20 cm. fields. June 15, 1933—Observation: Complete menopause. No symptoms. Right breast shows some thickening. but has reduced in size considerably. Skin recurrence in the left axilla. Treatment: 1,200 r posterior left axilla, 15×15 cm. field, anterior left axilla, 15×15 cm. field. July 18, 1933—Observation: Skin nodules in the axilla reduced. Patient feeling well. Complains of slight hoarseness. October 13, 1933—Observation: Patient complained of some pain in the back. Films show metastases to both femora and pathological fracture of 1st lumbar vertebra. Treatment: 1,200 r to the lumbar spine posteriorly, 10×20 cm. field; 1,200 r right lateral pelvis, 20×20 cm. field. November 10, 1933: Patient free of pain. Right breast enlarging rapidly. Treatment: 1,200 r anterior right breast, 1,200 r lateral right breast, 15×15 cm. fields. When last heard from, about April 1934, the patient had a large mass in the right upper abdominal quadrant and was in very poor condition.

Comment. This patient showed only a slight temporary improvement and belongs in that group of cases which show little if any response to sterilization.

Case vii (MG12321). Female, aged thirty-five. Lump in the left breast for five years. Simple (?) left mastectomy on January 29, 1929. Excision of the lump from the center of the scar on February 27, 1929, followed by roentgen treatment; unable to say by whom or to give dose. Mass in left axilla on April 1, 1931. Radical dissection on April 17, 1931. Adenocarcinoma grade 1 in aberrant breast tissue. June 20, 1932, removal of mass from scar, adenocarcinoma grade II. Implantation of two 1 mc. seeds into gland in the left axilla. October 13, 1934, gland noted in the right axilla. November 15, 1932, seen in this clinic. Pain in the right breast and moderately enlarged gland in the right axilla. Treatment: 1,200 r to the right axilla, 1,200 r to the right anterior breast. Patient refuses sterilization. June 13, 1933—Observation: Patient complaining of dyspnea. Film of the chest shows no evidence of metastases. August 4, 1933—Observation: Film shows metastases in the pelvis. Treatment: 800 r anterior pelvis, 800 r posterior pelvis, 20×20 cm. field. September 26, 1933—Observation: Menopause. Sterilization effected. Pain in the pelvis relieved. Complains of pain in the right side of the face. Films show complete destruction of head and neck of the right side of mandible. Treatment: 200 r to angle of jaw, 5×5 cm. field, for the relief of pain. May 15, 1934—Observation: Patient feels very well. No complaints. Face asymmetrical. July 17, 1934—Observation: Severe pain in the right mandible. Films show some regeneration of destroyed part of the right mandible. Treatment: 2,000 r to the right jaw, 10×10 field, 300 r per day. Pain relieved completely with second treatment. August 28, 1934—Observation: No pain. Some swelling of the right jaw. November 11, 1934—Observation: Pain in the cervical region. October 16, 1934—Observation: No change. Pain persisting.

Comment. Although the patient did not complain of pain of the right jaw until November 26, 1933, we believe that the lesion must have been present for some time. The regeneration of the bone during the period of nine months can hardly be attributed to the dose of 200 r given to relieve her pain. We believe the regression of this lesion may have been due to the elimination of the ovarian hormone.

Case viii (MG 12419). Female, aged forty-one. On April 14, 1932, radical left mastectomy for tumor of two months' duration. Pathological report, carcinoma of high malignancy. June 26, 1932, miscarriage of two months pregnancy. December 20, 1932, dilatation and curettage for therapeutic abortion of two months pregnancy. Sterilization advised. Treatment: 700 r to anterior pelvis, 700 r to posterior pelvis, 15×15 cm. fields. April 25, 1933—Observation: No menstrual flow since January 27, 1933. No menopausal symptoms of any kind. September 19, 1933—Observation: Small nodule in left axillary fold. No treatment. March 7, 1934—Observation: Nodule still present. Treatment: 1,800 r to anterior left breast. October 8, 1934—Observation: Condition good.

Comment. Generally speaking carcinomas of the breast appear to grow more rapidly in pregnant than in non-pregnant women. This patient is an Italian woman who has several children and sterilization

was indicated to prevent subsequent pregnancies if for no other reason than to guard against the deleterious effect thereof on the tumor. This patient had no serious menopausal symptoms which might contraindicate sterilization by irradiation in cases of this type.

Case IX (MG12262). Female, aged thirty. Radical left mastectomy on September 19, 1932. Pathological report, adenocarcinoma grade II. Seen in this clinic on October 18, 1932. Treatment: Posterior pelvis 700 r, anterior pelvis 700 r, left posterior chest 900 r, left anterior chest 1,200 r, 15×15 cm. fields, left axilla, 1,000 r, 10×10 cm. field. January 24, 1933—Observation: Menstruation ceased. No palpable glands. Complains somewhat of menopausal symptoms. May 23, 1933—Observation: Feeling well. No signs or symptoms of metastases. Still complains of menopausal symptoms. August 16, 1933—Observation: Still complains of menopausal symptoms. Feeling well otherwise. Treatment: 600 r to each side of the head over pituitary region. October 24, 1933—Observation: Patient feeling fine. Only very slight menopausal symptoms since treatment over pituitary. No evidence of metastases. October 11, 1934—Observation: Patient well. No symptoms of any kind.

Comment. This patient had no evidence of metastases. We are unable to say whether or not the appearance of metastases may be retarded by roentgen irradiation of the ovaries. The nature of the disease is so serious, however, that we believe sterilization should be carefully considered in all young patients with carcinoma of the breast. This is the only one of our cases to suffer from serious menopausal symptoms. We are unable to say whether or not the relief from these symptoms was due to irradiation of the pituitary gland.

Case X (BM7572). Female, aged thirty-five. Recurrent carcinoma of the left breast. Seen in this clinic on June 20, 1933. Four 0.5 cm. nodules over the left anterior chest wall; 3 cm. mass over fourth left anterior costal cartilage. Total of 2,200 r to the mass over cartilage, 10×10 cm. field; 1,800 r to remainder of the left anterior chest, 20×20 cm. field. July 25, 1933—Observation: Patient feeling well. No skin nodules palpable. Sterilization advised. Treatment: 600 r anterior pelvis, 600 r posterior pelvis, 20×20 cm. fields, 1,400 r to the gland in the right axilla, 10×10 cm. field. October 31, 1933—Observation: No evidence of recurrence. Patient feeling very well. March 8, 1934—Observation: Patient feeling very well. No complaints of any sort. No evidence of recurrence. October 12, 1934—Observation: Condition excellent. No evidence of recurrence. No menopausal symptoms.

Comment. To date no recurrence or metastases have been found in this case. This may be due to sterilization. We do not know whether or not sterilization delays the appearance of metastasis.

Case XI (BM7936). Female, aged thirty-six. In February, 1932, simple right mastectomy. Pathological report adenocarcinoma, high malignancy. Recurrent mass in the right axilla on June 1, 1933. Seven months pregnancy. Therapeutic abortion because of rapid increase in the size of the mass, in the right axilla. Seen in this clinic on August 28, 1934. Treatment: 1,000 r anterior right shoulder, 1,000 r posterior right shoulder, 800 r right axilla, 600 r posterior pelvis, 600 r anterior pelvis, 20×20 fields. October 31, 1933—Observation: Mass in the axilla reduced considerably. Excision done. Treatment: 2,000 r anterior right supraclavicular region for gland, 10×10 field. December 4, 1933—Observation: Patient feeling very well. Menstruation ceased, no menopausal symptoms.

Comment. This appears to have been a favorable result. While the follow-up is incomplete we have heard indirectly that the patient had been getting along very well until a few weeks ago. She is now beginning to fail slowly. There have been no untoward menopausal symptoms.

Case XII (MG9198). Female, aged thirty-three. Simple (?) right mastectomy in June, 1927, followed by roentgen therapy to chest. Pathological report, malignant adenocarcinoma. November, 1927, recurrence in right parietal region. April 2 to 21, 1928, patient was given 576 mg. of lead phosphate intravenously. Seen in this clinic April 26, 1928. Several small skin nodules along scar, several 2 cm. glands in left axilla; two 2 cm. tumor masses over right parietal region. Limitation of motion of right hip.

Treatment about 800 r anterior pelvis, 800 r posterior pelvis, 20×20 cm. fields. About 800 r anterior right chest, 20×20 cm. field, 800 r right axilla, 10×15 cm. field. August 13, 1928—Observation: Films of the skull and pelvis showed definite increase in density of metastatic lesions, filling in with new bone and nodules in skull have almost disappeared. November 6, 1928—Observation: Films of the skull and other bones continue to show improvement. February 5, 1929, general condition good, slight pain in left femur. Treatment about 800 r to left femur. June 28, 1929, patient's color not as good as last time. New lump in scalp. From this time on the patient gradually became worse and died about eight months later.

Comment. It was thought at the time that the marked improvement in this case may have been due to the injections of colloidal lead. We now believe that the favorable result was due to sterilization. The noteworthy thing in this case is the regression of the nodules in the scalp and the filling in of the metastatic lesions in the skull. She received no roentgen therapy to this region. The lesions in other bones showed equally striking results. We believe that these also were probably due to sterilization.

CONCLUSIONS

1. Certain cases of carcinoma of the breast in young women show marked improvement after irradiation of the ovaries with a sterilizing dose of roentgen rays.

2. We believe that this improvement is related to the sterilizing effect of roentgen rays on the ovaries.

3. Improvement may be evidenced by disappearance of metastatic nodules in the skin, shrinkage of glands showing metastatic involvement, a better blood picture, change of the osteolytic type of bone lesion to the osteosclerotic type, alleviation of pain and a subjective feeling of general good health.

4. No conclusions can be drawn at present on any effect roentgen irradiation of the ovaries may have on the time interval of appearance of metastases after irradiation.

5. Only one of our patients has shown more than slight menopausal symptoms.

6. At present we have no reason to believe that sterilization prolongs the duration of life in these patients. Our observation leads us to believe, however, that the course of sterilized cases is fairly good, terminating in a relatively sudden decline, whereas the course of unsterilized patients is a steady painful decline during which the patient is unable to live her usual life.

7. Although no such comparable evidence of hormonal influence has been shown to exist in other malignancies, experimentation in this direction deserves more attention and should be carried out.

8. We believe all women with carcinoma of the breast who have not reached the menopause should receive ovarian irradiation.

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TREATMENT OF CANCER OF THE BLADDER BY DIVIDED DOSES OF ROENTGEN RAYS AT LONG DISTANCES*

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IN JUNE, 1935, Keyes, Hocker and myself reported our observations on a series of 16 multiple tumors of the bladder treated by divided doses of roentgen rays at long distances. It was pointed out that a technique had been evolved which, in the later cases of the series, had resulted in a considerable number of complete regressions in these low grade multiple tumors.

We are now prepared to report our observations in detail in a series of 48 cases of tumor of the bladder. Fourteen of these patients were diagnosed and treated in the Carpenter Memorial Clinic of the Homeopathic Hospital, Wilmington, Delaware (Table I). The patients originated with Dr. Victor D. Washburn and were treated by him with the consulting services of Doctors Hocker, Hynes and myself. I am indebted to Dr. Washburn and to the Carpenter Memorial Clinic for the privilege of reporting these cases. The remaining 34 cases were seen in the office of Drs. Keyes, McLellan and myself and treated there by Dr. Hocker (Table II).

Among these tumors, all histologically verified by one or more biopsies, there were 17 single tumors and 31 multiple tumors. The latter were all Grade II or lower, while the 17 single tumors were all Grade II and higher, and all of the infiltrating variety.

Treatment in 8 of the cases was undertaken for palliation only, for the relief of pain or hemorrhage. All of these patients had extensive tumors and several already had metastases. Each of these patients is dead.

Of the remaining 40 cases treatment has been completed a sufficient length of time (three months to one year) to allow of one or more subsequent cystoscopic observations in all but 4. This report is based upon the cystoscopic observation of the remaining 36 cases.

In these 36 cases, complete regression of the tumor or tumors was noted in 20. Incomplete regression requiring further treatment was noted in 11, while in 5 the treatment apparently had no influence on the size of the tumor. Of these 5 cases, 2 are dead—the only deaths in the series other than the palliative cases already referred to.

No true recurrences were noted in any of the 36 cases. New tumors appeared in other locations in the bladder—in one case in which a complete regression had been previously noted, and in 3 cases in which the regression had been incomplete. Of the 20 patients, whose tumors completely regressed, 6 were single tumors of Grade II or higher, while the remainder were all multiple tumors of low grade. Of the 11 cases with incomplete regression 4 were single tumors, the remainder multiple.

We have a definite conviction, as set forth by Keyes, that some of our incomplete regressions were obviously due to an insufficient amount of treatment. When we compare the total amount of radiation in the early cases with that received by more recent patients, it will be noted that our technique has gradually changed from the delivery of a total of 6,000 r to two skin portals, to 12,000 or 15,000 r to three or four skin fields, as in many of the more recent cases.

We began the treatment of this series with the technique previously used in the treatment of teratoma testis. This technique consisted in the application of the

* Read at the Thirty-sixth Annual Meeting, American Roentgen Ray Society, Atlantic City, N. J., Sept. 24–27, 1935.

TABLE I

FOURTEEN CASES TREATED AT THE CARPENTER MEMORIAL CLINIC, WILMINGTON, DELAWARE

No.	Name	Date—First Treatment	Type of Tumor	Filter	Distance cm.	Skin Fields	No. Daily Portals	Daily Dose to Each Portal	Total Dose	Results
								r	r	
1	W. A.	June, 1935	Grade III	Thoraeus	100	3	2	100	8,800	General condition poor
2*	P. B.	May, 1932	Grade IV Infiltrating	(X-ray for palliation only—Bladder not treated)						Expired 5/5/35
3	O. B.	Sept., 1935	Grade II Multiple	Thoraeus	100	3	2	200	9,000	Cystoscopy 9/10/35—No tumors
4	N. F.	Jan., 1935	Grade II Multiple	0.5 mm. Cu 1.0 mm. Al	100	4	2	100	8,500	Cystoscopy 8/30/35—2 minute projections
5	J. G.	March, 1935	Grade I Multiple	Thoraeus	100	3	2	200	9,000	Cystoscopy 9/10/35—No tumors found; pink areas at site
6	W. H.	March, 1935	Grade III Multiple	Thoraeus	100	3	2	200	9,000	Cystoscopy 9/10/35—No tumors; red areas at site
7*	C. H.	Feb., 1935	Grade IV Infiltrating	Thoraeus	100	3	2	100	9,000	Ill at Soldiers Home, Washington, D. C. No report on condition of bladder
8*	W. K.	Feb., 1935	Infiltrating	Thoraeus	100	3	2	100	5,400	Discontinued—condition poor—Expired 3/18/35
9	W. L.	Feb., 1935	Grade I	Thoraeus	100	2	2	100	5,900	Cystoscopy 7/19/35—Tumor smaller
10*	A. McV.	Jan., 1935	Infiltrating Multiple	0.5 mm. Cu 1.0 mm. Al	100	2	2	100	6,000	4/29/35—Entire bladder inflamed 7/21/35—Bladder symptoms subsiding. Expired 8/12/35
11	E. M.	March, 1935	Grade II Multiple	Thoraeus	100	2	2	100	6,000	8/23/35—No regression
12	C. R.	Jan., 1935	Grades I-II Multiple	0.5 mm. Cu 1.0 mm. Al	100	2	2	100	6,000	6/7/35—No tumors
13	R. T.	June, 1935	Grade II Multiple	Thoraeus	100	3	2	200	9,000	Too early for examination
14	A.Van B.	April, 1935	Grades II-III Multiple	Thoraeus	100	3	2	100	9,000	8/19/35—No regression; tumor seems to be growing

* Palliation only.

TABLE II

THIRTY-FOUR CASES TREATED IN OFFICE OF DRS. KEYES, MCLELLAN AND FERGUSON

No.	Name	Date First Treatment	Type of Tumor	Filter	Distance cm.	Skin Fields	No Daily Portals	Daily Dose to Each Portal	Total Dose	Results
								r	r	
1	J. W.	7/18/34	Grade II Multiple	0.5 mm. Cu 1.0 mm. Al	70	2 ant. 2 post.	2	400	7,100	Died, Feb., 1935
		10/4/34			50	1 ant. 2 post.	1	300	4,400	
2	S.	7/20/34	Grade IV Multiple	0.5 mm. Cu 1.0 mm. Al	70	2 ant. 2 post.	1	400	8,000	Died, April 1935
3	S. C. G.	7/23/34	Grade II Multiple	0.5 mm. Cu 1.0 mm. Al	70	2 ant. 2 post.	1	400	6,400	Recurrence; under treatment at present
		8/27/35		Thoraeus	100	2 ant. 2 post.		100	Proposed 12,000	
4	Mrs. S.	7/23/34	Multiple	0.5 mm. Cu 1.0 mm. Al	70	1 ant. 1 post.	1	400	4,800	
		2/19/35		Thoraeus	100	1 ant. 1 post.	2	100	5,000	Negative for tumor, June, 1935
5	J. M.	7/24/34	Multiple	0.5 mm. Cu 1.0 mm. Al	70	1 ant. 1 post.	1	400	4,000	Wound opened July, 1935, to hospital
6	B.	8/20/34	Multiple	0.5 mm. Cu 1.0 mm. Al	70	2 ant. 2 post.	1	400	8,000	Well, August, 1935
7	S.	8/21/34	Single	0.5 mm. Cu 1.0 mm. Al	70	2 ant. 2 post.	1	400	6,800	No evidence of tumor, Sept., 1935
8	LaM.	9/10/34	Multiple	0.5 mm. Cu 1.0 mm. Al	70	1 ant. 2 post.	1	300	7,200	Died, Feb., 1935
9	K.	9/12/34	Multiple	0.5 mm. Cu 1.0 mm. Al	70	1 ant. 2 post.	1	400	6,000	Well
10	R. K.	9/18/34	Grade I Multiple	0.5 mm. Cu 1.0 mm. Al	70	1 ant. 2 post.	1	400	6,000	Well
11	S.	9/29/34	(Bl. neck)	0.5 mm. Cu 1.0 mm. Al	70	2 ant. 2 post.	1	400	8,000	Well
12	E.	10/1/34	Grade I Multiple	0.5 mm. Cu 1.0 mm. Al	70	1 ant. 2 post.	1	300	5,000	Died, May, 1935
		1/2/35		Thoraeus	100	1 ant. 1 post.	2	100	7,800	
13	H.	10/8/34	Grade II Multiple	0.5 mm. Cu 1.0 mm. Al	70	1 ant. 2 post.	1	400	6,000	Well
14	E. B.	10/15/34	Grade I	0.5 mm. Cu 1.0 mm. Al	70	2 ant. 2 post. 1 perineal	2	400	8,900	Tumor much smaller; fulgurated, June, 1935

TABLE II (*Continued*)

No.	Name	Date First Treatment	Type of Tumor	Filter	Distance cm.	Skin Fields	No. Daily Portals	Daily Dose to Each Portal	Total Dose	Results
								r	r	
15	P. G.	10/29/34	Grade III Multiple	0.5 mm. Cu 1.0 mm. Al	70	2 ant. 2 post.	1	300	7,200	Dying
16	P.	11/1/34	Multiple	0.5 mm. Cu 1.0 mm. Al	70	2 ant. 2 post.	1	400	4,800	Died, Feb., 1935
17	W. K.	9/19/34	Multiple	0.5 mm. Cu 1.0 mm. Al	70	2 ant. 1 post.	1	400	3,600	Died, Spring, 1935
18	K.	12/3/34	Single	0.5 mm. Cu 1.0 mm. Al	70	1 ant. 2 post.	1	400	3,600	Well
19	B.	12/8/34	Multiple	0.5 mm. Cu 1.0 mm. Al	70	2 ant. 2 post. 1 perineal	2	400	7,600	Well
20	L.	1/8/35	Grade I Multiple	Thoraeus	100	1 ant. 2 post.	2	100	9,900	One very small tumor July; radium implanted
21	R.	1/16/35	Multiple	Thoraeus	100	1 ant. 1 post.	2	100	5,400	Much reaction at end of treatment; well in June, 1935
22	E.	1/28/35	Single	Thoraeus	100	2 ant. 1 post.	2	100	9,000	May, 1935, remains of tumor fulgurated
23	J. H.	2/10/35	Grade II	Thoraeus	100	2 ant. 1 post.	2	100	9,000	Excellent results, no trace of tumor
24	R. C.	4/1/35	Grade II Multiple	Thoraeus	100	1 ant. 1 post. later— 2 ant. 2 post.	2	100	5,400	One small tumor, Sept., 1935
25	Mrs. W.	4/11/35	Grade II	Thoraeus	100	2 ant. 2 post.	2	100	12,000	Radium implantation into base of tumor, August, 1935
26	C.	5/1/35	Single	Thoraeus	100	1 ant. 1 post. later— 2 ant. 2 post.	2	150	6,450	Well
27	B	5/6/35	Grade II	Thoraeus	100	2 ant. 2 post.	2	100	8,400	Treatment stopped because patient developed cystitis; well, Sept., 1935
28	T. C.	5/15/35	Grade II Multiple (Recurrent)	Thoraeus	100	2 ant. 2 post.	2	100	11,200	Well, August, 1935

TABLE II (*Continued*)

No.	Name	Date First Treatment	Type of Tumor	Filter	Distance cm.	Skin Fields	No. Daily Portals	Daily Dose to Each Portal	Total Dose	Results
								r	r	
29	G.	5/20/35	Grade II Multiple	Thoraeus	100	2 ant. 2 post.	2	100	12,000	Well, August, 1935
30	L.	5/27/35	Grade III	Thoraeus	100	2 ant. 1 post.	2	150	5,550	Well
31	Z.	6/24/35	Grade I+	Thoraeus	100	2 ant. 1 post.	2	100	2,100	Treatment not finished; patient developed cystitis
32	L. W.	7/8/35	Grade I+ Multiple	Thoraeus	100	1 ant. 2 post.	2	100	4,800	Treatment deferred as patient developed cystitis
33	Mrs. N.	4/17/35	Grade II Multiple	Thoraeus	100	2 ant. 1 post.	2	100	9,000	Radium implanted into one remaining tumor, Sept., 1935
34	M.	4/22/35	Grade I+ Multiple 8 yrs. ago, now single	Thoraeus	100	2 ant. 2 post.	2	100	11,200	Tiny tumor fulgurated, Aug., 1935

following factors: 200 kv., 0.5 mm. copper, 1 mm. aluminum, 70 cm. target skin distance, 300 r daily to each of two portals. With this technique it is possible to deliver to the pelvis 2,000 to 2,700 r to each of four portals. However, this total was seldom realized in our early cases due to rectal mucositis, and rectal and bladder tenesmus.

The technique has gradually changed after consultations with Dr. Quimby to that which is used at present as follows: 200 kv., Thoraeus filter (equivalent of 1.62 mm. of copper), 100 cm. target skin distance, 100 r daily to each of two opposite portals. Four skin fields are used, the remaining two being treated on alternate days. With this technique totals of 3,000 to 4,000 r per field may be easily reached, thereby delivering a total of 12,000 to 16,000 r to the four skin portals. From these factors Dr. Quimby has estimated that a bladder tumor at the average depth of 10 cm. in the body would receive 10 to 13 threshold erythema doses respectively, from 3,000 to 4,000 r delivered to each of four skin fields; this provided that the four beams actually converged in the bladder. While we make a very careful effort to converge the fields, it is evident that they do not and we must allow for a maximum 20 per cent loss. With this allowance we are still able to deliver by this technique 8 to 11 threshold erythema doses to a bladder tumor.

Of 17 of the more recent cases treated by this technique there were 9 complete regressions, checked by cystoscopic examination. In one, a single new tumor appeared six months after completion of treatment. In 4 cases there was regression but it was incomplete and the tumor required further treatment by other means, usually fulguration and radon implantation through the cystoscope. In one case there was no regression, in 2 the treatment has been too recently completed to observe the result and in the remaining case there was complete regression of the original tumors in the bladder, but almost immediately there

was a new crop of multiple tumors which proved entirely resistant to further treatment and the patient finally succumbed.

SUMMARY

1. A series of 48 cases of tumor of the bladder treated by divided doses of roentgen rays at long distances is reported.

2. Of 36 cases, all verified by biopsy and subsequently observed cystoscopically, there were 20 complete regressions with the appearance of a new tumor in but one of these cases.

3. In the cases in which regression was incomplete, subsequent treatment was much simplified and usually consisted in fulguration and radon implantation in the base of the remaining tumor or tumors through the cystoscope.

4. Treatment by this technique can be carried to a total of 3,000 to 4,000 r to each of four portals without marked constitutional effect and with very little local irritation to the skin, bladder and rectum.

5. The rate of primary regression reported in this series of tumors of the bladder exceeds that observed with any previous form of irradiation with which we are familiar.*

* More than one year has elapsed since this report was prepared. For this reason every case has been carefully checked as to the condition on June 1, 1936. The following changes are found.

In Table I the status of these patients remains unchanged with the exception of Case 13 which has since been found free of tumor.

In Table II two patients, No. 4 and 10, had one recurrence each but are now well. Cases 5, 14, 20, 24, 31, 33 and 34 are now free of disease. Case 7 has metastases and is dying. Cases 15 and 25 are dead, the latter having proved to be a primary tumor of the cervix rather than of the bladder.

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THE RADIOSENSITIVITY OF THE CELLS OF THE MAMMARY GLAND*

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THE action of roentgen rays and radium upon cells and tissues is highly variable. Some types of cells are highly radiosensitive and are seriously affected when exposed to these rays. Other types of cells are more resistant and are affected only by massive or repeated exposure. Many studies of the radiosensitivity of various species of cells have been reported. Desjardins[7,8] recently summarized the literature in this field and classified the normal cells and tissues and tumors as to their radiosensitiveness. He stated that although the factors responsible for such specificity have not yet been determined, the sensitiveness peculiar to each kind of cell appears to be related chiefly to the natural life cycle. The lymphoid cells with a short life cycle appear to be most sensitive, with epithelial cells of various kinds next in order, followed by endothelial cells, connective tissue, muscle, bone and nerve cells.

The determination of the sensitivity of the mammary epithelium to roentgen rays is of interest from many angles. In cases of the irradiation of the body in the region where the glands are located, the question arises whether the dosage administered may permanently influence the subsequent growth of the gland. In cases of gynecomastia or excessive growth of the mammary glands the condition might be treated most satisfactorily by destroying the ability of the duct epithelium to grow further. In such cases the period of maximum sensitivity to the rays should be known. The increasing prevalence of physiological or endocrine mastitis in the nulliparous demands new methods of treatment. May not such cases be treated by means of irradiation to the extent that the secretory activity of the epithelial cells be destroyed? Finally, it is thought that knowledge of the response of the mammary epithelium to roentgen rays may offer a new mode of attack on the problem of mammary tumors and cancers. This would involve the irradiation of the gland to an extent such that further growth would be prevented and presumably prevent the alteration of normal epithelial cells into malignant cancer cells.

The object of this paper is to report the result of a series of experiments to determine the radiosensitivity of the epithelium of the mammary gland of the rabbit during various phases of growth, secretion and involution. Within the past few years the hormones stimulating growth and secretory activity have been determined. It thus seemed highly desirable to determine the precise effect of roentgen rays upon the mammary epithelial cell during the definite and distinct physiological epochs through which it passes.

While some work has appeared indicating the effect of roentgen rays on the mammary glands of experimental animals, the extent of the development of the gland under observation and the changes which might be expected were little understood. For the proper interpretation of these results, it is necessary to describe the condition of the gland and the changes which would normally occur with the subsequent treatment. Therefore, instead of reviewing the literature at this point, the previous experiments will be discussed in connection with the presentation of the observations.

Hormone Control of the Growth and Secretory Activity of the Mammary Gland.

* Contribution from the Department of Dairy Husbandry, Missouri Agricultural Experiment Station. Journal Series No. 438. This study has been aided in part by a grant from the Committee on Effects of Radiation upon Living Organisms of the National Research Council.

TABLE I

SUMMARY OF RESULTS ON THE EFFECT OF IRRADIATION ON THE PREPUBERTAL MAMMARY GLAND

Animal No.	Pre-irradiation Treatment	X-Ray Dose Minutes*	Post-irradiation Treatment	Observations
R323	None	2	20 rat units of estrogenic hormone daily for 20 days	Extensive growth of the duct system
		5		Extensive growth of the duct system
		10		Extensive growth of the duct system
		15		Growth of the duct system reduced one-half
R34	None	20	"	Growth of duct system reduced one-half
		30		Growth of ducts completely inhibited
R331	None	30	"	Growth of ducts completely inhibited
		60		Growth of ducts completely inhibited
R336	None	30	"	Growth of ducts completely inhibited
		60	"	Growth of ducts completely inhibited
R322	20 rat units of estrogenic hormone daily for 7 days	1	20 rat units of estrogenic hormone daily for 13 days	Very little growth, ducts distended with fluid
	"	2	"	Very little growth, ducts distended with fluid
	"	3	"	No growth, ducts distended with fluid
	"	4	"	No growth
R338	"	4	"	Extensive growth of ducts, branching slightly retarded
	"	7	"	Diameter of gland reduced to one-half of control
	"	9	"	Some duct growth
R339	"	10	"	Duct growth diameter reduced one-half
	"	12	"	Duct growth diameter reduced one-third
	"	14	"	Growth considerably retarded, diameter reduced to one-fourth size of normal stimulated gland
R316†	"	5	"	Marked retardation of growth. Ducts distended with secretion
	"	10	"	Similar to above, but ducts less distended with fluid
	"	15	"	Complete inhibition of growth of the duct system
R314†	"	20	"	No growth. Control gland also affected
	"	25	"	No growth. Control gland also affected
	"	30	"	No growth. Control gland also affected
	"	35	"	No growth. Control gland also affected

* 1 minute = 144 r.

† As the control glands of R314 showed an effect from the long-continued irradiation of the glands, the lead shield protecting the body was doubled. No further evidence of irradiation of the control glands was noted.

In taking up the question of the radiosensitiveness of the epithelium of the mammary gland it is necessary to review briefly the various physiological epochs included in the extrauterine growth and development of this gland. As an integral part of the reproductive system, the mammary gland passes through periods of extremely slow growth during the prepubertal period, when the duct system shows scarcely any

change, to periods of intense duct and lobule-alveolar growth under the impetus of estrus and pregnancy. Following parturition, the growth phase is replaced by a period of intense secretory activity involving the synthesis and discharge of milk in a cyclic manner. At weaning time, milk secretion is quickly suppressed. There then follows an involutionary process which includes the rapid disintegration of the lobule-alveolar system built up during pregnancy with the retention, however, of the extensive duct system.

The humoral control of these various stages of growth and secretory activity has been reviewed by Turner.[16] It will suffice here to state that ample proof is now available for the conclusion that the initial pubertal growth of the duct system of the gland is stimulated by the secretion of the estrogenic hormone (estrin, theelin) from the ovary. In gonadectomized rabbits, Turner and Frank[17] were able to stimulate the growth of an extensive duct system with daily injections of 20 rat units or more of this hormone.

Following coitus, with subsequent ovulation and formation of corpora lutea, the further branching of the two-layered epithelium of the duct system and the extensive growth of alveoli lined by a single layer of epithelial cells occurred. The study of Turner and Frank[18,19] in the rabbit demonstrated that alveolar growth was stimulated by the combined action of 20 rat units of the estrogenic hormone and 1 rabbit unit of the hormone of the corpus luteum (corporin or progestin). This period of intense growth is largely completed by the end of pseudo-pregnancy or the middle of normal pregnancy. During the latter part of pregnancy, the epithelial cells gradually assume functional activity.

At the approach of parturition the secretion present in the gland takes on the characteristics of colostrum. Following parturition there is a great burst of secretory activity. The studies of Stricker and Grueter,[15] Corner,[6] and many others have since demonstrated that the secretory activity observed was due to a lactogenic hormone produced by the anterior lobe of the pituitary (hypophysis).

*Description of Apparatus.** The mammary glands of the experimental animals were irradiated by means of a Victor roentgen-ray apparatus with a Universal broad-focus Coolidge tube. The apparatus was operated at the following settings: primary voltage, 205 volts; secondary voltage, 140 kv. (peak); and secondary current, 4 ma. At a target distance of 12 inches, the mammary glands received 144 roentgens per minute. The measurement of the international roentgens was made in actual contact with the skin, using a Victoreen dosimeter.

FIG. 1. Shield used to protect the rabbit during the irradition of the mammary gland. The glands are exposed by means of hemostats pulling the gland through an opening at the side of the shield.

Technique. In preparation for irradiation, the animal was immobilized on its side on an operating board. The entire body of the animal was then protected by means of a metallic lead shield $\frac{1}{4}$ of an inch in thickness fitted over the board.** The

* We are greatly indebted to Dr. L. J. Stadler of the Missouri Agricultural Experiment Station for the use of the roentgen-ray apparatus used in the experiments to be reported and to Nolan Walker and Garland Francis, roentgen technicians, for invaluable aid in irradiating the mammary glands of the animals.

** At first a single shield $\frac{1}{8}$ inch in thickness was used. As the control glands of R314 were affected also, a second $\frac{1}{8}$ inch shield was added.

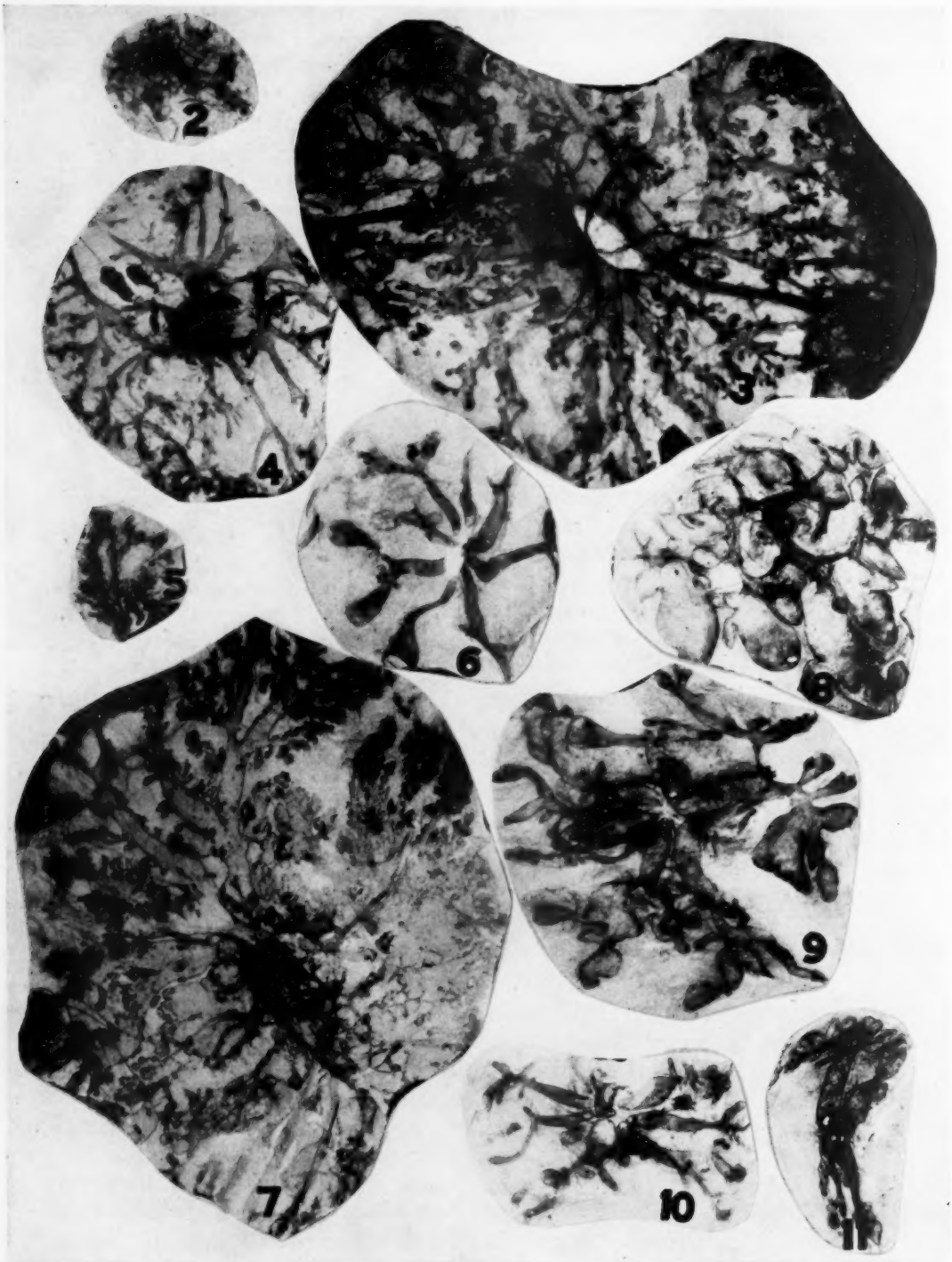

Fig. 2. A mammary gland of an immature female rabbit (R316) before the injection of the estrogenic hormone was begun (×2).

Fig. 3. A mammary gland from the above rabbit (R316) after twenty daily injections of 20 rat units of the estrogenic hormone (×1.5).

Fig. 4. A mammary gland of an immature rabbit (R34) irradiated for twenty minutes before the injection of the estrogenic hormone was begun. The gland was taken after twenty daily injections of the hormone (×1.5).

irradiation of the mammary gland was effected by means of an opening at the side of the shield and opposite the ventral part of the animal through which the gland was drawn. The skin over the gland was held fast by means of hemostats of suitable size, thus exposing a semicircular area (about $1\frac{1}{2}$ to 2 inches in diameter) of the skin and gland to the roentgen rays. Only one gland was irradiated at a time (Fig. 1). Usually from two to four mammary glands of each animal were irradiated, the others serving as controls. The dosage was increased by lengthening the time of exposure. In all instances the roentgen dose for each gland was administered in a single period of irradiation, without a filter.

The experimental and control glands were studied by means of histological sections and whole mounts, the latter being prepared by a method previously described (Turner and Gomez[20]).

EXPERIMENTAL

In describing the following experiments, a brief outline of the anatomy of the mammary glands of the rabbit will aid in understanding the work. The rabbit has two rows of glands extending from the thoracic to the inguinal region. The most anterior pair of glands might even be classed as cervical, as they are usually found on the loose skin of the neck. The second pair of glands is located over the thoracic cavity, the third at the points of the last ribs, while the fourth pair (when only four pairs are present) is located in the inguinal region. When five pairs of glands are present the extra pair is located anterior to the inguinal pair on the abdomen.

The glands spread out in a thin flat sheet below the skin. When the skin is pulled out for exposure to the roentgen rays, the gland is pulled with it.

Irradiation of the Prepubertal Mammary Gland. From birth up to the beginning of puberty, each mammary gland of the rabbit consists of from 4 to 8 short simple tubular ducts extending scarcely beyond the base of the teat (Fig. 2). Growth of the duct system is minimal as this is a period of quiescence.

The first of the series of experiments had as its objective the determination of the radiosensitiveness of the epithelial cells of these rudimentary ducts before the stimulus for growth had begun at the approach of puberty. The mammary glands of a group of three young female rabbits (four to five months old) were irradiated for increasing intervals ranging from two to sixty minutes (Table 1).

In order to determine the effect of irradiation, the growth of the mammary duct system was then stimulated by means of the estrogenic hormone (20 rat units daily in oil) for twenty days. Control glands taken immediately prior to the time of irradiation showed the ducts to be very small. The animals were sacrificed twenty-four hours after the last injection. This period of hormone stimulation caused the growth of an extended duct system in the normal glands (Fig. 3). The rudimentary glands irradiated for two and five minutes were slightly smaller in diameter, indicating some inhibitory action of the rays. However, this was very slight and in general the ducts appeared to be normal in structure. The gland irradiated for ten minutes was also somewhat below normal in diameter but in this case the gland appeared somewhat abnormal due to the greater distention of the ducts with fluid. After fifteen and twenty minutes, the ability of cells of the ducts

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Fig. 5. A mammary gland of the above animal (R34) irradiated for thirty minutes, then injected with 20 rat units of the estrogenic hormone daily for twenty days.

Fig. 6. A mammary gland from an immature female rabbit (R316) after seven daily injections of 20 rat units of the estrogenic hormone (×2).

Fig. 7. A gland of an immature female rabbit (R338) first stimulated for seven days with 20 rat units of the estrogenic hormone, followed by an irradiation for four minutes, then continued for thirteen days on the estrogenic hormone. Note the irradiated zone marked by the retardation of growth and arborization of the ducts (×1.5).

Fig. 8. A gland of an immature female rabbit (R316) treated similarly to the one above except that the irradiation continued for five minutes (×1.5).

Fig. 9. A gland of the above animal (R316) irradiated for ten minutes (×1.5).

Fig. 10. A gland of the above animal (R316) irradiated for fifteen minutes (×1.5).

Fig. 11. A gland of an immature female rabbit (R314) injected with the estrogenic hormone according to the plan outlined above but irradiated for twenty minutes (×1.5).

to grow was very markedly retarded. The glands were only about one-third the diameter of the control and the type of development was distinctly abnormal, the ducts being greatly distended with fluid. In addition, the arborization of the individual ducts was greatly retarded. The deeply staining end buds, one of the most conspicuous morphological characteristics of the actively growing duct, were absent (Fig. 4). The duct system of the mammary glands irradiated for thirty and sixty minutes was prevented from further growth beyond that present at the time of irradiation. The type and extent of these glands were comparable to the unstimulated controls (Fig. 5).

These experiments indicated that the rudimentary duct epithelium, before the growth stimulus of the estrogenic hormone had become effective, was relatively resistant to roentgen rays. Though irradiation for five minutes (720 r) slightly depressed the subsequent growth, and twenty minutes (2,880 r) very markedly, it was only after thirty minutes (4,320 r) that the growth of the duct system was totally inhibited.

Effect of the Estrogenic Hormone on the Sensitivity of the Prepubertal Gland. The radiosensitiveness of the cells of actively growing ducts stimulated by the estrogenic hormone was determined in a second series of experiments. A group of 6 immature female rabbits (four to five months old) were first given a preliminary treatment with 20 rat units of the estrogenic hormone daily for seven days. After thus stimulating the growth of the duct system, the glands were irradiated for intervals ranging from one to thirty-five minutes (Table 1). Control glands were removed from each of the animals at the beginning of the hormone injection and at the time of irradiation. In order to detect the effect of irradiation, the injection of the hormone was continued for a period of thirteen days. The animals were sacrificed twenty-four hours after the last injection.

Before beginning the hormone treatment, the mammary glands consisted of short rudimentary ducts extending scarcely beyond the base of the teat. After seven days of the hormone treatment, the ducts had grown considerably. Secondary branches and end buds were formed at the distal end of each individual duct (Fig. 6). Extending the period of the hormone treatment caused a further extension of the duct system of the normal glands (Fig. 3).

The glands of the first rabbit (R322) were irradiated for intervals ranging from one to four minutes. For some unexplainable reason, the gland removed at the time of irradiation appeared slightly abnormal and at the end of the period of hormone treatment the control unirradiated glands had developed only to about one-third the size of the normal glands of other rabbits. The results of the irradiation of the gland for four minutes in this case indicated rather complete suppression of mammary duct growth. In contrast a gland in a second rabbit (R338), also given an exposure of four minutes, showed only slight retardation of duct growth (Fig. 7). In a third animal (R316) irradiated for five minutes the growth of the ducts was greatly inhibited although they were greatly dilated with fluid (Fig. 8). Seven and nine minute exposures in rabbit R338 still permitted up to one-third the normal extension of the duct system.

The glands irradiated for ten to fifteen minutes showed some individual variation, but in both animals the longer periods practically stopped all subsequent growth (Figs. 9 and 10). Twenty minutes of irradiation, or longer, prevented all subsequent growth (Fig. 11). The results obtained on the longer exposure in R314 and to a less extent in R316 were not entirely satisfactory as the controls showed some effect of the roentgen rays. The lead shield protecting the animals was doubled after these observations were made.

While variations were noted in the radiosensitiveness of the glands of the rabbits, it appeared that even the most resistant glands were inhibited in their further growth by periods of irradiation of fifteen to twenty minutes. It appeared that the sensitiveness of the duct epithelium was increased from thirty to fifty per cent by stimulating active growth with the estrogenic hormone.

Irradiation of the Mature Virgin Mammary Glands. The mature virgin mammary gland consists of an extensive duct system (Fig. 3). At this time the doe may be mated or pseudopregnancy may be induced. In either case a rapid proliferation of the lobule-alveolar system follows during a period of fifteen to sixteen days.

In this series of experiments the object was to determine the radiosensitiveness of the epithelial cells of the pubertal ducts before the stimulus for growth and proliferation of the lobule-alveolar system had begun at the time of

TABLE II

SUMMARY OF RESULTS ON THE EFFECT OF IRRADIATION UPON PUBERTAL, PREGNANT AND PSEUDO-PREGNANT MAMMARY GLANDS

Animal No.	X-Ray Dose Minutes	Protocol of the Experiments	Observations
R325	2	Irradiated immediately after breeding	Complete hyperplasia of the mammary gland
	5		Complete hyperplasia of the mammary gland
	10		Complete hyperplasia of the mammary gland
	15		Complete hyperplasia of the mammary gland
R330	20	Irradiated immediately after breeding	Marked retardation of growth of the lobules
	25		Complete inhibition of lobule growth
R37	20	Irradiated immediately after breeding	Marked inhibition of lobule growth. No lactation
	25		Complete inhibition of lobule growth
R36*	30	Irradiated immediately after breeding	Complete inhibition of lobule growth
	60		Complete inhibition of lobule growth
R337	15	Irradiated at the time of injection of antuitrin-S	Complete hyperplasia of the mammary gland
	20		Marked retardation of lobule growth
	25		Complete inhibition of lobule growth
	30		Complete inhibition of lobule growth
R332	30	Irradiated on second day of pseudo-pregnancy	Complete inhibition of lobule growth
	60		Complete inhibition of lobule growth
R341	20	Irradiated on third day of pseudo-pregnancy	No apparent inhibition of lobule development
	30		Complete inhibition of lobule growth
	40		Complete inhibition of lobule growth
R324	2	Irradiated on fourth day of pseudo-pregnancy	Complete hyperplasia of the gland parenchyma
	5		Complete hyperplasia of the gland parenchyma
	10		Complete hyperplasia of the gland parenchyma
	15		Slight retardation of lobule growth
R42	10	Irradiated on sixth day of pseudo-pregnancy	Complete hyperplasia of the gland parenchyma
	15		Complete hyperplasia of the gland parenchyma
R43*	20	Irradiated on sixth day of pseudo-pregnancy	Complete retardation of further growth of lobules
	25		Complete retardation of further growth of lobules

* The mammary glands of the animals were examined by biopsy at parturition or at the end of pseudo-pregnancy.

conception or at the initiation of pseudo-pregnancy. The mammary glands of four nulliparous female rabbits were irradiated, for intervals ranging from two to sixty minutes, within a few hours after coitus. The mammary glands of a fifth animal were irradiated for intervals of fifteen to thirty minutes immediately after the intravenous administration of 200 rat units of antuitrin-S.* The observations on the effect of irradiation upon the mammary gland parenchyma were made at the time of the termination of pregnancy or pseudo-pregnancy. Unless otherwise stated, the animals were sacrificed at this time.

When the skin of the animal was carefully removed following parturition, the mammary glands, irradiated for intervals ranging from twenty to sixty minutes, revealed on the surface of the glands a more or less circularly depressed irradiated zone, about an inch in di-

* The antuitrin-S was kindly furnished by Dr. Oliver Kamm of Parke, Davis and Co.

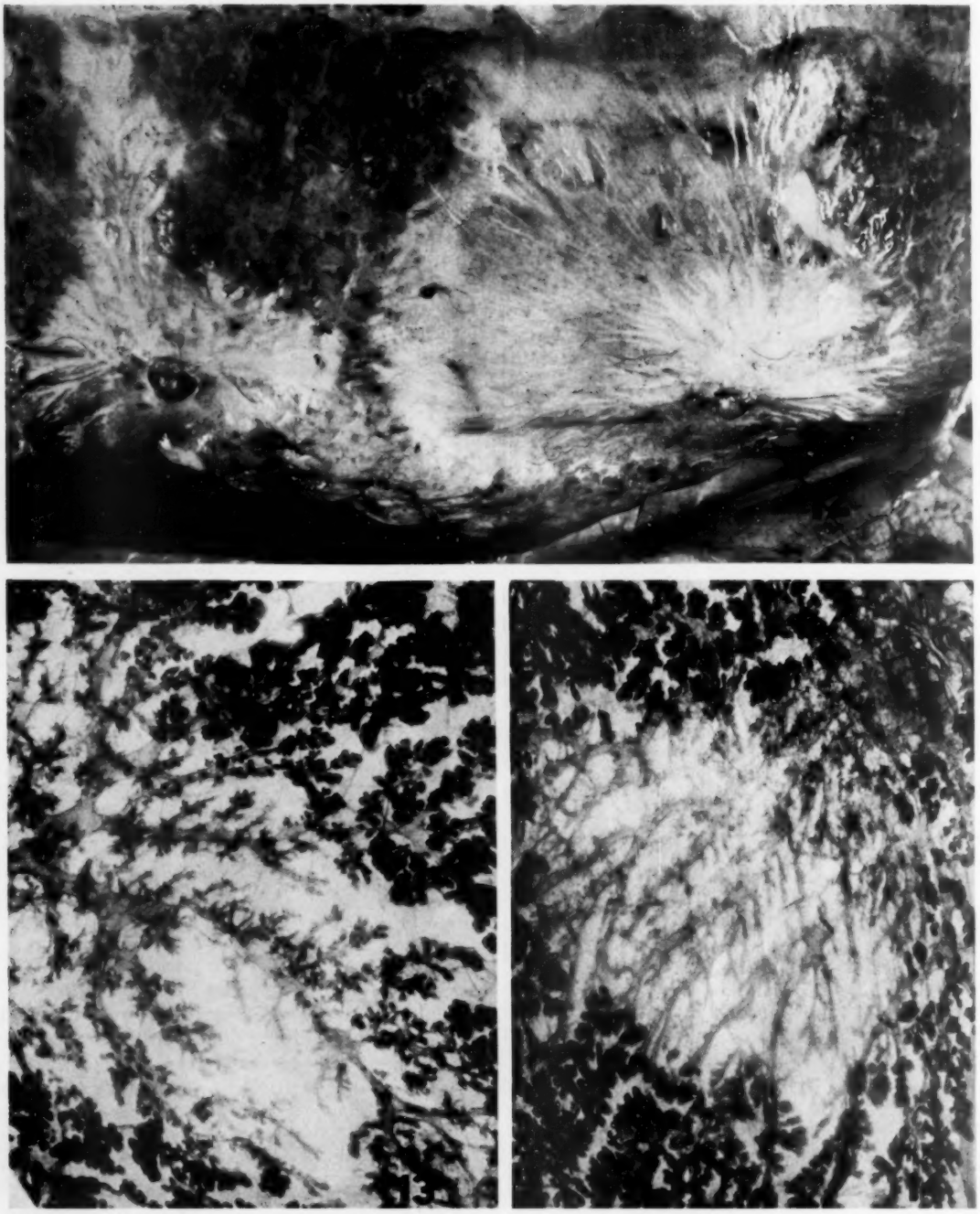

Fig. 12. Photograph of the mammary glands of R330 in situ at the time of parturition. The gland at the left was irradiated for twenty minutes and at the right for twenty-five minutes at the time of breeding. Note the irradiated zone marked by a conspicuous circular depression of the gland tissue (×1).

Fig. 13. Mammary gland of a sexually mature nulliparous female rabbit (R337) irradiated for twenty minutes immediately before the intravenous injection of antuitrin-S. The gland was taken at the end of pseudo-pregnancy (fifteen days after the injection) (×1.5).

Fig. 14. Mammary gland of the same animal (R337) irradiated for twenty-five minutes. Note irradiated zone marked by the complete absence of the lobule-alveolar system (×1.5).

ameter. This zone was markedly differentiated from the surrounding gland tissue, being white in color due to the preponderance of connective tissue. The large ducts traversing this zone were conspicuous in the fresh gland due to the presence of milk in the lumina (Fig. 12). Sections of the outer zone of gland tissue showed a normal picture of alveolar development and milk secretion (Figs. 15 and 16), whereas within the irradiated zone only a duct system was present (Fig. 17).

Microscopic examination of the mammary glands irradiated for twenty minutes revealed a very marked degree of retardation of growth of the lobule-alveolar system. The greater portion of the gland parenchyma within this zone consisted of ducts; a few small lobules, however, were also observed within the irradiated zone. The unirradiated glands revealed complete hyperplasia of the mammary gland parenchyma. The glands irradiated for twenty-five to thirty minutes revealed a complete inhibition of growth of the lobule-alveolar system (Figs. 13 and 14). The mammary glands irradiated for intervals of two to fifteen minutes showed no evidence of an irradiation zone either in fresh or in fixed and stained preparations.

The second of this series of experiments was to determine the radiosensitiveness of the epithelial cells of the duct system at various intervals after the stimulus for growth of the lobules had been initiated by pseudo-pregnancy. Four sexually mature nulliparous female rabbits were each given 200 rat units of antuitrin-S intravenously. The mammary glands of the animals were then irradiated for intervals ranging from two to sixty minutes on the second, third, fourth, and sixth day after the injection of the hormone (Table II). Unless otherwise specified, the animals were sacrificed on the sixteenth day following the administration of antuitrin-S. The glands irradiated for intervals ranging from thirty to sixty minutes during the first four days of pseudo-pregnancy all revealed a complete inhibition of the growth of the lobule-alveolar system. With irradiations ranging from two to twenty minutes, however, a complete hyperplasia of the mammary gland parenchyma was observed. While very little or no roentgen effect was noticeable in the gland irradiated for twenty minutes, a complete inhibition of the growth of the lobules occurred in the gland irradiated for thirty minutes. This seems to indicate that in the early stage (one to four days) of pseudo-pregnancy, the epithelial cells were as radiosensitive as those of the pubertal glands. The mammary glands irradiated for twenty and twenty-five minutes on the sixth day of pseudo-pregnancy showed almost if not complete retardation of the lobule-alveolar system. With ten and fifteen minute periods of irradiation, no evidence of the retardation of growth of the lobule-alveolar system was observed.

These observations indicated that the epithelial cells of the duct system, when growth was approximately complete (i.e., after the rapid growth during the early stages of puberty) required about twenty-five minutes (3,600 r) of irradiation to completely inhibit subsequent lobule-alveolar growth.

In the early stages of pseudo-pregnancy (two to four days) when the lobule-alveolar system was just beginning to develop, the sensitivity appeared to be about the same as earlier, i.e., about twenty-five minutes being required to completely inhibit growth. After six days the sensitivity of the cells had increased, as about twenty minutes (2,880 r) of irradiation inhibited further growth.

Irradiation of the Mammary Gland at the End of Pseudo-pregnancy. Following the growth of the lobule-alveolar system at the end of pseudo-pregnancy, Gardner and Turner (1933) showed that lactation comparable to that observed at the end of normal pregnancy could be induced by means of the lactogenic hormone of the anterior pituitary. The object of the next experiment was to determine the radiosensitiveness of the epithelium of the alveoli previous to the initiation of lactation.

The mammary glands of two rabbits were irradiated for intervals ranging from two to sixty minutes at the end of pseudo-pregnancy. The animals were each given 1 c.c. of the lactogenic hormone (galactin, prolactin) daily for six days. The animals were sacrificed twenty-four hours after the last injection.

Examination of the mammary glands in situ showed a lactation response of 4+, rated according to the method of Gardner and Turner. The gland irradiated for two minutes was in full lactation and similar to the normal controls. After five minutes a slight depression of the irradiated zone appeared as lactation was induced, i.e., during the six days of the injection of the lactogenic hormone. Sections showed

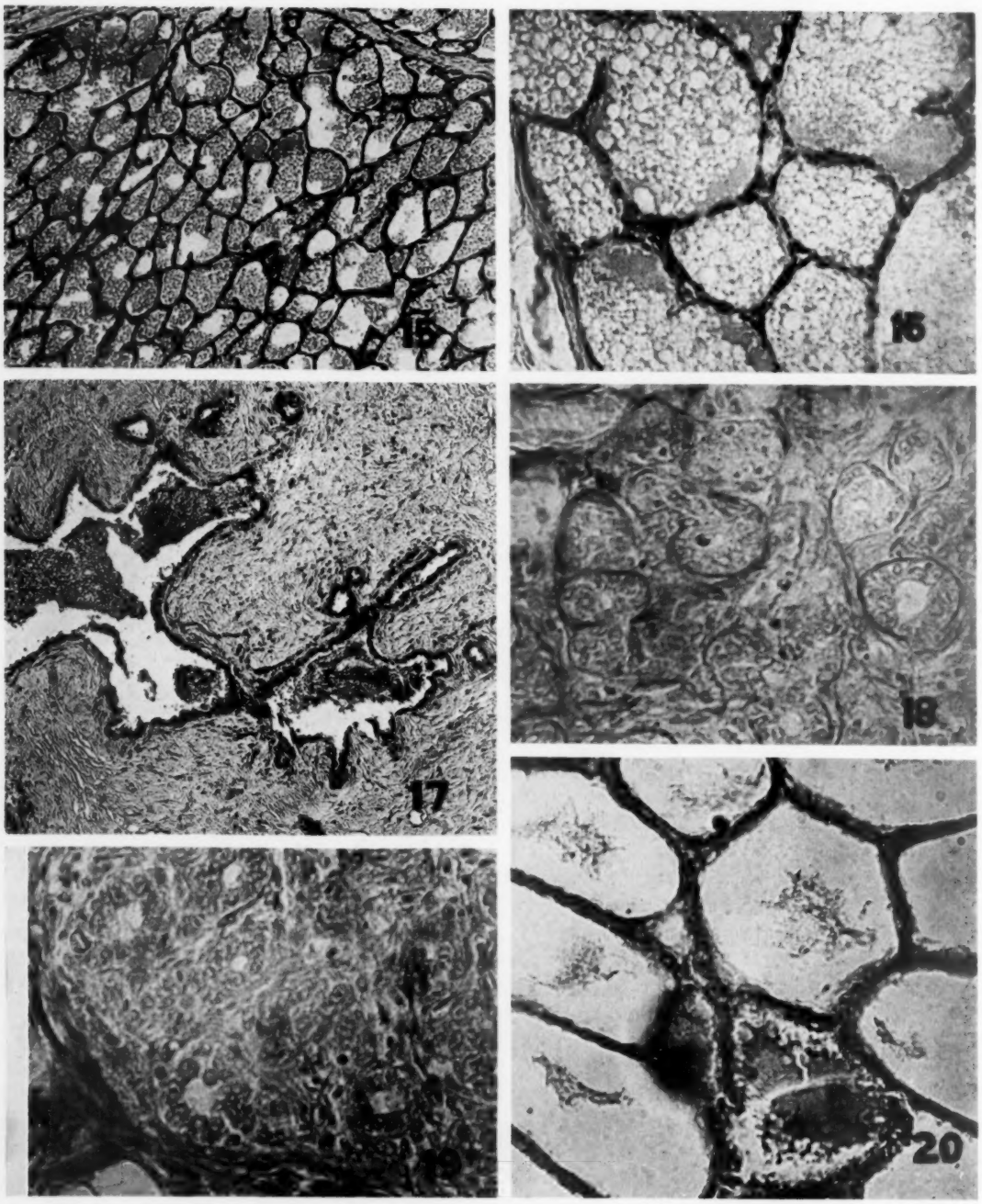

FIG. 15. Microphotograph of a section of the normal mammary gland of a primiparous rabbit (R_{330}) taken at the time of parturition (×30).

FIG. 16. Same as Figure 15, but magnified 120 times.

FIG. 17. Photomicrograph of a section of the mammary gland of a primiparous rabbit (R_{330}) irradiated for twenty-five minutes. The specimen was taken immediately after parturition (×30).

FIG. 18. Photomicrograph of a section of the mammary gland of a pseudo-pregnant rabbit (R_{334}) irradiated for five minutes before the injection of the lactogenic hormone was begun. The functional activity of the alveolar cells was completely inhibited (×120).

FIG. 19. Photomicrograph of a section of the mammary gland of the above animal (Fig. 18), irradiated for ten minutes prior to the injection of the lactogenic hormone (×120).

that the alveoli were small and compact, not being expanded with milk. Change of alveolar epithelium was indicated also by the chromophobic properties of the cells (Figs. 18 and 19).

Lactation in the glands irradiated from ten to sixty minutes was completely inhibited, milk appearing only in the larger ducts which extended into the unirradiated gland. The depressed irradiated zone could be seen through the skin.

These observations indicate that the epithelial cells lining the lobule-alveolar system developed at the end of pseudo-pregnancy or the middle of pregnancy are extremely sensitive to roentgen rays. Somewhat less than five minutes' (720 r) exposure quite definitely inhibited their subsequent ability to secrete milk.

Irradiation of the Mammary Gland during Lactation. It was of interest next to determine the sensitiveness of the mammary cells during the intense secretory activity following parturition in comparison with the growth phase.

The mammary glands of a rabbit which had been in lactation for fourteen days were irradiated for ten and fifteen minutes. After irradiation, the does were returned to their cages with their litters, and lactation was continued for ten days so that the effect of irradiation might show itself. The irradiated glands were examined daily for external evidence of a roentgen effect upon the secretory activity of the cells. These glands showed no evidence of roentgen effect at the termination of the experiment.

The mammary glands of rabbits which had been in lactation for twenty-four hours (R51) and twenty days (R38) respectively, were irradiated for twenty minutes. Upon examining the glands ten days later, there appeared a slight discoloration of the irradiated area of the former rabbit. In both animals the glands revealed a complete suppression of the secretion of milk. The cessation of secretory activity was further confirmed by the microscopic examination of the sections of the irradiated gland of the rabbit in lactation for twenty days. The alveoli, however, were still distended with clear fluid. The alveolar cells were for the most part pycnotic, or chromophobic, and in some alveoli, were sloughing off the basement membrane (Fig. 20).

The mammary glands irradiated for twenty-five minutes and at intervals ranging to sixty minutes, on the second, seventh, fourteenth and twentieth days of lactation, on biopsy at the end of ten days following irradiation all revealed a very marked depression of the irradiated zone from the surrounding gland tissue. These zones were conspicuously discolored due to the absence of milk in the lumina of the alveoli and ducts and the preponderance of connective tissue. Upon microscopic examination the alveoli of the glands irradiated for thirty minutes or more showed histological changes similar to those of the glands irradiated for twenty minutes.

At all stages of lactation (twenty-four hours to twenty days) the secretion of milk was inhibited by periods of irradiation for twenty minutes (2,880 r) or more.

The Permanency of the Effect of Irradiation. The preceding experiments are believed to indicate quite definitely that when the mammary glands are irradiated for a sufficient period, the further growth and the functional activity of the mammary gland may be at least temporarily inhibited. The permanency of the action of roentgen rays was still to be determined. For these experiments a number of animals were irradiated during various stages of development and lactation as previously described but instead of sacrificing the animals at the termination of the experiment when the exposure had been sufficient to cause either the cessation of growth or lactation, they were kept for varying periods of time. Subsequently, pregnancy or pseudo-pregnancy was induced one or more times and frequently lactation was induced after pseudo-pregnancy by means of the lactogenic hormone. Between these periods of growth and lactation, involution of the glands for periods ranging from fifteen to ninety days was permitted.

In 8 animals thus variously treated for periods up to 150 days, the response was the same. Whenever the exposure to roentgen rays was sufficient to temporarily inhibit either growth or lactation, the irradiated area involuted to a duct system and then upon repeated stimulation for growth or lactation failed either to again grow a lobule-alveolar system or to lactate (Figs. 21–24).

FIG. 20. Photomicrograph of a section of the mammary gland of a rabbit (R38) in lactation for twenty days irradiated for twenty minutes. The gland was taken ten days after irradiation. Compare the cellular structure and the contents of the lumina of the alveoli with that of normal lactating gland shown in Figure 16 (×120).

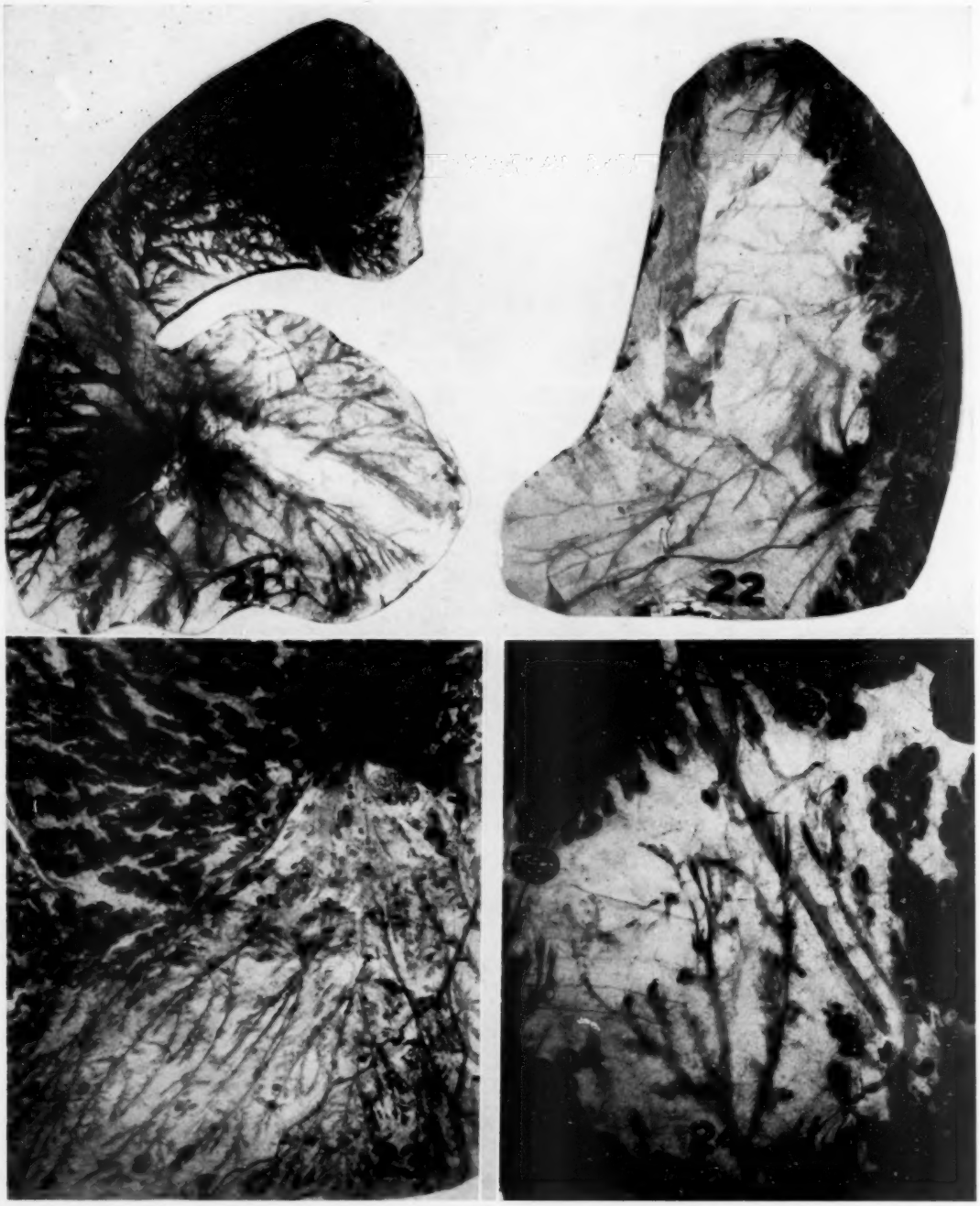

FIG. 21. The gland of a rabbit (R44) irradiated for twenty-five minutes on the second day of pseudo-pregnancy. A biopsy performed at the end of pseudo-pregnancy revealed a complete inhibition of lobule-alveolar growth. The glands were then involuted for ninety days, followed by stimulations of two successive pregnancies separated by a lactation period of thirty days. The animal was sacrificed at the termination of the second pregnancy (×1.5).

FIG. 22. The gland of a rabbit (R36) irradiated for thirty minutes at the time of breeding. The gland was taken 125 days after irradiation. The animal had had two pregnancies, separated by a period of normal lactation. Thirty days after the termination of the second pregnancy, pseudo-pregnancy was induced by an intravenous injection of antuitrin-S. The animal was sacrificed at the end of pseudo-pregnancy (×1.5).

FIG. 23. The gland of a rabbit (R52) irradiated for twenty-five minutes on the seventh day of lactation. A

TABLE III

SUMMARY OF RESULTS SHOWING THE EFFECT OF IRRADIATION UPON THE FUNCTIONAL MAMMARY GLAND

Animal No.	Condition of the Animal at the Time of Irradiation	X-Ray Dose Minutes	Observations
R334	Pseudo-pregnant 15 days irradiated, followed by lactogenic hormone for six days	2	Good lactation (4+)
		5	Slight depression of the irradiated zone
			Complete inhibition of secretory activity
		10	Complete inhibition of secretory activity
		15	Complete inhibition of secretory activity
R340	Pseudo-pregnant 15 days irradiated, followed by lactogenic hormone for six days	30	Marked depression of irradiated zone. Complete inhibition of secretory activity. Effect similar to the 30 minute irradiated gland
		60	
R38	20 days in lactation	20	No external evidence of irradiated zone after 10 days
		30	Complete suppression of secretory activity and desquamation of the epithelial cells
R32	14 days in lactation	10	No external evidence of irradiated zone
		15	Secretory activity was not suppressed
R39	14 days in lactation	40	Discoloration of the irradiated zone 48 hours after irradiation. Complete suppression of secretory activity, with desquamation of the alveolar cells after 10 days
		60	
R51*	24 hours in lactation	20	Slight discoloration of the irradiated zone after 10 days. Marked to complete suppression of lactation observed on biopsy on the 10th day after irradiation
		40	Complete suppression of secretory activity
R52*	7 days in lactation	25	Slight discoloration of the irradiated zone
		30	Complete suppression of secretory activity observed 10 days after irradiation

* The animals were used for further observation on the permanency of the effect of irradiation.

The fact that the duct system persists even when apparently incapable of regenerating lobules is quite remarkable and difficult to understand. Are the cells lining the ducts still capable of limited metabolic activity but no longer able to respond to the stimulus of the various hormones? This question must await further study.

DISCUSSION

The earliest work on the sensitivity of the epithelial cells of the mammary gland appears to be that of Cluzet and Soulié[5] (1907) working with guinea pigs. They observed a retardation of the growth and

biopsy performed ten days after irradiation showed a circularly depressed area. The gland was involuted for thirty days after the young were weaned. Following the period of involution the animal was bred and again rebred, at the end of the intervening period of lactation. The animal was sacrificed at the termination of the last gestation period (×1.5).

FIG. 24. The gland of a rabbit (R51) irradiated for twenty minutes twenty-four hours after parturition. A biopsy performed ten days after irradiation showed a very marked circularly depressed area. The gland was then involuted for ninety days. Following the period of involution, the animal had three successive pregnancies, separated by periods of normal lactation. The animal was sacrificed at the end of the third gestation period (×1.5).

initiation of milk secretion when the glands were irradiated at various times during pregnancy and shortly after parturition. Cluzet and Bassal[3,4] (1908–1909) and Cluzet[2] (1909) continued studies with the rabbit. They reported the modification of the duct system of virgin rabbits when irradiated prior to coitus. Alterations were also produced when the glands were irradiated during pregnancy. They also observed that the effect of the irradiation was permanent.

These observations were extended by Kushtaloff[11] (1910) using rabbits and dogs. He confirmed the observations of Cluzet and associates but observed also the retardation of lactation with increasing periods of irradiation. Nunberg[13] (1910), on the contrary, arrived at the conclusion that roentgen rays did not cause atrophy of the highly developed mammary gland even in large doses; in fact, it was suggested that irradiation might stimulate the function of the mammary gland.

Of interest also were the clinical observations of Muhlmann,[12] Harms[10] (1925) and Richarz[14] (1925). They observed in the case of girls irradiated over the chest in the treatment of tuberculosis that later one breast failed to develop, indicating that the irradiation inhibited the pubertal growth of the gland. They suggested caution in the use of roentgen rays over the breast of children to prevent the destruction of the mammary gland. Earlier Bouchacourt[1] (1908) noted the regression of the hypertrophied breast following irradiation.

The present study was undertaken to determine more definitely the exact effect of roentgen rays on the mammary gland epithelium at very definite stages of development and in the light of the recent studies of the hormone regulation of growth and milk secretion. It was believed also that the improved standards of measuring roentgen rays would place the observations on a more comparable basis with observations on the sensitivity of other types of cells.

As with all biological phenomena, considerable variation in response was noted. The dosages suggested as inhibiting further growth at various stages of development should not be taken as absolute but only approximate. For more accurate determination of response a large number of glands should be irradiated at each level.

SUMMARY AND CONCLUSIONS

1. The irradiation of the rudimentary duct system of the young rabbit for five minutes (720 r) depressed the subsequent rate of growth slightly, twenty minutes (2,880 r) very markedly, and thirty minutes (4,320 r) entirely.

2. When the rudimentary ducts were first stimulated to growth by the injection of the estrogenic hormone for seven days, their further growth was inhibited by periods of irradiation of from fifteen to twenty minutes (2,160 to 2,880 r). It thus appeared that the sensitivity of the duct epithelium to roentgen rays was increased from 30 to 50 per cent by stimulating more rapid growth of the ducts.

3. When the growth of the duct system of mature virgin rabbit was approximately complete, about twenty-five minutes (3,600 r) of irradiation was required to completely inhibit subsequent lobule-alveolar growth. Similar results were obtained up the fourth day of pseudo-pregnancy. After the sixth day of pseudo-pregnancy the sensitivity of the glands appeared to increase slightly as twenty minutes (2,880 r) inhibited further growth.

4. The epithelial cells lining the fully developed lobule-alveolar system present at the end of pseudo-pregnancy or the middle of pregnancy were observed to be extremely sensitive. Somewhat less than five minutes' (720 r) exposure definitely inhibited their subsequent ability to secrete milk.

5. At all stages of lactation (twenty-four hours to twenty days) the secretion of milk was inhibited by periods of irradiation of twenty minutes (2,880 r) or more.

6. Whenever the exposure to roentgen rays was sufficient to temporarily inhibit either subsequent growth or lactation, the irradiation area regressed to a duct system. Subsequent pregnancies or pseudo-pregnancies failed to stimulate the growth of the lobule-alveolar system or lactation, indicating that irradiation permanently affected the cells concerned.

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DOSIMETRY IN RADIATION THERAPY

I. GAMMA-RAY MEASUREMENTS IN ROENTGENS

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I. RELATIONSHIP BETWEEN THE OPEN AIR AND ENCLOSED IONIZATION CHAMBERS

WITHIN the past few years, the air ionization method of measuring the intensity of roentgen radiations has been well established experimentally and in actual practice. The "roentgen"* has been accepted internationally as a quantity unit for roentgen radiations, and has been intercompared by the various national physical institutions with a satisfactory degree of accuracy.

These international comparisons were made with the standard open air ionization chamber, an instrument which has served very well for the radiations produced between 10 and 300 kv. For radiations produced beyond 300 kv., however, and especially for the gamma radiations from radium, the standard air chamber can be used only with great difficulty.

While the present types of the standard air chamber fail to determine short wave radiation in roentgens, the roentgen itself, as a unit, can be used to express some function of the true intensity of any air-ionizing electromagnetic radiation. While this fact is almost axiomatic, the unit cannot easily be measured with physical validity in the very short wave spectral region by means of the ordinary standard chamber, because the long range photoelectrons which are produced in the measured air volume by these ultra radiations fail, effectively, to lose all their energy in secondary processes within the delimited air volume of the narrow beam directed through the measuring chamber.

In the proper spectral range, the precision of the standard chamber allows accurate comparisons of the roentgen to be made within less than 1 per cent—a physically necessary factor in establishing the unit in various remote institutions. For practical measurements, the small "air wall" ionization chamber has been used in conjunction with the open air chamber, to which it has been related as a secondary standard, and as a means of transferring the roentgen to actual dosage measurements in therapy. In this case, of course, the true roentgen measurements are those made in free air. The small chamber instruments, standardized by the open air type, have a precision of observation within about 2 per cent, providing a degree of accuracy entirely sufficient for radiotherapeutic practice.

On the other hand, primary measurements with a small chamber instrument which are evaluated from a knowledge of its own physical and geometrical constants are less certain than the free air measurements largely because the ionization within the enclosed air volume is influenced by a "wall effect." That such an instrument can nevertheless be used to measure roentgens with sufficient accuracy for use in radiation therapy follows from physical studies made upon the characteristics of small thimble chambers themselves.

* At the Third International Congress of Radiology in Paris, July, 1931, the following definition of the unit was accepted:
"The international unit of roentgen radiation shall be the quantity of roentgen rays which, when the secondary electrons are fully utilized and the wall effect of the ionization chamber is avoided, produces in one cubic centimeter of atmospheric air at 0° Centigrade and 76 centimeters mercury pressure such a degree of conductivity that one electrostatic unit of charge is measured at saturation current. The international unit shall be called the 'roentgen' and shall be designated by the letter 'r.' The effective intensity of the radiation shall be expressed in 'r' per minute or 'r' per second."

II. PHYSICAL STUDIES ON THE ENCLOSED IONIZATION CHAMBER

Fricke and Glasser,[9] in a study of the density of air ionization which was produced in completely enclosed volumes by ionizing radiations, were the first (1925) to describe chambers with a so-called "air wall" effect. The materials of these chambers were chosen of a combination of chemical substances of low atomic weight in order to create an enclosing wall of the same "effective atomic number" as air. In this way, it was possible to formulate a first approximation to free air ionizing conditions in the enclosed volume.

A few years later (1929) Braun and Küstner[3] made a comparative study of the validity of primary measurements of the roentgen by both enclosed and open air chamber methods. These authors tabulated a series of conditions under which the actions of the two methods are comparable from the conditions of the definition of the roentgen, and from the air wall considerations suggested by Fricke and Glasser. These conditions, *essentially describing the procedure intended to make a true count (electrically) of ion density in irradiated air, were listed somewhat as follows:*

A. For the standard air chamber (from the international definition of the roentgen).
   1. Full use (of the ionizing energy) of the electrons found in air.
   2. Avoidance of a wall effect (secondary radiation and ionization produced by material, other than air, of the chamber itself and of immediately surrounding objects. This wall effect usually markedly increases the observed ionization density).
   3. Maintenance of saturation conditions (sufficiently powerful electrical field applied across the irradiated volume to collect every ion formed).
   4. Measurement of the critical radiated volume.
   5. Measurement of the temperature and pressure of the air (to reduce air molecular density always to normal conditions).
   6. Measurement of the quantity of electricity produced by ionization.

B. For the small enclosed chamber (from Fricke and Glasser).
   1. Construction of the chamber of "air wall material."
   2. Maintenance of saturation conditions.
   3. Measurement of the chamber volume.
   4. Measurement of temperature and pressure of the air.
   5. Measurement of the quantity of electricity produced by ionization.

The small ionization chamber has been purposely made of air wall material with the intention of fulfilling the first two conditions required of the standard open air chamber. Braun and Küstner[3] in 1929 recognized this fact by restating that the first two conditions listed for the standard air chamber were to be satisfied by the first condition in the case of the enclosed chamber. *Avoidance of a wall effect, a criterion of the correctness of method A, is not a physically necessary condition to method B.* Here a wall effect ionization and secondary ionizing radiation from the enclosed walls can exist and still produce no more ions within the enclosed volume than if it were surrounded entirely by air. (In discussing the wall effect of the small chamber here, the reduction in intensity of the radiation passing through the wall is not included because it is observably negligible [see Table 1] except for very soft radiations.)

TABLE I

RELATIVE IONIZATION IN 1 C.C. GRAPHITE CHAMBER OF VARIOUS WALL THICKNESSES

0.25 mm. graphite	94.9
1.25 mm. graphite	102.0
2.25 mm. graphite	102.0
3.25 mm. graphite	102.0
4.25 mm. graphite	101.0
5.25 mm. graphite	100.0
6.25 mm. graphite	100.0
6.00 mm. graphite (one piece)	100.0

From their studies on both types of instrument, Braun and Küstner concluded that primary measurements in the roentgen-ray spectrum were best made with the open air chamber; at that time, they computed an accuracy within ± 1.5 per cent for the open air chamber, and ± 6.3 per cent for the thimble chamber instrument,

when primary measurements with each were made on roentgen rays. The chief sources of uncertainty were determination of the small volume of their thin-walled chambers, and the presence of a wall effect varying with different roentgen-ray wave lengths. These authors, nevertheless, using graphited cellophane thimble chambers (with very thin walls: 0.03 and 0.3 mm.) were able to make primary measurements with the small chamber that differed, in a single case by 3.6 per cent, and in an average by only 0.3 per cent, from the standard chamber over a range of radiations produced from 60 to 180 kv.

III. FURTHER DESCRIPTIONS OF AIR WALL MATERIALS

Since the original work of Braun and Küstner, other authors have studied small

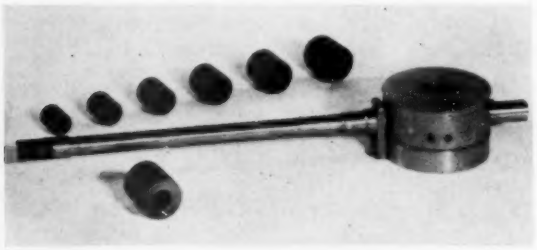

Fig. 1. Condenser unit of ionometer with 1 cubic centimeter graphite chamber of various wall thicknesses.

chamber characteristics and have added conditions which were believed to be necessary to the proper evaluation of roentgens by the thimble chamber method. Meyer[25,26,27,28] and Miehlnickel[29] attributed the wave length dependence of the small chamber chiefly to the ratio of chamber surface to chamber volume, and to the electron density in the wall material itself. That there is a significance to the electron density in and about the enclosed volume of the small chamber is undoubtedly correct, especially for the short wave spectrum where the production of Compton electrons becomes larger for a given quantity of radiation. No quantitative relation, however, is presented to show the outcome of this effect, and in actual measurement it can only be observed as a part of the total results. In this case, our criterion for the evaluation of an electron density effect is: how observed and computed free ion densities compare with one another.

Albrecht[1] in discussing the absolute determination of the roentgen in the gamma-ray spectrum with the small chamber, presented further conditions which were deemed to be important in producing the equivalent air wall surrounding for the ionized volume. The material was to have at the same density as air:

1. The same number of photoelectrons produced as in air.
2. The same number of Compton electrons produced as in air.
3. The same absorption as that of air for the electrons released.

These added conditions for an ideal air wall material are indisputable, and more closely define the condition to be sought. Yet, since the actual attainment of such conditions has not taken place, the end-result is what we most desire, regardless of the mechanism by which it is produced.

In the process of his study, Albrecht observed a wall effect in gamma-ray measurements dependent upon the thickness of the wall material, and, in the case of graphite, he observed a maximum ion density in the enclosed volume with a wall thickness of 4 millimeters. Later, Keller[19] also observed this same action, as did Mayneord and Roberts.[24] Friedrich, Zimmer and Schulze[10] included the wall thickness effect in a condition calling for saturation in the chamber in their measurements of the roentgen in the gamma-ray spectrum.

The wall thickness effect of increased ionization, familiarly related to the maximum range of photoelectrons in any material, has been observed in almost all cases with canalized radiation entering a single wall or single wall area of the small chamber. We have conducted a series of experiments with a small ionization chamber standing free in a large volume of

gamma-radiated air (Figs. 2 and 3) and have varied the wall thickness of a graphite chamber material from 0.25 mm. to 6.25 mm. by using a series of precisely machined graphite caps, fitting over one another (Fig. 1). Our results in relative observed ionization densities are summarized in Table I.

From these measurements, we find that an enclosed chamber made of a light material such as graphite, and having a wall thickness of 1 millimeter or more, presents values that are independent of a wall thickness effect *when observations are made in a large volume of radiated air.* Evidently in such a condition, when the fast photoelectrons expelled from within the enclosed volume are compensated for by high speed electrons penetrating the enclosure from the surrounding air—a state of equilibrium exists, in which the divergence of corpuscular radiation is zero, within the limits of the volume of the small chamber. There seems to be an agreement, then, with the application of Gray's[15] "principle of equivalence" describing the ratio of energy loss by beta particles in a cavity and in a solid. Mayneord and Roberts[24] found results comparable to ours in their own investiga-

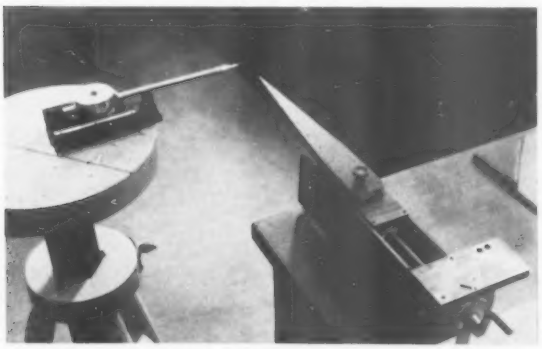

Fig. 2. Set-up of radium capsule and condenser ionometer.

tion of the problem. Yet another corroborating evidence is the long list (Table III) of independent observations of the value of *roentgens** per milligram-element-hour at 1 centimeter distance, commonly designated as *r/mgeh-cm.*, which show a close agreement with one another, though observed with chambers of many materials and various wall thicknesses, several of which are much less than the so-called

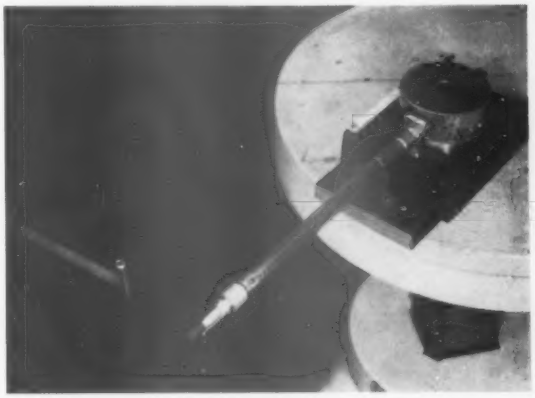

Fig. 3. Set-up of radium capsule and condenser ionometer.

"saturation thickness." These listed measurements are necessarily made in free air to avoid secondary radiations from any materials of high atomic weight. We shall consider Table III later, in a discussion of the value of *r/mgeh-cm.* itself.

IV. ROENTGEN UNITS AND THE RADIUM IONIZATION CONSTANT

The whole problem of measuring in **roentgens** is that of effectively counting a certain number of ion pairs formed in a unit volume of free air due to an ionizing radiation of a certain fixed intensity. Upon this basis the true value of the intensity of energy flow of the various ionizing electromagnetic radiations can be reached through studies of energy absorption in air and through investigation of the work expended in producing the total number of ion pairs formed by the type of radiation present. (See for example, article by Lauritsen.[21]) If it can be shown that the small ionization chamber, immersed in a comparatively large volume of ionized air, acts under certain conditions as though its enclosed volume were very nearly at the condition of "free" air, then the small chamber instrument can be used

* In this paper, gamma-ray roentgens will be italicized.

TABLE III

AIR IONIZATION DATA

EVALUATED CHIEFLY FROM ENCLOSED AIR VOLUME MEASUREMENTS OF GAMMA RADIATION IN *r/mgeh* AT 1.0 CM. (0.5 MM. PT FILTER)

Author	Method of Determination (Filter Used in the Measuring Process)	*r/mgeh-cm.*	
		Value Presented (Corresponding Filter)	Value Reduced to 0.5 mm. Pt Filter, or Recalculated
Eve[5]	Thin cardboard ionization chamber, coated within with lampblack, volumes of order of 1 liter, distances of radiation order of 1 meter to Ra source; sufficiently filtered to remove gamma rays of the Ra B	7.4 Equivalent to 6 mm. Pb	—
Glasser and Mautz[12]	Spherical graphite ionization chambers, air volumes 0.5 and 1.0 c.c., wall thickness 1.0 mm.; measurement in free air; (Pt radium needle, 0.5 mm. Pt)	8.05 (0.5 mm. Pt)	8.8 (Recalculated from observed value at 10 cm. distance)
Jona[18]	Wulf ionometer with air wall chamber (2–3 c.c. volume) radium-chamber distances of 4–5 cm.; 100 mg. Ra (2.6 mm. brass) measurement reported in "R" (value presented not reduced to point conditions)	6.5 R (2.6 mm. brass)	7.0 (not reduced to point conditions)
Mayneord[22]	Calculation from the caloric energy of γ-ray emission from Ra (B+C), the absorption of γ-rays in air, and the energy required to produce one pair of ions (most probable values)	8.7 (0.5 mm. Pt)	8.7
Mayneord[22]	Ionization measurement with small celluloid chamber (1 mm. wall thickness) calibrated by standard chamber in roentgen-ray wave lengths	9.2 (0.5 mm. Pt)	9.2
Reitz[33]	Ionization measurement, aluminum and paper ionization chambers, volume of order of 1 liter, distance to gamma-ray source approximately 1 meter, sufficient filtration to reduce Ra B gamma radiations, and secondary beta rays from metal to zero, approximately	7.4 (6 mm. Pb)	—
Reitz[33]	Same measuring conditions as above except 2 mm. Pb filter used with γ-ray source	8.6 (2 mm. Pb)	9.0
Sievert[34]	Graphited celluloid spherical condenser chambers, outer diameter of air volume: 0.8 cm.; separation from γ-ray source: 3.0 cm.; (value presented evidently not computed as for point source and receiver)	7.55 (0.35 mm. Au +0.30 mm. Pt)	8.0 (not reduced to point conditions)
Mayneord[23] and Gray[15]	Calculation from Eve's constant, evaluated from data by Reitz (see above) and from ionization measurements by Gray in an aluminum scattering medium, using chambers of Al, graphite, S, of 1–2 c.c. volume	8.9 (0.5 mm. Pt)	8.9

Table III (*Continued*)

Author	Method of Determination (Filter Used in the Measuring Process)	*r/mgeh-cm.*	
		Value Presented (Corresponding Filter)	Value Reduced to 0.5 mm. Pt Filter, or Recalculated
Mayneord and Roberts[24]	Small graphite chamber, air volume 2 c.c., wall thickness 4 mm. (equivalent to range of secondary electrons from the air gases)	8.3 (0.5 mm. Pt)	8.3
Jaeger[17]	Calculation from values observed by Eve and Reitz for ionization produced, presumably, only by the gamma radiation from RaC; presented thus as a minimal value. (Also quotes Behnken and Jaeger, see below)	7.35 Equivalent to 6 mm. Pb	—
Behnken and Jaeger[3]	[Reported by Jaeger[17]] Thimble-chamber measurements, chamber volumes 4 c.c. and 2.5 c.c.; 42.5 mg. Ra. 40 mm. long lying in groove on lead plate, with 0.5 mm. Pt sheet above as filter; data reduced to ideal condition of point source and receiver; 8 per cent additional radiation effect assumed, and corrected for	8.8 (0.5 mm. Pt)	8.8
Friedrich, Zimmer and Schulze[10]	Spherical chamber of graphite; wall thickness 4 mm.; volume 0.33 c.c.; distances of 15 cm. (approx.); lead cone shield used to determine secondary radiation from surrounding air; calculation to 1 cm. distance, and 1 c.c. volume	10.6 (0.3 mm. Pt +1.5 mm. brass)	—
Friedrich and Schulze[11]	Spherical and cylindrical chambers of graphite; wall thickness 4 mm.; volume varied; lead cone shield; calculated to 1 cm. distance and 1 c.c. volume.	7.6 (0.3 mm. Pt +1.5 mm. brass) 5.2 (6.67 mm. Pb)	7.8
Stahel	[Reported by (10)] Ionization measurement with liquid microionization chamber converted to value for air	7.5 (2 mm. Pt)	9.0
Murdoch and Stahel[30]	[Reported by (10)] Ionization measurement with liquid microionization chamber converted to value for air	7.62 (1.0 mm. Pt)	8.11 (0.5 mm. Pt)
Glasser and Rovner	Measurement in free air with ionization chambers of 0.03 c.c.; 0.046 c.c., 0.061 c.c. volume, made of graphite; wall thickness 1.0 mm.; filter, 0.25 mm. monel metal +0.5 mm. Pt. Observations reduced to condition of point source and receiver. Geometrical and physical constants, only, used to evaluate roentgens	8.8 (0.5 mm. Pt)	8.8
Glasser and Rovner	Measurement in free air, radiation from 2 gm. pack, thimble chamber of bakelite, 1 mm. wall thickness volume = 2 c.c.; distances of order of 1 meter; filter sufficient to eliminate soft secondary rays from walls of pack. Geometrical and physical constants used, as well as standard chamber calibration	8.9 (0.5 mm. Pt)	8.9

as a modified standard measuring device. That is to say, that in this case, *just as in that of the large open air chamber*, the ionization intensities can be observed in terms of primary measurements on the physical and geometrical constants of the instrument itself.

Let us consider the air ionization data of measurements made on gamma radiations from radioactive sources with instruments using enclosed ionizing volumes. From these we can draw some conclusions regarding the significance of ionization density measurements of gamma-ray intensities.

It is well known that the atoms of the radioactive disintegration products of radium, when existing in equilibrium proportions with a fixed amount of their parent atoms, produce radiation at a rate that remains practically constant over a great span of years, and under extreme variations in the physical environment. The disintegration products Ra B and Ra C, which emit gamma radiations, thus serve, in definite amounts, as excellent standard sources of a radiation of fixed intensity, analogous to, but much more constant and reproducible than the "standard candle" of the visible spectrum. Since standardizing measurements on gamma rays are made on fixed quantities of some Ra salt, the factors determining the observed effect are primarily two: the quantity of salt, and the distance between the source of the radiation and the receiver.

The factor of distance makes it essential that for precise measurement both the source and the receiver occupy only point volumes. This very necessary mathematical fiction is effectively realized when a small radium needle and a small ionization chamber are several centimeters apart, or when the distance between the source and a large volume chamber are of the order of 1 meter.

Secondarily, since the radioactive salt is the source of a shower of high speed beta particles, these corpuscular radiations must be screened off with sufficient filtration so that, ideally, only gamma radiations leave the source (0.5 mm. Pt effectively absorbs the beta rays from the salt). The components of these gamma radiations coming from Ra B are more easily absorbed than the Ra C gamma components, and are largely absorbed from the primary beam by small thicknesses of metal filter, 6 mm. of Pb being adequate to reduce them approximately to zero.[32]

Actually, the measurements are further restricted by the necessity of making them in free air to avoid secondary effects from materials of high atomic number, or even from large masses of light material.

We have previously introduced the values of r/mgeh-cm. as evidence of the negligible effect of "wall thickness" on air ionization measurements, with large volumes of radiated air surrounding the enclosed chamber. Let us now consider the magnitude of the constant itself.

At first glance (Table III), the values of r/mgeh-cm. presented seem to be quite various, but it is interesting to see that their differences generally correspond to the filter used, and to whether or not point conditions obtained in the measuring procedure. The measured values presented fall, apparently, into two general groups: those of a magnitude in the region of 9.0, and those evaluated at approximately 30 per cent lower.

These two separate values stand quite logically when it is recalled that the low values represent air ionization produced by radiation heavily filtered to remove entirely the softer Ra B components, and the higher values represent air ionization, generated with a comparatively light filter at the source. The separation of these two groups of values has arisen from the convention followed by Eve[5,6] in observing the ionization produced by Ra C *only* (using a filtration equivalent to 6 mm. Pb in order to remove the gamma components of Ra B), and from the general use of 0.5 mm. Pt as a filter in therapy. (Since the absorption coefficients of Ra B and Ra C gamma radiations are in themselves complex, it is not desirable to attempt to reduce the observations at 6 mm. Pb filtration back to a precise value at 0.5 mm. Pt.)

V. EXPERIMENTAL DETERMINATION OF THE VALUE: r/MGEH-CM.

We have made further measurements on the value of the conversion unit, *r/mgeh-*

cm., at the Biophysics Laboratory of the Cleveland Clinic Foundation, and at the Tumor Clinic of the Michael Reese Hospital in Chicago. *As reported in Table III, our value of the ionization constant for gamma radiations of Ra B and Ra C filtered by 0.5 mm. Pt is 8.8 r/mgeh-cm.*

When these measurements are compared with the best values deduced from the original report of Glasser and Mautz[12] in 1930 taken from their observations at distances of 2 cm. and beyond, we obtain the values shown in Table II.

TABLE II

IONIZATION INTENSITIES MEASURED AT A POINT AT VARIOUS DISTANCES FROM A POINT SOURCE

Distance in Centimeters	Present Values	Glasser-Mautz (1929) Values Corrected for Air Density
1.0	8.8	
2.0	2.20	2.19
3.0	0.98	0.985
4.0	0.55	
5.0	0.35	0.35

Our measurements of the gamma radiation ionization intensities in Cleveland were made with a condenser ionometer,[13] using the arrangement of source and receiver shown in Figures 2 and 3; the observations are presented in Figure 4.

A description of the technique follows:

A small chamber adapter (Fig. 3) was attached to the condenser unit of the ionometer and upon this, several small chambers were used in succession. (A complete distance-intensity curve was obtained with one chamber at a time.) The length of the air column was made the variable factor between the different chambers in order to determine the manner in which the intensity measurement at a given distance was affected by the finite extent of the receiver.

The measurements with the condenser ionometer were made by a direct method, with the assumption that the graphite shells of the ionized volumes acted as an air wall for the filtered gamma rays observed. The intensity values obtained were evaluated from the physical constants of the measuring instrument itself.

The electrical capacity of the ionization system was determined to a precision of 1 per cent by a substitution method using a capacity bridge. The volt sensitivity of the electrometer was observed at each exposure by the use of a 600 volt battery, an accurate high ohmage resistor, and a type K potentiometer.

The gamma radiation source was 25.3 milligrams of Ra contained in a monel metal capsule. A platinum capsule with walls 0.05 cm. thick served as the container for the radium

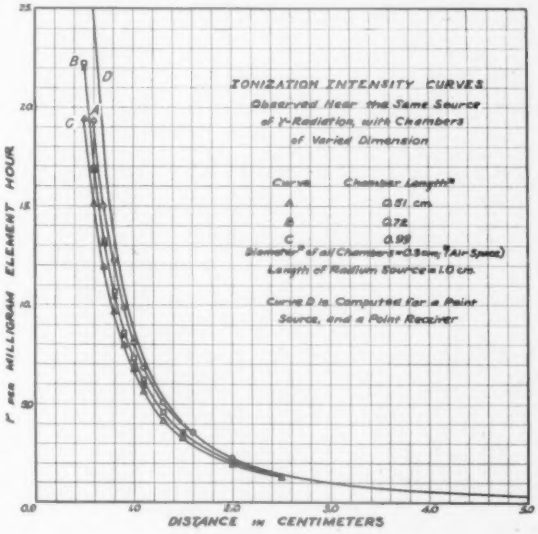

FIG. 4. Ionization intensity curves.

tube, and as a filter for the radiation. (A thin sleeve of graphite served to center the monel tube precisely within the Pt container.)

In order to minimize scattering, the Pt container was mounted on the end of a wooden shaft, as shown in the figures, so that both source and receiver were freely supported in air. The wooden shaft was fixed to the sliding plate on the bed of a small Michelson interferometer* which had an accurate screw thread. The distance between the axes of the radium tube and the ionization chamber could be determined with good precision from the readings of the vernier head on the screw of the instrument. Temperature and barometric pressure were recorded with each series of readings, and from these values the usual gas density corrections were applied. Corrections for dielectric leakage were used when necessary. Each recorded value of ionization intensity followed as the mean of at least three discharge observations.

* Prof. D. C. Miller of Case School of Applied Science kindly permitted us the use of this instrument.

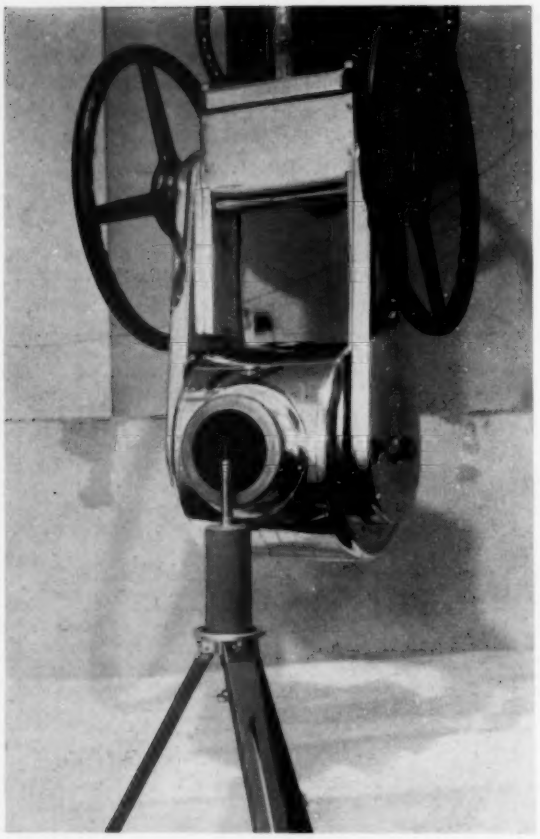

FIG. 5. Two gram radium pack.

The ionization intensity values observed with the different chambers (Fig. 4) are significant in defining experimentally the conditions under which point conditions may actually be realized.

The curves obtained with chambers *A*, *B* and *C* definitely show the effect of the spatial extent of each chamber upon the measured number of *roentgens* per milligram-element-hour.

In viewing the intensity curves, one must keep in mind that it is the vertical (intensity) separation between the curves that is important. Close to the radium capsule, one finds the maximum of difference between the measured values, for the divergence of radiation energy is at its highest there. As one would expect, the longest chamber, *C*, shows the least value of intensity at various axial distances from the radium capsule because the end regions of its ionizing volume are most remote from the source of radiation.*

As the distance from the source increases for all of the chambers, the differences in their measured intensities become less and less until the curves finally converge.

At the region of convergence and beyond one may assume that *the source and receiver are acting as true points*, and that the inverse square law then properly describes the variation of intensity with distance.

For these small chambers, a convergence of the intensity values occurs beyond 2 cm. The observed intensities at distances greater than 2 cm. fits an inverse square law. If one traces the inverse square intensity curve back toward the source, an

* When the comparatively large size thimble chamber of radiotherapeutic practice (usual volume: 2 c.c.) is used to measure the air ionization due to filtered gamma rays from a radioactive source, one must be certain that the distances are sufficiently great to insure point conditions. For a radium needle 1 cm. long, and an approximately spherical ionization chamber volume of 2 c.c., the measurements must be made with a separation of at least 5 cm. between source and receiver.

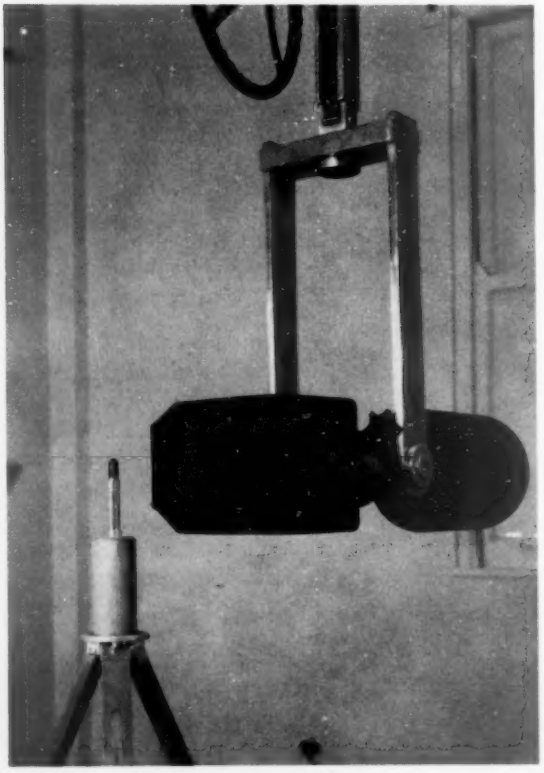

FIG. 6. Four gram radium pack.

intensity value for a point source and receiver may be determined at 1.0 cm. *This value is 8.8 r/mgeh-cm.*

In order to compare these measurements, necessarily made with small volume chambers on a small source and at short distance with those made by a standard type of ionometer (air volume 2 c.c.) on a large radioactive source of gamma radiations, we have made a series of ionization measurements on the 2 gram and 4 gram packs at the Tumor Clinic of Michael Reese Hospital.* Figures 5 and 6 show the size relation of the thimble chamber of the Victoreen condenser units to the pack apertures. The condenser units were placed at a greater distance from the source than shown (actually 25 cm. to 75 cm.) in order to obtain true point conditions.

The minimum distance for true point conditions could easily be determined with exactitude by comparison of an integrated intensity value for the radiation from the distributed source, with values computed from the inverse square law, assuming a point source. The radiation was filtered by an added 1 mm. Cu+1 mm. Al to remove the soft secondary components from the walls of the orifices of the packs.

From these measurements with a Victoreen condenser r-meter calibrated by a standard air chamber in the roentgen-ray spectrum, we observed, *for gamma radiation from Ra B+Ra C, filtered by 0.5 mm. Pt, a value of 8.9 r/mgeh-cm.*

Since these closed chamber measurements are reproducible, the factor of difference between them and an ideally functioning open air chamber can be expressed by a constant quantity, be it 0.9 or 1.1, when the uncontrovertible proof is finally given of the absolute value of the *roentgen* in terms of a radium standard.

As an attendant consideration to these conclusions, the problem of measuring the true roentgen in air should not be confused with that of measuring an intensity unit in tissue. It is the air ionization unit, in relation to the accompanying electromagnetic energy, which forms an accurate step in the evaluation of tissue dosages.

* Dr. Max Cutler, Director of the Tumor Clinic, very generously arranged for our convenience in making these measurements.

VI. SUMMARY AND CONCLUSIONS

Experimental studies of the standard air chamber during the past few years have shown it to be incapable, in its present form, of measuring the true value of free air ionization produced by radiations of very short wave lengths.

These limitations of operating range do not seem to affect ionization measurements made with the small enclosed type of chamber when measurements are made in a large volume of irradiated air.

A series of studies of the adequate nature of air wall materials for enclosed chambers has been put forth by many authors, and seems to find a useful unification of result in the measured values of the radium ionization constant: *r/mgeh-cm.*

The constant *r/mgeh-cm.* can thus properly serve as a standard upon which to base the ionization measurements of ultra short wave radiations.

We have conducted further measurements on the value of *r/mgeh-cm.* and have obtained results in general agreement with our earliest measurements, and with the work of other authors. Our value of the air ionization constant for gamma radiations of Ra B and Ra C, filtered by 0.5 mm. Pt, is 8.8 *r/mgeh-cm.*

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Thirty-seventh Annual Meeting: Cleveland Hotel, Cleveland, Ohio, Sept. 29-Oct. 2, 1936.

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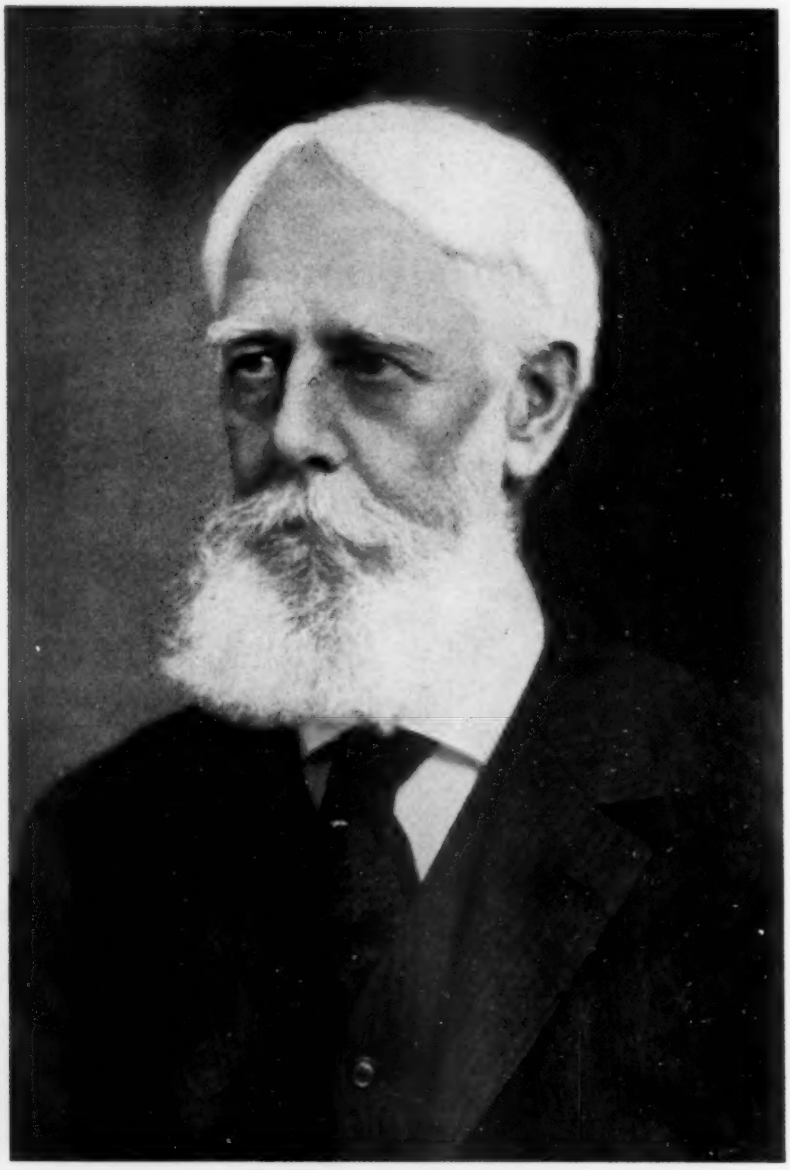
Twenty-second Annual Meeting, 1937: To be announced.

EDITORIAL



FRANCIS HENRY WILLIAMS
1852-1936

FOR five years following the discovery of the roentgen rays, the bookshelves of the pioneer American medical radiologist held principally the published records of the observations of physicists who had undertaken the greater part of the earliest investigation of the subject. He awaited the appearance of a monograph which

would deal purposefully with the *clinical* application of x-rays. His patience was rewarded by the publication of the records of five years' practical accomplishment, carefully and thoroughly prepared, in the form of a book of over six hundred and fifty pages, entitled "The Roentgen Rays in Medicine and Surgery," from the pen of Francis H. Williams of Boston. In its three editions, all of which appeared within the short span of three years, this book remains as a monument to an extraordinarily useful life of over eighty-four years that was terminated on June 22, 1936—useful in an earlier career of clinical medical practice and teaching, but supremely effective through forty years of unremitting devotion to study of the roentgen rays and of radium and to the application of their physical effects to the problems of medicine.

Born in Uxbridge, Massachusetts, Doctor Williams was a son of Henry Willard and of Elizabeth (Dewe) Williams. At the age of twenty-one he was graduated from the Massachusetts Institute of Technology. The year following his graduation was spent in a tour around the world, which included a visit to Japan as a member of the United States Transit of Venus Expedition. In 1877 he received the degree of Doctor of Medicine from Harvard University, and the following two years he devoted to medical study in Europe. In 1879 he began his long career as a practising physician in Boston. At the Harvard Medical School he was appointed, in 1884, an Instructor in Materia Medica and during the years following 1885 became successively Instructor in Materia Medica and Therapeutics, Assistant Professor of Materia Medica and Therapeutics and Assistant Professor of Therapeutics. In 1891, he married Miss Anna Dunn Phillips of Boston.

It was as Visiting Physician to the Boston City Hospital that Doctor Williams began in 1896 his work with the roentgen rays. At first, he was compelled, through lack of hospital facilities, to take his patients to the Rogers Laboratory of Physics at the Massachusetts Institute of Technology to examine them with the fluoroscope. During the winter of 1896 he made there many such investigations of pulmonary tuberculosis and other chest cases transported from his wards at the City Hospital, so firm was his belief in the value of the roentgen rays as an aid in the diagnosis of thoracic conditions. Eventually, a small room in the basement of the hospital was granted him by the trustees, where for nineteen years—until 1915—he carried on his work in radiology in addition to his duties as Visiting Physician. In the course of these years the roentgen-ray department of the Boston City Hospital was officially established. In 1913 he was appointed Senior Physician.

Even before the period of his devotion to radiology, Doctor Williams's work in general internal medicine gave evidence of his mental discernment and vision. In 1892, he had initiated bacterial examinations at the Boston City Hospital and in 1894 was the first in his community to use antitoxin in the treatment of diphtheria. Thus it is easy to appreciate the intensity of his interest, stimulated by this quality of perspicacity, in the discovery of the roentgen rays in 1895 and of radium three years later.

Doctor Williams's previous clinical experience definitely influenced his attitude toward the status of the roentgen-ray examination in diagnostic problems. To his mind, such a procedure involved as close a clinical relationship as do those of palpation, auscultation or percussion; moreover, in its use he foresaw greater diagnostic revelations than most pre-existing clinical methods could promise. As a means to this end, the rational application of the fluoroscopic screen in diagnosis attracted him at once, although, in his work at the Boston City Hospital during the short but intensive "fluoroscopic era" which obtained everywhere from 1896 to 1900, he successfully withstood the importunate demand for the almost exclusive use of the fluoro-

scope in every diagnostic problem, even those of minor surgery, to which the roentgen rays could be applied at that day. As he subsequently wrote: ". . . it was the confidence I had in the possibilities of the fluoroscope to assist in the diagnosis of diseases of the lungs and heart that led me to begin and develop this method of examination."

This belief in a new and promising method broadened Doctor Williams's viewpoint as an internist to a degree quite beyond his time, because he perceived how much the diagnostic powers of even the most skillful clinician might thereby be strengthened. By the beginning of 1898, hardly over two years from the moment of Röntgen's discovery, and through the medium of the fluorescent screen, he had publicly discussed the application of the roentgen rays to the diagnosis of thoracic aneurysm, pericardial effusion, cardiac hypertrophy, cardiac transposition, emphysema, pleurisy with large or slight effusion, pneumothorax, hydropneumothorax and pulmonary tuberculosis. In addition, he demonstrated that early or central pneumonitis can be revealed by roentgen rays when auscultatory evidence of their presence is not discernible. He also established the superiority of the fluoroscope in paramediastinal diagnosis over the roentgenographic methods then available. In 1899, Doctor Williams and Dr. Walter B. Cannon carried out some of the very earliest investigations, by means of the fluoroscope, on the human alimentary tract. In two children of seven and ten years of age, they demonstrated the relationship of visceral position to subjective posture, the excursion of the stomach in respiration and its changes in shape during digestion.

The common experience of the pioneer, whatever his field of endeavor, was shared by Doctor Williams. His belief and confidence in the efficiency of the fluoroscopic screen in the hands of the trained observer and his diagnostic conclusions derived from his own use of it courted skepticism and even antagonism from his clinical colleagues. One of his treatises on the subject was rewarded by this editorial appendage to a review of it: "The author is evidently an enthusiast. It is unfortunate that he has confined himself so largely to work with the fluoroscope. Observations made in this manner are liable to errors of personal interpretation . . . "

Doctor Williams was an early exponent of the theory (a thoroughly sound one before the day of efficient output rectification) that no source of gas-tube energization could equal in excellence the static machine, and that it remained only to amplify the current capacity of such an apparatus by increasing the number and diameter of its stationary and revolving plates. He and his able coadjutor, Dr. William Rollins, therefore designed a machine with plates so large (nearly seven feet in diameter) that the chamber of dehydrated air in which they revolved was actually a *room* of the hospital x-ray department. The increased output of this apparatus ensured the fluoroscopic results of which Doctor Williams took such effective advantage.

Doctor Williams paid no heed to the theory promulgated many years ago that the rays emanating from a tube under excitation by a static machine can have no deleterious effect on the human skin. From the very start of his work he felt that radiations of such power of penetration must be inimical to the integrity of living tissues, and forthwith Doctor Rollins and he adopted every means to protect themselves and their patients. Many of these methods were described in the literature, and had their importance been more deeply appreciated by Doctor Williams's younger and perhaps more thoughtlessly ardent contemporaries, profound physical misery and great loss of precious lives might have been avoided. Both he and Doctor Rollins reached the completion of their long and useful careers without physical blemish resulting from the untoward effect of radiation from either roentgen rays or radium.

Doctor Williams recently wrote that his

attention was first called to radium in the year 1900 by this invaluable associate, who put into his hands a capsule containing chloride of radium, with the suggestion that it might be used for therapeutic purposes. This occurred during the *year preceding* the famous "Becquerel burn" of 1901, from which historians have been prone to date the inception of curie therapy.

Doctor Williams's pre-medical years of education at a great technological institution was undoubtedly the reason of his possession of so many instruments of precision for accessory use in his work, as was the able cooperation of his friend, Dr. William Rollins, likewise possessed of a sound technical education. This cooperation, extending over the course of many years resulted in the production of many devices aiding the practical application of both the roentgen rays and radium; among them, the fluorometer, for the mensuration of roentgen rays (1902) as well as for the estimation of the proportions of electrons (beta particles) and gamma rays given off from radium salts (1903); the "see-hear," a fluorescent screen combined with a phonendoscopic diaphragm, for noting intrathoracic sights and sounds simultaneously; a mechanical stereoscopic fluoroscope involving the use of two discs rotating on one shaft, in contradistinction to the type wherein a Coolidge-tube alternator and an alternating eye-shutter are synchronized electrically.

Doctor Williams was fascinated by the physics of radiotherapy, especially that of the roentgen rays and radium, but he was likewise ever the clinician; it is obvious that his predilection for therapeutic work was in great measure due to his early training as a teacher of therapeutics. He was of that older school of physicians which has not lost sight of the fact that *cure* is the sole desire of the patient, or at least relief, if cure is not to be his lot. The impulse that led to his transition from the environment of his bedside ministrations to the equally absorbing and equally clinical field of the roentgen-ray "laboratory" was a fortunate thing for American Radiology and its developmental progress.

Through his authoritative work and his prolific writings, Doctor Williams was well known in the greater medical centers of the world. He was a Fellow of the American Association for the Advancement of Science and of the American Academy of Arts and Sciences. He was President, from 1917 to 1918, of the Association of American Physicians; an Active Member of the Massachusetts Medical Society, of the American Medical Association and of the Société de Radiologie Médicale de France; a Corresponding Member of the K. K. Gesellschaft der Aerzte in Wien, and an Honorary Member of the American Radium Society, of the American Roentgen Ray Society and of the Radiological Society of North America. Doctor Williams had been a life Member of the Corporation of the Massachusetts Institute of Technology since 1882 and a member of its Executive Committee during the course of the first twenty-five years of its existence.

During the later years of his life, Doctor Williams did not frequently appear at the meetings of scientific bodies of which he was an honorary member. His attendance at the Twenty-fifth Annual Meeting of the American Roentgen Ray Society will be affectionately remembered by those who were privileged to listen to his "Reminiscences of a Pioneer in Roentgenology and Radium Therapy." In more recent years he, in turn, recalled this meeting and the unalloyed pleasure it afforded him. At this time, his generous and kindly nature was again manifested in his gift to the Society of a card-catalogue of the work of over ten thousand contributors to the radiologic literature, with abstracts.

In 1930, Doctor Williams retired from active practice, but he continued his personal contributions to the literature, as is shown by the appearance, during the course of his eighty-fourth year, of a small volume on "Radium Treatment of Skin Diseases, New Growths, Diseases of the Eyes and Tonsils." Herein is reviewed his

work of many years, with especial reference to the regions mentioned. It illustrates copiously the many ingenious instruments of his design for the application of radium to these areas, under proper filtration.

By those who saw Doctor Williams more often and perhaps knew him better, his sedate and dignified bearing, with its least touch of diffidence, will be clearly remembered. The image of his tall figure, moving with its graceful stride through his wards at the Boston City Hospital or the rooms of its radiological department that he loved so well, makes a lasting imprint on the minds of those who were fortunate enough to have been contemporaries of his active and completely efficient life, and to have learned from him much, both by precept and example. This life has added both lustre and dignity to the Science of Radiology, and affords stimulation to those who would help to perpetuate its ideals in like manner.

PERCY BROWN

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

Items for this section solicited promptly after the events to which they refer.

MEETINGS OF ROENTGEN SOCIETIES*

UNITED STATES OF AMERICA

AMERICAN ROENTGEN RAY SOCIETY
Secretary, Dr. F. P. Pendergrass, University Hospital, Philadelphia, Pa. Annual Meeting: Cleveland, Ohio, Sept. 29–Oct. 2, 1936.

AMERICAN COLLEGE OF RADIOLOGY
Secretary, Dr. B. H. Orndoff, 2561 N. Clark Street, Chicago, Ill. Annual meeting, 1937: To be announced.

SECTION ON RADIOLOGY, AMERICAN MEDICAL ASSOCIATION
Secretary, Dr. J. T. Murphy, 421 Michigan St., Toledo, Ohio. Annual meeting, 1937: To be announced.

RADIOLOGICAL SOCIETY OF NORTH AMERICA
Secretary, Dr. D. S. Childs, 607 Medical Arts Bldg., Syracuse, N.Y. Annual meeting: Cincinnati, Ohio, Nov. 30–Dec. 4, 1936.

RADIOLOGICAL SECTION, BALTIMORE CITY MEDICAL SOCIETY
Secretary, Dr. W. B. Firor, 1100 N. Charles St., Baltimore. Meets third Tuesday each month, September to May.

RADIOLOGICAL SECTION, CONNECTICUT STATE MEDICAL SOCIETY
Secretary, Dr. Max Climan, 242 Trumbull St., Hartford, Conn. Meets annually in May. Special meetings may be called by the Chairman.

RADIOLOGICAL SECTION, LOS ANGELES COUNTY MEDICAL SOCIETY
Secretary, E. N. Liljedahl, Los Angeles, Calif. Meets on the second Wednesday of each month at the County Society Building.

RADIOLOGICAL SECTION, SOUTHERN MEDICAL ASSOCIATION
Secretary, Dr. Roy G. Giles, Temple, Texas. Annual meeting, Baltimore, Md., Nov. 17–20, 1936.

BROOKLYN ROENTGEN RAY SOCIETY
Secretary, Dr. E. Mendelson, 120 E. 19th St., Brooklyn, N. Y. Meets monthly on first Tuesday, October to April.

BUFFALO RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Joseph S. Gian-Franceschi, 610 Niagara St., Buffalo, N. Y. Meets second Monday of each month except during summer months, place of meeting selected by the host.

CHICAGO ROENTGEN SOCIETY
Secretary, Dr. R. G. Willy, 1138 N. Leavitt. Meets second Thursday of each month October to May inclusive at the Palmer House.

CINCINNATI RADIOLOGICAL SOCIETY
Secretary, Dr. H. G. Reineke, General Hospital Cincinnati, Ohio. Meets third Monday of each month, October to May, inclusive.

CLEVELAND RADIOLOGICAL SOCIETY
Secretary, Dr. North W. Shetter, 14600 Detroit Ave. Meetings are held at 6:30 P.M. at the Cleveland Chamber of Commerce Club rooms on the fourth Monday of each month from October to April, inclusive.

DENVER RADIOLOGICAL CLUB
Secretary, Dr. K. D. A. Allen, 452 Metropolitan Building, Denver, Colorado. Meets on any month having a fifth Monday.

DETROIT ROENTGEN RAY AND RADIUM SOCIETY
Secretary, Dr. E. R. Witwer, Harper Hospital. Meets monthly on first Thursday from October to May, at Wayne Country Medical Society Building.

FLORIDA STATE RADIOLOGICAL SOCIETY
Secretary, Dr. Gerard Raap, Miami, Florida. Meetings held twice a year, May and November.

ILLINOIS RADIOLOGICAL SOCIETY
Secretary, Dr. Cesare Gianturco, 602 W. University Ave., Urbana, Ill. Regular meetings held quarterly.

INDIANA ROENTGEN SOCIETY
Secretary, Dr. C. C. Taylor, Indianapolis, Ind. Meeting held the second Sunday in May annually.

LONG ISLAND RADIOLOGICAL SOCIETY
Secretary, Dr. M. Dannenberg, 1464 Eastern Parkway, Brooklyn, N. Y. Meets on third Thursday of each month from October to May, at 8:30 P.M.

MICHIGAN ASSOCIATION OF ROENTGENOLOGISTS
Secretary, Dr. C. S. Davenport, St. Lawrence Hospital, Lansing, Mich. Three meetings a year, Fall, Winter, and Spring.

MILWAUKEE ROENTGEN RAY SOCIETY
Secretary, Dr. S. A. Morton, Columbia Hospital, Milwaukee, Wis. Meets monthly. Place of meeting designed by the president.

MINNESOTA RADIOLOGICAL SOCIETY
Secretary, Dr. L. G. Rigler, University Hospital, Minneapolis, Minn.

NEBRASKA STATE RADIOLOGICAL SOCIETY
Secretary, Dr. D. A. Dowell, Medical Arts Bldg., Omaha, Nebr. Meets third Wednesday evening of each month.

NEW ENGLAND ROENTGEN RAY SOCIETY
Secretary, Dr. E. C. Vogt, 300 Longwood Ave., Boston, Mass. Meets monthly on third Friday, Boston Medical Library.

RADIOLOGICAL SOCIETY OF NEW JERSEY
Secretary, Dr. P. S. Avery, New Brunswick, N. J. Meets annually at time and place of State Medical Society. Mid-year meetings at place designated by the president.

NEW YORK ROENTGEN SOCIETY
Secretary, Dr. E. F. Merrill, 30 W. 59th St., New York. Meets monthly on third Monday, New York Academy of Medicine, at 8:00 P.M.

NORTH CAROLINA ROENTGEN RAY SOCIETY
Secretary, Dr. Major Fleming, Rocky Mount, N. C. Annual meeting at time and place of State Medical Society. Mid-year scientific meeting at place designated.

CENTRAL NEW YORK ROENTGEN RAY SOCIETY
Secretary, Dr. C. F. Potter, 820 S. Crouse Ave., Syracuse, N. Y. Three meetings a year—January, May, and November.

PACIFIC ROENTGEN CLUB
Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

PENNSYLVANIA RADIOLOGICAL SOCIETY
Secretary, Dr. L. E. Wurster, Williamsport, Pa. Next annual meeting June 5 and 6, 1936, Lycoming Hotel, Williamsport, Pa.

PHILADELPHIA ROENTGEN RAY SOCIETY
Secretary, Dr. Thomas Loughery, Germantown Hospital. Meeting first Thursday of each month from October to May inclusive, at 8:15 P.M., in Thompson Hall, College of Physicians, 19 S. 22d St.

ROCHESTER ROENTGEN RAY SOCIETY, ROCHESTER, N. Y.
Secretary, Dr. Camp C. Thomas, 476 Lake Ave. Meets on second Thursday from October to May, inclusive, 8 P.M., Rochester Academy of Medicine Building.

ST. LOUIS ROENTGEN RAY SOCIETY
Secretary, Dr. P. C. Schnoebelen, Missouri Bldg., St. Louis, Mo. Meets first week of each month. Time and place of meetings designated by president.

SOUTH CAROLINA X-RAY SOCIETY
Secretary, Dr. R. B. Taft, 105 Rutledge Ave., Charleston. Meets at time and place of South Carolina State Medical Association.

TENNESSEE RADIOLOGICAL SOCIETY
Secretary, Dr. F. B. Bogart, 311 Medical Arts Bldg.

* Secretaries of Societies not here listed are requested to send the necessary information to the Editor.

Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

Texas Radiological Society
Secretary-Treasurer, Dr. J. H. Smith, Lubbock, Texas
Meets annually one day preceding the meeting of the Texas State Medical Association.

University of Michigan Department of Roentgenology Staff Meeting
Secretary, Dr. C. B. Peirce, University Hospital, Ann Arbor, Mich.
Meets each Monday evening from September to June, at 7 P.M. at University Hospital.

University of Wisconsin Roentgen Club
Secretary, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis.
Meets monthly on last Thursday, October to April, Service Memorial Institute, at 4:30 P.M.

Virginia Roentgen Ray Club
Secretary, Dr. V. W. Archer, University Hospital, University, Va.
Meets annually in October.

Cuba

Sociedad Cubana de Radiologia y Fisioterapia
Secretary, Dr. Francisco Padron, Enrique, Villuendas 64, Havana, Cuba. Meets monthly in Havana.

British Empire

British Institute of Radiology Incorporated with the Röntgen Society
Meets on the third Thursday of each month, from November to June inclusive, at 8:15 P.M., at 32 Welbeck St., London, W. 1, or as advertised.

Electro-Therapeutic Section of the Royal Society of Medicine (Confined to Medical Members)
Meets on the third Friday of each month during the winter at 8:30 P.M. at the Royal Society of Medicine, 1 Wimpole St., London, W. 1.

Section of Radiology and Medical Electricity, Australasian Medical Congress
Secretary, Dr. H. M. Cutler, 139 Macquarie St., Sydney, New South Wales.

Radiological Section of the Victorian Branch of the British Medical Association
Secretary, Dr. Colin Macdonald, Lister House, 61 Collins St., Melbourne, Australia.
Meets monthly at Melbourne during the winter.

Section on Radiology, Canadian Medical Association
Secretary, Dr. A. H. Rolph, 160 St. George St., Toronto, Ont.

Radiological Section, New Zealand British Medical Association
Secretary, Dr. P. C. Fenwick, The Hospital, Christchurch. Meets annually.

Continental Europe

Belgian Society of Roentgenology
Secretary, Dr. J. Boine, Avenue des Alliés, 134, Louvain (Belgium).
Meets monthly on second Sunday at d'Egmonds Palace, Brussels, except in the summertime.

Sociedad Española de Radiologia y Electrologia
Secretary, Dr. J. Martin-Crespo, Fuencarral, 7, Madrid, Spain. Meets monthly in Madrid.

Société de Radiologie Médicale de France
Meets monthly on second Tuesday, except during months of August and September, 12 Rue de Seine, Paris.

Société Suisse de Radiologie (Schweizerische Röntgen-Gesellschaft)
Secretary for French language, Dr. A. Grosjean, La Chaux de Fonds.
Secretary for German language, Dr. Scheurer, Molzgasse, Biel.
Meets annually in different cities.

Société Francaise d'Electrothérapie et de Radiologie Médicale
Meets monthly on fourth Tuesday, except during months of August and September, 12 Rue de Seine, Paris.

Association of German Roentgenologists and Radiologists in Czecho-Slovakia
Secretary, Dr. Walter Altschul, German University, Prague, 11.52.

Deutsche Röntgen-Gesellschaft (Gesellschaft für Röntgenkunde und Strahlenforschung)
Meets annually in April, alternating one year in Berlin, one year in some other German city. Meets in addition every two years with the Gesellschaft deutscher Naturforscher und Aerzte.
Permanent secretary, Professor Dr. Haenisch, Klopstockstrasse 10, Hamburg, Germany.

Süd- und Westdeutsche Röntgengesellschaft
Meets annually in different cities.

Nord- und Ostdeutsche Röntgengesellschaft
Meets annually in different cities.

Dutch Society of Electrology and Roentgenology
Holds two meetings a year in Amsterdam, one in the Spring, and one in the Fall.

Societa Italiana Radiologia Medica
Secretary, Professor M. Ponzio, University of Turin, Turin.

Societatea Romana de Radiologie si Electrologie
Secretary, Dr. G. Gatoschi, Str. Isvor 14–16, Bucarest.
Meets second Monday in every month with the exception of July and August.

All-Russian Roentgen Ray Association, Leningrad, USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson.
Meets annually.

Leningrad Roentgen Ray Society
Secretaries, Drs. S. G. Simonson and G. A. Gusterin.
Meets monthly, first Monday at 8 o'clock State Institute of Roentgenology and Radiology, Leningrad.

Moscow Roentgen Ray Society
Secretaries, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konobejevsky.
Meets monthly on the first Monday at 8 o'clock, the place of meeting being selected by the Society.

Polish Society of Radiology
Secretary, Dr. Jan. Kochanowski, 45 Gornoslazka St., Warsaw. Meets annually.

Warsaw Section, Polish Society of Radiology
Secretary, Dr. B. Krynski, 11 Zielna St.
Meets once a month except in the summertime.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association. Each of the following societies, with exception of the Denmark Society, meets every second month except in the summertime.

Society of Medical Radiology in Sweden
Meets in Stockholm.

Society of Medical Radiology in Norway
Meets in Oslo.

Society of Medical Radiology in Denmark
Secretary, Dr. G. Biering, Copenhagen.
Meets on the second Wednesday of each month from October to July in Copenhagen, at 8 o'clock in the State Institute of Roentgenology.

Society of Medical Radiology in Finland
Meets in Helsingfors.

Vienna Roentgen Society
Meets first Wednesday of each month, at 6.30 P.M. at Zentral-Röntgen Institut des allgemeinen Krankenhauses Alserstrasse 4.

Orient

Japan X-Ray Association
c/o Orthopedic Surgery, Tokyo Imperial University.
Meets annually in April.

Kinki Roentgen-Abend Society
Director, Dr. Prof. Taiga Saito, Ogawaoike Tyoto Japan. Meets bi-monthly on third Sunday.

PRELIMINARY PROGRAM
of the
MIDSUMMER RADIOLOGICAL CONFERENCE
in the
ROCKY MOUNTAINS, DENVER

Sponsored by the
Denver Radiological Club
August 5, 6, 7, 1936

All Meetings Held in the Venetian Gardens
Hotel Shirley-Savoy

Guest Speakers

(as they appear on program)

Eugene P. Pendergrass, M.D., F.A.C.R., Professor of Radiology, School of Medicine, University of Pennsylvania, Philadelphia

John D. Camp, M.D., F.A.C.R., Assistant Professor Roentgenology, Mayo Foundation, University of Minnesota, Associate in Roentgenology, Mayo Clinic, Rochester, Minn.

J. M. Martin, M.D., F.A.C.R., Professor of Radiology, Baylor University, Dallas, Texas

Clyde K. Emery, M.D., M.R.C.S., L.R.C.P. Assistant Professor Radiology, California Institute of Technology, Pasadena, Calif. Director Radiation Therapy, Cedars of Lebanon Hospital, Hollywood, Calif.

Visiting Speakers of the Radiological Club of Omaha

Howard B. Hunt, M.D., F.A.C.R., Associate Professor Radiology, University of Nebraska, Medical School, Omaha, Nebr.

Anders P. Overgaard, M.D., F.A.C.R., Omaha, Nebr.

Albert F. Tyler, M.D., F.A.C.R., Attending Radiologist, St. Joseph and Immanuel Hospitals, Omaha, Nebr.

T. Tennyson Harris, M.D., Roentgenologist, Clarkson Hospital, Omaha, Nebr.

James F. Kelly, M.D., F.A.C.R., Professor Radiology, Creighton University School of Medicine, Omaha, Nebr.

Edward W. Rowe, M.D., F.A.C.R., Lincoln, Nebr.

Wednesday Afternoon, August 5th

12 to 2:00 P.M. Registration

2:00 P.M. H. P. Brandenburg, M.D., Presiding, President, Denver Radiological Club.

2:15 P.M. W. W. King, M.D., Address of Welcome, President, Colorado State Medical Society, Denver

2:30 P.M. "Recent Advances in Diagnostic Radiology," Ernst A. Schmidt, M.D., Denver.

3:00 P.M. "The Small Intestine," Eugene P. Pendergrass, M.D., F.A.C.R., Philadelphia.

3:45 P.M. "Gastro-intestinal Tract of Children," John S. Bouslog, M.D., Denver.

4:15 P.M. Discussion opened by John D. Camp, M.D., F.A.C.R., Rochester, Minn.

4:30 P.M. Adjournment

4:30 P.M. Clinical Conferences.

Wednesday Evening, August 5th

8:00 P.M. Joint meeting with the Medical Society of the City and County of Denver, T. E. Beyer, M.D., Presiding, President of the Medical Society of the City and County of Denver.

Guest Speakers:

John D. Camp, M.D., F.A.C.R., Rochester, Minn., "Osteoporosis and Its Importance in Medical Diagnosis"

J. M. Martin, M.D., F.A.C.R., Dallas, Texas, "The Physician's Responsibility to the Cancer Patient"

Dutch Lunch in Rathskeller.

Thursday Morning, August 6th

9:00 A.M. Symposium on Gastro-intestinal Disease, Arranged by the Radiological Club of Omaha Chairman—Howard B. Hunt, M.D., F.A.C.R., Omaha

9:15 A.M. "Roentgen Diagnosis of Lesion of the Esophagus," Anders P. Overgaard, M.D., F.A.C.R., Omaha

9:30 A.M. "The Value of the True Lateral Examination of the Duodenum," Albert F. Tyler, M.D., F.A.C.R., Omaha

10:00 A.M. "X-ray Diagnosis of Lesions of the Colon," T. Tennyson Harris, M.D., Omaha

10:30 A.M. "The Value of the Preliminary Film without Opaque Media in the Diagnosis of Abdominal Conditions," James F. Kelly, M.D., F.A.C.R., Omaha

11:00 A.M. "Radiography of the Biliary Tract, before, during and following Operation," Howard B. Hunt, M.D., F.A.C.R., Omaha

11:30 A.M. "Malignancy Originating in the Small Bowel," Edward W. Rowe, M.D., F.A.C.R., Lincoln, Nebr.

12:00 noon Discussion opened by Lorenz W. Frank, M.D., President of the Denver Internists Club, Denver

12:30 P.M. Adjournment

12:30 P.M. Luncheon.

Thursday Afternoon, August 6th

1:00 P.M. to 2:30 P.M. Round Table Discussion of the Problems of Diagnostic Radiology, Chairman—W.W. Wasson, M.D., Denver

2:30 P.M. Symposium on Diagnostic Radiology, S. B. Childs, M.D., Presiding, Denver

"Roentgenologic Findings in Patients with Sciatica and Low-Back Pain," John D. Camp, M.D., F.A.C.R., Rochester, Minn.

3:30 P.M. Discussion opened by Henry W. Wilcox, M.D., President of the Orthopedic Cub of Denver, Professor of Surgery, University of Colorado, Medical School, Denver

3:45 P.M. Heart Measurements, Elizabeth H. Newcomer, M.D., Denver, Nathan B. Newcomer, M.D., Denver

4:00 P.M. Discussion opened by T. D. Cunningham, M.D., Denver

4:30 P.M. Adjournment

4:30 P.M. Clinical Conferences.

THURSDAY EVENING, AUGUST 6TH

6:15 P.M. Social Hour.
Private room to be announced later.

7:00 P.M. Informal Banquet, Venetian Gardens, H. P. Brandenburg, M.D., Presiding, President, Denver Radiological Club

FRIDAY MORNING, AUGUST 7TH

9:00 A.M. "Review of Year's Progress in Radiation Therapy," Paul R. Weeks, M.D., Denver

9:30 A.M. "Radiation Therapy in the Treatment of Carcinoma of the Intraoral Cavity, Larynx, and Pharynx," J. M. Martin, M.D., F.A.C.R., Dallas, Texas

10:30 A.M. "The Management of Carcinomas of the Breast," Clyde K. Emery, M.D., M.R.C.S., L.R.C.P., Pasadena, Calif.

11:30 A.M. Discussion opened by W. W. Wasson, M.D., Denver.

12:15 P.M. Adjournment.

12:30 P.M. Luncheon.

FRIDAY AFTERNOON, AUGUST 7TH

1:00 P.M. Round Table Discussion of Therapeutic Radiology, Sanford Withers, M.D., Presiding, Denver

2:00 P.M. "Chaoul Therapy as Practiced in European Clinics," Eugene P. Pendergrass, M.D., F.A.C.R., Philadelphia.

2:45 P.M. "Radiation Therapy as a Rational Treatment for Fibroids, Menorrhagia, Ovarian Dysfunction, Inflammations, Fungus and Pyogenic Infections, etc." Leonard G. Crosby, M.D., Denver

3:15 P.M. "The Place of Super-voltage X-ray in the Treatment of Malignancies," Clyde K. Emery, M.D., M.R.C.S., L.R.C.P., Pasadena, Calif.

4:00 P.M. Discussion opened by Frank B. Stephenson M.D., Denver

4:30 P.M. Adjournment.

4:30 P.M. Clinical Conferences

INDIANA ROENTGEN SOCIETY

The Ninth Annual Meeting of the Indiana Roentgen Society was held in Indianapolis on June 7, 1936. Dr. John D. Camp of Rochester, Minn., addressed the Society, his subject being "X-ray findings in Spinal Cord Tumors." The following officers were selected for the coming year: *President:* E. M. Van Buskirk, M.D., Fort Wayne; *President-elect:* J. N. Collins, M.D., Indianapolis; *Vice-president:* H. H. Inlow, M.D., Shelbyville; *Secretary-Treasurer:* Clifford C. Taylor, M.D., Indianapolis.

The many friends of Dr. Leopold Jaches will be pleased to learn of his appointment as Assistant Clinical Professor of Roentgenology at Columbia University.

DEPARTMENT OF TECHNIQUE

Department Editor: Robert B. Taft, M.D., M.S., 105 Rutledge Ave., Charleston, S. C.

A SIMPLE ROENTGENOGRAPHIC TECHNIQUE FOR UNILATERAL DENSITY OF THE CHEST

By E. ROBERT WIESE, M.D.
Home for Consumptives
CHESTNUT HILL, PENNSYLVANIA

MARKED differences of density in the two hemithoraces due to fluid, pleural thickening, operative procedures (thoracoplasty), etc., still present difficulties to the average roentgenologist. Various techniques have been devised to surmount these but unfortunately the majority of the methods are rather complicated.

The technique suggested by Sampson[1] necessitates two exposures of the same photographic plate, and halving of the exposure by means of the lead plate he uses is not easy. The use of an opaque plastic, as presented by Gershon-Cohen[2] presents technical difficulties and requires too much time to invite general acceptance. It requires the removal of the tube from the holder, "an eye-piece . . . mounted upon a wire in such a way that the eye can occupy the same position as the focal spot of the tube," drawing upon a stiff sheet of transparent cellulose or glass an outline corresponding to the healthy chest with a grease pencil and then spreading an opaque plastic upon that outline.

After trying out various means of simplifying the methods now employed, the following has proved useful. We have found that the heavy wrapping immediately surrounding some brands of smoking tobacco (Granger, for example), when applied to the healthy part of the chest, contains sufficient material impervious to the roentgen ray to absorb any excessive amount of the radiation.

The metallic material is usually tightly adherent to a heavy waxed paper and, when smoothed out, any number of such wrappings, placed one upon the other, may be used. They may be either stitched together or fastened by narrow strips of adhesive tape. Should such wrappings prove not sufficiently heavy to absorb the unnecessary rays, we suggest the use of thin, pure lead foil fastened either to some thin cloth or paper. Either the wrapper (or wrappers), or the lead foil, should be cut with a heavy scissors (an old bandage scissors has proved of value) and then secured to the healthy side of the chest with narrow strips of adhesive tape. The technique of exposure of the chest varies, of course, in individual cases.

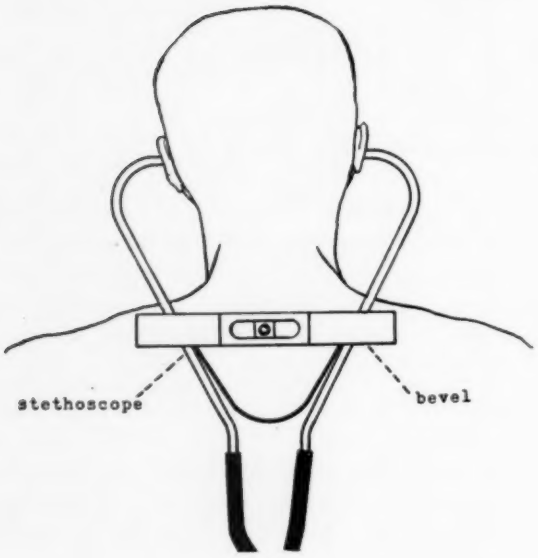
This method presents advantages that should appeal to roentgenologists: it is economical, it is simple, it is practical and it produces diagnostic plates.

[1] Sampson, H. L. Double-exposure roentgenological chest technique. *Am. Rev. Tuberc.*, 1935, *31*, 50–53.

[2] Gershon-Cohen, J. Radiographic examination of the chest employing opaque plastic for equalization of radiographic densities. *Radiog. & Clin. Photog.*, 1935, *11*, 10–13.

A SIMPLE METHOD OF EXACT CENTERING OF THE HEAD

By WILLIAM R. STECHER, M.D.
EASTON, PENNSYLVANIA



A STETHOSCOPE is placed in the patient's ears, with tubing resting upon the back of patient, for postero-anterior projections, and upon the chest of the patient, for anteroposterior projections. An inexpensive bevel is positioned transversely upon the metallic stethoscope tubing, and the head is adjusted until exact level of the bevel is obtained. If very fine coning is employed, viz., nasal accessory sinuses, the stethoscope will not interfere with the view during exposure. It is important to obtain firm pressure with the ear pieces of the stethoscope, and if the spring effect is insufficient, a rubber band can be supplemented. The accompanying illustration is self-explanatory.

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ROENTGEN DIAGNOSIS

HEAD

PAULIAN, D., and SFINȚESCU, S. Reperajul ventricular in epilepsie. (Ventricular landmarking in epilepsy.) *Primul Congres Național de Radiol. și Electrol. Med.* București, October 26–28, 1934, Communicări, pp. 82–87.

The authors performed, between July, 1932, and July, 1934, ventricular landmarking according to the technique of Laruelle (see previous abstracts in this JOURNAL) in a series of 100 cases of epilepsy. In tabulating the results obtained the following conclusions were reached: (1) By disregarding the lesser variation in size of the lateral ventricles which appears of little significance it was found that the greatest percentage of anomalies in decreasing order refers to the visibility of the third ventricle (which indicates a certain degree of dilatation), to the false roots, to the enlargement of one of the lateral ventricles and finally to the marked enlargement of the third ventricle. These modifications are no doubt indicative of stasis resulting from the disturbed circulation of the spinal fluid due to some obstruction in its circulation. (2) From the therapeutic standpoint the cases can be divided into two groups: (*a*) 80 cases in which only one single examination was made and the patients discharged without further observation and (*b*) 20 cases in which the procedure was repeated from two to five times at shorter or longer intervals over a period of one to one and a half years. It is remarkable that in all 20 cases the convulsive spells have completely disappeared. It is the author's contention that the ventricular landmarking has helped to bring to normal the circulation and absorption of the spinal fluid. In several of these cases later roentgenograms revealed a normal ventricular appearance.—*T. Leucutia.*

NECK AND CHEST

BENETATO-MODVAL, MARIA. Aspectul radiologic al mamelei normale și patologice. (Roentgenologic aspect of the normal and pathologic breast.) *Cancerul*, April-June, 1934, *2*, 95–104.

The author studied a number of roentgenograms of the breast with soft tissue exposure, especially from the point of view of possible differentiation between benign and malignant tumor. It was found that the regularity of the border and the invasion of the surrounding structures permits a certain amount of differentiation. Thus, the benign tumors appear with regular borders, whereas the malignant neoplasms show irregular contour with infiltrating bands either towards the cutaneous surface of the mammary gland or especially toward the retromammary space. Normally the retromammary space appears in the form of a narrow clear zone in front of the pectoral muscle. In malignant tumors, when the glandular tissues alone are involved, the space is maintained, but as soon as deeper invasion takes place the retromammary space becomes partially or entirely obscured. It is the author's impression that the method cannot be used with certainty to differentiate all malignant neoplasms from benign tumors but that it may be of value in estimating the operability of the malignant neoplasm. If the retromammary space is extensively invaded one might assume that the pectoralis muscles and the deeper structures are also involved, a fact which might make a malignancy inoperable. Thus, the method has a very limited value.—*T. Leucutia.*

JOHANNESSON, CARL J. Intrapulmonary infection of bronchogenic origin. *Northwest. Med.*, May, 1935, *34*, 176–178.

Bronchogenic extension in cross-infection usually involves the area between the second and fourth ribs. The author's observations indicate that bronchogenic extension of infection to the opposite apex is quite rare. The mechanical factors are discussed and the comment is made that the secondary lesion is almost always peripherally situated, involving the parenchyma. The advisability of patients with destructive infectious lesions in one lung not resting or sleeping on the normal side is stressed. Roentgenologists should carefully study this area of predilection if the secondary infection is to be detected in an early stage.—*W. R. Brooksher.*

Bendove, Raphael A., and Gershwin, Benjamin S. Morphologic varieties of bronchiectasis in the adult; their probable pathogenesis and clinical differentiation. *Arch. Int. Med.*, July, 1934, *54*, 131–144.

The authors review the recent contributions on the respiratory and expulsive functions of the bronchi and give six classifications of bronchiectasis, each of which is characterized by a more or less destructive clinical syndrome and is considered to be the result of different pathogenic factors both structural and functional. These subdivisions are the tubular, cylindric, varicose and globular type and bronchiolectasis and bronchiectatic abscess.

In the tubular form the bronchi appear as hollow cylinders or tubes when injected with iodized oil. Catarrhal or inflammatory conditions of the mucosa are, as a rule, the initial pathologic process. This type follows repeated attacks of chronic bronchitis.

In the cylindric type the bronchi look like solid cylinders when opaque oil is injected. The involved portions resemble the dry leafless branches of a tree in winter. The dilated bronchi have lost much of their resilience as a result of degenerative and sclerotic changes in the myoelastic layers. There are several variations of this type.

In certain bronchi in which has been injected iodized oil, the resulting shadows look like swollen, knotted and tortuous cords which sometimes stretch from the trachea to the bronchioles. The authors call this type varicose bronchiectasis. This form is always found in cases of pulmonary fibrosis.

Bronchiolectasis is very similar to the varicose type except in distribution, it being more in the periphery than the varicose bronchiectasis. Inflammatory lesions of the periphery are the precursors of this type.

In a small number of cases the iodized oil reveals minute globules or capsules filled with fluid scattered throughout the diseased area. The appearance is that of a bunch of grapes. The French clinicians consider this type to be due to syphilis. However, the authors feel that any lesion causing a localized ulceration of the bronchial mucosa may lead to this type of bronchiectasis.

The sixth type is that of primary bronchiectatic abscess. This type is usually caused by an infected foreign material and not infrequently developed following tonsillectomy.

It was observed that each of the six morphological types described had its corresponding clinical syndrome which if not pathognomonic, was always indicative of a bronchiectatic condition. The tubular type was revealed by bronchorrhea and a moderate but continuous cough. The sputum was never purulent nor foul smelling. The ordinary roentgen plate shows no distinctive pathological condition.

The symptom-complex of the cylindric type of bronchial dilatation varies with its distribution. Cough may be absent in the early stages but is a distressing symptom in the later stages. The morning expectoration is most abundant. Sputum is purulent and fetid.

The symptoms of the varicose type are usually submerged under those of the concomitant pulmonary disease. Pain may be a complaint. The clinical findings of bronchiolectasis are also marked by the pulmonary involvement which initiates the condition.

The globular type of bronchiectasis may betray itself by a sudden severe hemoptysis. If infection supervenes the symptoms may simulate another type of bronchiectasis. Neither physical signs nor roentgenologic findings are of diagnostic aid in this type. Bronchography is the only means of diagnosis.

The findings of the bronchiectatic abscess may resemble that of an acute pulmonary abscess or pursue a subacute course with fever, general malaise, lassitude, anorexia, loss of weight and other symptoms.

The authors believe that no diagnosis of bronchiectasis is complete unless the location, distribution and above all, the type have been determined. The therapeutic procedure depends upon this information. They discuss the therapy of the different types.—*J. H. Harris.*

Warner, W. P., and Graham, Duncan. Lobar atelectasis as a cause of triangular roentgen shadows in bronchiectasis. *Arch. Int. Med.*, Dec., 1933, *52*, 888–904.

A brief review is given of the literature concerning the cause of the triangular basal shadows occasionally seen in a chest roentgenogram. The authors were able to demonstrate that these shadows were due to atelectasis of a lobe of the lung which was caused by bronchiectasis. Two cases are reported substantiating this conclusion. Six per cent of all their cases of bronchiectasis have shown this triangular basal shadow. In one of the cases reported the

bronchi were not obstructed but the terminal bronchioles were closed or practically closed by inflammatory swelling of the bronchial walls.

It was possible to produce the triangular basal shadow in lungs of dogs by completely obstructing a lower lobe bronchus by means of a rubber balloon inserted through a bronchoscope.

The authors believe that these shadows are always due to collapsed bronchiectatic lobes and when observed the diagnosis of bronchiectasis is warranted. Bronchographic studies should confirm the diagnosis, however.—*J. H. Harris.*

Traisman, Alfred S. Persistent congenital atelectasis. *Am. J. Dis. Child.*, April, 1935, *49*, 974–984.

Persistent congenital atelectasis in older infants is an interesting and comparatively rare condition. Traisman's patient was a girl aged eleven weeks. The roentgenogram made immediately after admission to the hospital showed an unusual zone of decreased density which extended from the upper part of the left lung to beyond the spine on the right side. There was partial obliteration of the upper half of the right pulmonary field with deviation of the mediastinal structures and trachea to the right. There was marked hyperaeration of the left pulmonary field, especially in the upper two-thirds (compensatory emphysema). The heart was displaced to the right but apparently was not enlarged. A roentgenogram in the lateral view showed a triangular area of increased density in the costophrenic angle posteriorly. This latter was assumed to be due to atelectasis. At post mortem the diagnosis was made of congenital atelectasis of the lower lobe of the left lung, extreme compensatory emphysema of the upper lobe of the left lung, acute tracheobronchitis, compression atelectasis of the entire right lung, displacement of the heart and mediastinum to the right and circulatory congestion of the liver, spleen and kidneys.

Traisman found a rather striking scarcity of case reports in the literature on persistent congenital atelectasis. In his case the infant showed definite cyanosis shortly after birth and continued to have cyanotic spells during the first month of life but during this period before admission to the hospital, no roentgenograms were taken. As a result a proper diagnosis of congenital atelectasis was not made and no treatment to correct the condition was given.

The treatment consists of inhalations of a mixture of from 5 to 10 per cent carbon dioxide and oxygen, which has proved of great value. Traisman emphasizes his conclusion that cyanosis in the new-born and young infants requires thorough clinical study and complete roentgenographic examinations.—*R. S. Bromer.*

Meller, Oscar. Röntgendiagnosticul tuberculozei intratoracice la copil. (Roentgen diagnosis of intrathoracic tuberculosis in children.) *Primul Congres Naţional de Radiol. şi Electrol. Med.*, Bucureşti, Oct. 26–28, 1934. Festivităţi, Rapoarte, pp. 185–239.

1. *Introduction.* Particular characters of the tuberculous infection in children. Our knowledge of tuberculosis in general and of infantile tuberculosis in particular has suffered during the past few years considerable revision. The morphology and dynamics of the tuberculous process in children being different from that in the adult, the roentgen aspects are likewise very different. Furthermore, there is a great variation at the various ages such as in sucklings, small children, school children and at puberty.

2. *Technical considerations.* The delicate structure of the pleuropulmonary apparatus and the still more delicate appearance of the pathological modifications require a special technique of roentgenography. The author prefers the vertical position in all instances with a distance of 60 cm. for infants and small children and teleroentgenography for school children and at puberty. In a series of cadaver experiments, by introducing fragments of various tissues into the lung, it was found that the roentgen visibility of the intrapulmonary structures is rather ill defined, a fact which indicates that many pathological lesions in an early stage escape detection.

3. *Anatomic-roentgenologic considerations of the hilus.* It also results from the above experiments that the present conception on the anatomic equivalent of hilus shadow must be revised in the sense that it represents the summation of several elements such as the pulmonary artery, bronchi, lymph nodes, lymphatic vessels and connective tissue. Both in the normal and the pathologic state the chief rôle is played by the lymphatic and hematologic stasis and by the secondary inbibition of the tissues of the hilar and interlobar space when the process is reversible. In contradistinction

to this the irreversible shadows have as substratum the well formed connective tissue. It is safe, therefore, to assume that the hilar shadow possesses a nonspecific character and that numerous other nonspecific influences may produce identical images.

4. *The primary lesion and primary complex.* It is a unanimous opinion that the tuberculous infection may start in infancy, leading up in adolescence to an infection of about two-thirds of all individuals. The lungs form no doubt the most important site of the primary focus which may vary in size from a roentgenologically invisible pinhead lesion to an invasion of an entire lobe. On the other hand, a great deal of the opacity demonstrated on the roentgenograms must be attributed to the perifocal nonspecific reaction. The dynamics of the lesion is in relation to the age of the patient rather than the size of the primary focus: in infants it nearly always leading to dissemination, and with advancing age showing a somewhat more benign course. After the primary lesion has once become ulcerated the prognosis is very grave and the dissemination is just a question of time, the exact moment of which is difficult to recognize and necessitates repeated roentgen examinations at various angles.

5. *Tracheobronchial adenopathy.* The adenopathy must form the center of our interest because the entire evolution of the tuberculosis is dependent on it. The roentgenological problem in this respect consists in diagnosing the active lesion early. In addition to demonstrating the tumefactions of the glands, in many instances the recognition of the secondary manifestations may lead in the right direction. Thus especially on the left side one often encounters a compression of the ascending bronchus with atelectasis and migration of the mediastinum.

6. *Perifocal reaction.* A further secondary manifestation is the perifocal reaction. The mediastinitis and interlobitis are best demonstrated in a position which is called by the author "exaggerated and combined lordosis" and which consists in placing the patient in exaggerated lordosis with the shoulder corresponding to the normal side directed forward, the incidence of the rays being posteroanterior. On other occasions, bronchiectasis and especially generalized dissemination may represent the predominating complicating factor. This latter may occur either by hematogenous, lymphatic or bronchial extension.

7. *Roentgen characteristics of tuberculosis in puberty.* The evolution of tuberculosis is quite malignant at the time of puberty, all forms of tuberculosis being represented. The dissemination occurs mostly by the hematogenous route and its localization and appearance represent intermediary stages between childhood and adult tuberculosis.

8. *Roentgen aspect of lungs in children vaccinated with BCG.* The author studied the roentgen appearance of the lungs in a number of children inoculated with BCG vaccine. In the new-born inoculated per os, within about thirty days after the inoculation a series of disorders are observed which Calmette called Bcgitis. They consist in a veritable impregnation of the organism by the attenuated virus leading to humoral changes on the one side, and to histopathologic changes, on the other. These latter represent inflammatory reactions localized chiefly to the lymphatic system and hilus. In a series of experiments the author was able to demonstrate bronchovascular and hilar roentgen changes in 80 per cent of vaccinated children. All of the shadows possessed an irreversible character. In reality the impregnation starts immediately after the inoculation but the reactions cannot be demonstrated roentgenologically at the beginning because of the increased heart shadow in the new-born. In a series of children who were inoculated and remained in a tuberculous environment, the intrathoracic changes were even more pronounced. The hilar shadows were more accentuated and complicated with veritable adenopathies, in some instances with calcification. However, of 78 cases thus examined, a dissemination has occurred in only seven. This ought to create a certain optimism, proving that the inoculation produces a roentgenologically visible impregnation, however, without harmful accidents. Furthermore, during the first few years of infancy, which is known to be the most dangerous age for tuberculosis, the malignant forms were encountered relatively rarely.—*T. Leucutia.*

OCTAV, BURILEANU. Röntgendiagnosticul tuberculozei la copil (Coraport pentru medicina internă). (Roentgen diagnosis of tuberculosis in children; medical report.) *Primul Congres Naţional de Radiol. şi Electrol. Med.*, Bucureşti, Oct. 26–28, 1934. Festivităţi, Rapoarte, pp. 240–248.

Intrathoracic tuberculosis of childhood pre-

sents a varied clinical aspect. This polymorphism is influenced by the age, physical state of the child at the time of contamination, the intensity and duration of the contamination and by the manner and time at which the allergy develops. Another important peculiarity of childhood tuberculosis is that it often remains quiescent for a long time, the symptomatology appearing very indefinite. For this reason the clinical examination alone may remain insufficient and one must resort to the tuberculin test, demonstration of the tubercle bacilli in the gastric contents and especially to roentgenography.

The author considers in detail the three types of clinical manifestations of tuberculosis: (1) the pulmonary tuberculosis of first inoculation; (2) the tracheobronchial adenopathy, and (3) the secondary pulmonary tuberculosis due to reinfection. He arrives at the following general conclusions: (1) There are forms of tuberculosis in sucklings and early infancy which may undergo spontaneous healing. These forms, unknown a short time ago, are demonstrated, thanks to the aid of roentgenography. (2) Systematic and repeated roentgen examinations are necessary to establish a diagnosis and to follow the evolution of a pulmonary tuberculosis in childhood. (3) In cases suspected of tuberculosis an early and precise diagnosis may thus be established, this leading to an efficacious and well selected therapeutic intervention.—*T. Leucutia.*

Georgescu, A., Oreviceanu, I., and Popper, M., Cercetări asupra aspectului radiologic al hilului normal şi patologic la copii în primul an. (Investigations on the roentgen aspects of the normal and pathologic hilus in children in the first year.) *Primul Congres Naţional de Radiol. şi Electrol. Medi.*, Bucureşti, October 26–28, 1934, Communicări, pp. 25–27.

A series of investigations were carried out in 160 children in the first year on the roentgen aspect of the hilar shadow, and the following general conclusions were reached: (1) All children who had no contact with tuberculosis and who were not subjected to tuberculosis vaccination presented a normal hilus and pulmonary fields free of any pathologic shadow. (2) The children who received antituberculosis vaccination (the so-called BCG) and who frequently have shown the phenomenon of transitory allergy have shown on roentgen study enlarged hilus and increased bronchial markings extending into the lung fields. (3) In several cases with abnormal pulmonary roentgen shadows but who have shown a negative tuberculin test, subsequent tests revealed that the infection was due to some other cause (localized pneumonia, hereditary syphilis), a fact which proves the value of the tuberculin test in preference to roentgenography.—*T. Leucutia.*

Roesler, H. Interatrial septal defect. *Arch. Int. Med.*, Sept., 1934, *54*, 339–380.

A case report and review of 62 cases of interatrial septal defect are given. The pathology and clinical symptoms are reviewed. The roentgenologic findings were those of a large heart, varying in shape from oval to globular and extending as a rule toward the left. The pulmonary conus and artery projected far to the left and upward and forward. The branches of the pulmonary artery at times showed increased pulsations and were sharply defined and enlarged. Mediastinal tumor and tuberculosis were erroneously diagnosed at times. The aortic knob was small and at times invisible. The enormously dilated right side of the heart caused only a moderate degree of axis deviation to the right in the electrocardiogram. —*J. H. Harris.*

Lazeanu, E. Importanţa diagnosticului radiologic al stazei in venele pulmonare la cardiaci. (Importance of roentgen diagnosis of statis in the pulmonary veins of cardiacs.) *Bul. Soc. de radiol. şi electrol. med. din Romania*, 1934, *3*, No. 5–6, 3–6.

The roentgen examination of the chest permits, in addition to a study of the dimensions of the heart, the demonstration of phenomena of pulmonary stasis which are of prognostic and therapeutic importance. As a rule the presence of a venous stasis indicates cardiac insufficiency which may occur concomitantly with other symptoms such as generalized edema, etc. The association of pulmonary stasis with dilatation of the left auricle in mitral stenosis represents, however, an important sign of circulatory disequilibrium which in many instances forms the one and only symptom of cardiac insufficiency. In this respect one may say that the pulmonary stasis is an early sign, permitting the prevention by rational therapy of more serious complications such as pulmonary edema, etc. It also helps to explain the cause of hemoptysis which is often observed in

such cases. The persistence or aggravation of the venous stasis in serial roentgenograms taken at shorter or longer intervals indicates an aggravation of the cardiac lesion, thus establishing a more grave prognosis.

The author arrives at the conclusion that a systematic roentgen examination at various intervals is imperative in all cases with mitral stenosis to estimate the capacity of compensation of the heart. This applies especially to women affected with mitral stenosis during the course of pregnancy in which the absence of pulmonary stasis forms the best sign of the tolerance to the pregnancy.

The roentgen syndrome of stasis of the pulmonary veins varies according to the intensity of the stasis. The first roentgen manifestation consists in dilatation of the pulmonary veins, this appearing in the form of accentuated hilar shadows with some clouding of their contours. When the stasis is more pronounced the clouding extends to the mid portion of the lungs, whereas in the advanced cases all of the lung fields become more or less obscure. This latter form usually leads to cardiac hemoptysis. If the intensive pulmonary stasis is associated with a progressive dilatation of the left auricle the prognosis becomes exceedingly grave.—*T. Leucutia.*

Moolten, Sylvan E. Hodgkin's disease of the lung. *Am. J. Cancer*, June, 1934, *21*, 253–294.

The author gives a detailed report of the clinical and post-mortem finding of 8 cases of Hodgkin's disease of the lungs. He compares the microscopic picture of lung tissue of these cases with that of infectious granulomas of known etiology (e.g. tuberculosis and actinomycosis), and from the comparison draws conclusions as to the etiology of Hodgkin's disease. He concludes that these cases permit the deduction that this disease is a primary inflammatory reaction of granulomatous character rather than a neoplasm. The lesion in the lung appears to permeate such resistance structures as the walls of arteries and such delicate structures as the walls of alveoli by a uniform infiltration and not by mechanical compression and destruction. The evidences favor the view that the disease is brought about by the diffusion of a virus which stimulates the local proliferation of the mesenchymal elements.

There is a marked difference between the action of neoplastic and Hodgkin's infiltration as regards the bronchial and alveolar epithelium, the Hodgkin's infiltration tending to conserve this epithelium rather than ulcerate it as does neoplastic infiltration.

A discussion is given of the comparative features of the hypothetical virus of Hodgkin's with the known virus of tuberculosis and actinomycosis. He concludes that as in about 10 per cent of all cases of Hodgkin's disease of the lungs the primary lesion is pulmonary, it is not illogical to regard the lung actually as the portal of entry.

A classification of Hodgkin's disease of the lung is given having as its basis the conception of the disease as a form of inflammation with a definite pathogenesis and employing a terminology which reflects this point of view:

1. Granulomatous pan-bronchitis and bronchopneumonia (peribronchial form of granulomatous interstitial pneumonia).
2. Granulomatous pleurogenous pneumonia (pleurogenous form of granulomatous interstitial pneumonia).
   (a) Primary (rare).
   (b) Secondary (invasion from adjacent infiltrated structures, e.g. mediastinum).
3. Exudative lobar and lobular pneumonia.
   (a) Acute (gelatinous pneumonia).
   (b) Subacute and chronic (organizing pneumonia).
4. Miliary, submiliary, and multiple isolated nodular lesions (hematogenous, lymphogenous).—*J. H. Harris.*

Brown, Lloyd T. An x-ray study of the diaphragm. *J. Bone & Joint Surg.*, Jan., 1935, *17*, 133–140.

This study was undertaken to find out what effect, if any, improvement in the general health of children would have on the action and position of the diaphragm. The children studied, by their environment and associations, had been exposed to pulmonary tuberculosis, but showed no clinical or roentgen evidence of the disease. The routine of the children consisted of careful medical supervision by an internist, an expert in the care of tuberculosis, regular periods of play and study and rest periods under the supervision of trained nurses and a physiotherapist. The rest period was always started with the children in the position of hyperextension and a few simple exercises were used to train them in the correct use of the body.

It was found that in many of the children it was possible to make a very close correlation of the gain in weight, the increase in vital capacity, and the size of the chest, with the improvement in the body mechanics, an increase in the amount of the excursion of the diaphragm, a higher position of the diaphragm in the chest, and a lessening of the length of the pleural cavity.

Brown's conclusions follow:

1. The position and the amount of excursion of the diaphragm is affected by the shape of the chest.

2. In the case of a chest which is used in the position of expiration, the common one in faulty body mechanics, not only is the diaphragm in a lower position in the chest, but there is also less excursion.

3. In the case of a chest which is used in the position of good body mechanics, the diaphragm is in a higher position in the chest and there is a greater excursion of the diaphragm.

4. Accompanying these changes, there is also an improvement in the general condition of the patient as a whole—an increase in weight, an increase in vital capacity, and an improvement in the body mechanics.

From the point of view of the prophylaxis as well as of the treatment of pulmonary tuberculosis, a proper understanding of the relationship of body mechanics to respiration is essential. From the findings in his study, Brown advises in cases of pulmonary tuberculosis where surgery is considered necessary, a carefully planned procedure to improve the body mechanics either before or after operation as a logical step in the treatment. It is well recognized that in cases of tuberculosis of the lungs it is usual to find a high position of the diaphragm in the roentgenogram. This is evidently Nature's attempt to take some of the strain away from the infected part and to help reduce the size of the cavities. The position of good mechanics of the whole body not only follows out the line pointed to by Nature in raising the diaphragm in the chest, and by so doing lessens or removes the strain on the lungs or the cavities in them, but it also makes possible a better functioning of the rest of the body.—*R. S. Bromer.*

Forty, Frank. Congenital hernia through right dome of diaphragm. *Brit. J. Surg.*, Jan., 1935, *22*, 500–503.

The case reported is of interest because the congenital hernia caused acute intestinal obstruction in a man seventy years of age and because it occurred in the right dome of the diaphragm. At operation Forty found a circular opening in the right dome of the diaphragm through which at least 3 feet of small intestine had passed into the right pleural cavity. The intestinal obstruction was the result of the constriction due to the margins of the diaphragmatic opening. The hernia was reduced without difficulty and the right lobe of the liver, which had been dislocated to the left, returned to its normal position, thus guarding the opening in the diaphragm.

The author discusses the etiology and classification of diaphragmatic herniae briefly, giving his reasons for considering the hernia in his patient congenital in origin.—*P. J. Hodes.*

Dunhill, Thomas. Diaphragmatic hernia. *Brit. J. Surg.*, Jan., 1935, *22*, 475–499.

There are three stages in the development of the diaphragm. In the first the celomic space is continuous until the growth of the embryonic organs subdivides it into pericardial cavity, pleural space, and peritoneal cavity. It is clear therefore, if the pleuroperitoneal canals should remain open through deficiency in the growth energy of the parts whose proliferation normally closes them, then the pleural and peritoneal cavities will not be separated completely from one another. Because of this, the positive intra-abdominal pressure will carry some of the abdominal organs into the thorax. According to Dunhill this is one of the commonest types of hernia in infants and because the pleuroperitoneal canal remains open no sac is present.

During the second stage in the development of the diaphragm the pleuroperitoneal canal is closed by an ingrowth of its own walls. During this stage a true hernia may occur, for the pleura and peritoneum are complete and have closed their respective cavities. If any abdominal viscera are forced into the thorax at this time a sac will be present.

The diaphragmatic muscle spreads through the membranous diaphragm in the third stage of its development. The growth of the muscle may fail, leading to a deficiency in the muscular attachments of the diaphragm, although the peritoneum and pleura separate the cavities. This condition amounts to an absence of the crura together with the crural attachments and the result is a gap in the diaphragm.

The sites of the hernial orifices in the author's series of 25 patients are as follows:

Retrosternal (foramen of Morgagni)	1
Left dome	2
Costovertebral region—left (hiatus)	3
Esophageal region	
1. Hernia diaphragmatica transversa	3
2. Para-esophageal	2
3. Short esophagus	14

The author then describes the various types of diaphragmatic hernia.

The retrosternal, parasternal, or hernia through the foramen of Morgagni contained the terminal ileum, cecum, ascending and part of the transverse colon. The sac and its contents occupied the anterior mediastinum resting against the pericardium on the left, displacing the right pleura and lung backwards and to the right.

Herniae through the left dome are actually through the substance of the diaphragm and must therefore be distinguished from the costovertebral type. The points of entry and exit are away from the costovertebral angle and imply the position of the defect. The herniated structures are narrowed at the point of entry and exit and are fixed in the abdomen. This visceral fixation would not occur with eventration and helps to differentiate hernia from eventration. Because of the absence of a sac, Dunhill implied that the defect occurred during the celomic stage of diaphragmatic development.

The author prefers "costovertebral angle" hernia to the terms "pleuroperitoneal hiatus" and "foramen of Bochdalek" hernia. He believes that these herniae result from a congenital absence of the left crus and the muscular fibers continuous with it. In each of the 3 cases of this type a sac was present.

Herniae in the region of the esophagus are due to three different anatomical defects. The hernia transversa diaphragmatica is due to a non-development of the crura. The anatomical hiatus does not exist because of the crural defect. Furthermore, there is no posterior attachment of the diaphragm in the region of the aorta, the esophagus, and the vertebral column. The peritoneal sac ascends into the posterior mediastum through this gap.

The hiatus is present in the para-esophageal hernia but is dilated. The esophagus is of normal length, the hernial sac passing up through the hiatus lying beside the esophagus.

The short esophagus type of herniae are associated with a congenitally short esophagus, the cardia and portion of the stomach being situated within the thorax. The condition is due to the failure of the esophagus to elongate in its descent from the cervical region. Because of this the stomach is partially arrested in the posterior mediastinum. The arrested portion is surrounded by a sac so that it is a true hernia. The symptoms in this type of hernia due to stricture and ulceration may become very distressing.

This excellent article contains many fine diagrams which enhance the value of the discussion.—*P. J. Hodes.*

ABDOMEN

Lazeanu, E. Colecistografia. Technica şi interpretarea rezultatelor obţinute prin colecistografie. (Cholecystography; technique and interpretation of results obtained by cholecystography.) *Primul Congres Naţional de Radiol. şi Electrol. Med.*, Bucureşti, Oct. 26–28, 1934. Festivităţi, Rapoarte, pp. 97–116.

In this first article in a symposium on cholecystography, the author discusses the various procedures employed and compares their relative value. It is emphasized that the method permits the direct study of the gallbladder and that the diagnostic results exceed those of any other method of investigation.

In discussing the technique, special attention is given to the oral method which the author recommends as the method of choice. A review of the literature revealed that there are several fatal accidents known which must be attributed to the intravenous application of the dye and therefore he expresses the opinion that this method is not entirely harmless. He refers to the work of Gabeaux of Brussels who made an inquiry of 12,000 cases of cholecystography carried out by 25 Belgian roentgenologists, 6,000 of them being by the oral and 6,000 by the intravenous method. It was found that 11 of the roentgenologists preferred the intravenous and 12 the oral method, although admitting that the results of this latter are somewhat less precise and inconstant. One author used both methods and the last preferred the oral but resorted to the intravenous whenever the oral failed. It was shown that the intravenous method led in 2 cases to death, both of angina, in 15 cases to serious general

reaction and in 15 cases to a local reaction. The general reaction consisted of syncope, dyspnea, general toxicity, and the local reactions of neuritis, phlegmon, phlebitis, local edema, etc. The oral method often led to nausea but not one single serious accident was observed.

The author also discusses in detail the interpretation of the results both as it concerns the modifications of form and position and of the functional test. More recently there is a tendency to employ methods which accelerate the examination such as the method of Antonucci and Sandström. These are also considered in detail.—*T. Leucutia.*

Christide, E., and Făgărăşanu, I. Colecistografia in chirurgia veziculei biliare. (Cholecystography in surgery of the gallbladder.) *Primul Congres Naţional de Radiol. şi Electrol. Med.*, Bucureşti, Oct. 26–28, 1934. Festivităţi, Rapoarte, pp. 117–149.

The addition of cholecystography to the diagnostic armamentarium of the gallbladder has raised the precise diagnoses to nearly 90 or 95 per cent. This must be attributed to the fact that cholecystography permits a functional exploration of the gallbladder, whereas simple roentgenography was of value only in pointing out certain indirect signs of cholecystitis or by permitting the direct visualization of some of the biliary calculi.

To obtain the above results cholecystography must be executed with a correct technique, the examination being associated with a gastrointestinal series and the Meltzer-Lyon test. The true causes which may lead to false interpretation of cholecystograms are exceptional, such as porcelain gallbladder, gallbladders with opaque or purulent contents, calcified tuberculous nodes of the liver, etc. The other causes of error are the result of a faulty technique.

In estimating the value of cholecystography in surgery, one may say broadly that (1) the filling and normal emptying of the gallbladder indicate a normal gallbladder or more exactly a normally functioning gallbladder and (2) the nonfilling indicates in the absence of hepatic insufficiency a diseased gallbladder or at least a gallbladder which does not function normally. However a nonfilling does not necessarily mean sclerotic retraction, calculous cholecystitis, or stenosis of the cystic duct. There are discrete lesions such as, for example, a catarrhal inflammation, which may produce a temporary occlusion of the cystic duct. Thus the cholecystographic method should not constitute the sole factor in establishing an operative indication but the clinical examination should also be taken into consideration. In a series of 29 cases of cholecystography controlled at operation by the author, the percentage of precisely diagnosed cases was 93.2.

The author then discusses in detail, using many illustrations (1) the normal visible gallbladder, (2) the visible gallbladder in cholecystitis, pericholecystitis and stasis, (3) the opaque gallbladder with visible calculi and (4) the invisible gallbladder or negative cholecystography. The conclusion is reached that cholecystography has influenced enormously the surgical procedures in the treatment of gallbladder lesions. On the one hand, more precise operative indications are established; on the other, the entire course of operative intervention is better regulated, the preoperative preparation as well as the postoperative management of the patient being handled in a more skilled manner due to knowledge of the hepatic cellular function. Furthermore, in many instances with vague gastric symptomatology, cholecystography permits the establishment of whether or not other abdominal pathology as, for example, a chronic appendicitis, is associated with gallbladder disease.—*T. Leucutia.*

Pavel, I., and Volovici, B. Valoarea colecistografiei văzută din punct de vedere medical. (The value of cholecystography considered from the medical standpoint.) *Primul Congres Naţional de Radiol. şi Electrol. Med.*, Bucureşti, Oct. 26–28, 1934. Festivităţi, Rapoarte, pp. 150–173.

The report deals chiefly with the physiological interpretation and the diagnostic estimation of cholecystographic results and their comparison with the Meltzer-Lyon test. The requirements of a positive cholecystography are (*a*) satisfactory resorption of the opaque substance through the intestinal tract, (*b*) normal elimination of this substance through the liver, (*c*) normal function of the sphincter of Oddi, (*d*) permeability of the cystic duct, (*e*) integrity of the gallbladder and (*f*) normal concentration capacity of the gallbladder. The requirements of the Meltzer-Lyon test, on the other hand, are (*a*) permeability of the cystic duct, (*b*) integrity of the gallbladder proper, (*c*) persistency of the function of concentration and (*d*) persistency of contraction. A comparison of

these requirements shows that a negative cholecystography may be the result of a pathologic state of four organs (intestine, liver, gallbladder, and sphincter of Oddi), whereas the negative Meltzer-Lyon test implies a pathologic state of only one organ (gallbladder). The Meltzer-Lyon test thus represents a test of the total function of the gallbladder, while cholecystography, in addition to being a functional test of the gallbladder, constitutes a morphologic test, permitting the study of the position, form, relationship of the adjacent organs and occasionally the presence of calculi. This then indicates that in order to establish a more precise diagnosis both methods must be used.

After considering the diagnostic value of cholecystography on the basis of personal cases, which are carefully tabulated, the author establishes the following rules for the medical man in demanding a cholecystographic examination: (1) He should indicate if hypotension is present since it is proved that the intravenous injection of tetraiod itself results in a marked hypotension. This phase of hypotension lasts for about ten or fifteen minutes, there being at the same time acceleration of the respiration and pulse. It would appear safer to resort in all cases of hypotension to the oral method or when one is forced to apply the intravenous method to inject ephedrin concomitantly. (2) He should indicate if the patient has a tendency to nausea or vomiting, in which instance the intravenous method is preferred. (3) In case former examinations have shown a slow concentration of the dye he should advise the use of more rapid methods (Antonucci or Sandström method). (4) In case the patient is of asthenic type and there are signs of a simple atony of the gallbladder, he should ask the roentgenologist to preliminarily empty the gallbladder either by the Boyden meal or duodenal drainage, etc., and to apply the Graham method only after this preliminary procedure, otherwise a negative result may be obtained. (5) In case that at the clinical examination a pericholecystitis is suspected he should ask the roentgenologist to associate the cholecystography with a gastrointestinal series or barium enema in order to demonstrate possible adhesions.(6) If the patient presents a history of recurring attacks of infection, the recommendation of a simple film before cholecystography may lead to the detection of a stone. (7) If the patient suffers from diabetes he should recommend the roentgenologist to have the roentgen films made two or three hours instead of eight to twelve hours after the injection because the diabetic liver shows hyperpermeability for the dye.—*T. Leucutia.*

RADOJEVIC, STEVO. Nos expériences avec la cholécystographie par la voie intraveineuse. (Our experiences with cholecystography by the intravenous route.) *Primul Congres Național de Radiol. și Electrol. Med.*, București, Oct. 26–28, 1934. Festivități, Rapoarte, pp. 179–184.

In discussing the three above reports in the symposium, the author presents his own statistics of 1,881 cases of cholecystography performed by the intravenous route between 1927 and 1933. Four hundred and twenty-six cases were operated upon and it was found that the percentage of preciseness in the diagnosis was 89.5. The following technique was employed in all instances: a simple film of the gallbladder region was made in the morning on an empty stomach. At noon the regular lunch was given. In the afternoon at 4:30 two or three eggs were given to empty the gallbladder. At 6:30 p.m. iodtetragnost was administered intravenously after a preliminary injection of atropin to facilitate opacification of the gallbladder. The next morning at 9 o'clock roentgenograms were made with the patient on an empty stomach. In case of invisible gallbadder the roentgen examination was repeated two hours later, whereas if the gallbladder was visualized the Boyden meal was given three-quarters of an hour later and then a last roentgenogram made to study the evacuation of the gallbladder.

The cases are considered statistically in six groups, according to the type of lesion present, and the following conclusions are drawn: The intravenous method of cholecystography is recommended (1) because it presents no danger to the patient, there having been observed no serious accidents, (2) because it can be applied in ambulatory cases and (3) because it leads to a greater precision of the diagnosis, the correctly diagnosed cases amounting to 90 per cent.—*T. Leucutia.*

HĂNGĂNUT, M., and RĂDULEȚ, V. Câteva considerațiuni asupra cholecistografiei în baza a 942 cazuri. (Some considerations of cholecystography on the basis of 942 cases.) *Primul Congres Național de Radiol. și Electrol. Med.*, București, October 26–28, 1934, Comunicări, pp. 48–50.

In describing the procedure and results of examination of cholecystography in their cases the authors stress that the examination in vertical position is of greater advantage than the one in abdominal decubitus. Its advantages are that it permits a more accurate estimation of the form, tonicity, function and especially the relation of the gallbladder to the adjacent organs. Furthermore, the shadow, being underneath the liver and not superimposed by it, appears clearer. The cystic duct and the choledochus are also brought out to greater advantage than with the horizontal position.

The examination is always started with a preliminary roentgenoscopic study. The gallbladder is localized in the best possible position and obliquity and roentgenograms are made with a rotating Potter-Bucky diaphragm in complete apnea.

In publishing the postoperative control in those cases which were operated upon it was found that the percentage of correct diagnoses was very high, reaching in several groups of lesions 100 per cent.—*T. Leucutia.*

Hațieganu, Iuliu, and Hângănuț, Marius. Considerațiuni asupra cholecistografiei în diabet. (Considerations on cholecystography in diabetes.) *Primul Congres Național de Radiol. și Electrol. Med.*, București, October 26–28, 1934, Comunicări, pp. 54–55.

The authors by performing a series of experiments in diabetic patients concerning the elimination of the tetraiodophenolphthalein arrived at the following conclusions: (1) in sugar diabetes the cholecystogram must be ready within one and a half to two hours after the injection. A delay in its appearance indicates a hepatobiliary drainage; (2) the negative cholecystography in diabetes is of far greater interpretative value due to the increased elimination of the tetraiod; (3) the mechanism of a rapid elimination is explained on the one hand by the evident impermeability for the dye and all components which are eliminated through the bile and on the other by a biliary hyperfunction (hypercholia). It is the authors' belief that this hepatic hyperfunction is the result of hyperglycystia in which the liver and all the tissues take part; (4) the explanation of Antonucci on the rôle of glucose in rapid cholecystography in the sense that the glucose fixes the tetraiod, carrying it more quickly to the liver and thus producing a more rapid passage through it, does not appear to be justified.—*T. Leucutia.*

Schons, Edward. Value of cholecystography by the oral method, with an analysis of 189 operated cases. *Minnesota Med.*, May, 1935, *18*, 269–273.

The reliability of the oral method is stressed. In non-functioning gallbladders, the probability of disease is very high. In poorly functioning gallbladders, the probability of disease is again high, but not so high as in the non-functioning type. More care should be given to the study of the response to the fatty meal, as calculi and other abnormalities are more certainly excluded if a normal shadow is followed by a markedly contracted shadow after the ingestion of food. —*W. R. Brooksher.*

Spangler, Davis. Nine years' experience with gallbladder visualization. *South. M. J.*, Feb., 1935, *28*, 144–147.

Seven hundred and fourteen traceable cases of gallbladder visualization, of which 63 were by the intravenous method, were studied to determine the extent of agreement of the roentgen findings with the final clinical (medical or surgical) diagnosis. Thirty-four patients received more than one examination. Practically 100 per cent of cases with a roentgen diagnosis of calculi were so clinically confirmed. Clinical confirmation was obtained in 95 per cent of cases reported as "non-filling diseased gallbladder" on the roentgen examination, while 90 per cent of those with a diagnosis of "filled diseased gallbladder" were confirmed. The roentgen diagnosis of "normal gallbladder" agreed with the clinical diagnosis in 88 per cent of the cases. Pelvic disease, cardiovascular disease and a few disorders of the appendix and kidney were most commonly diagnosed clinically when there was disagreement with the roentgenological findings.—*W. R. Brooksher.*

Gaither, Ernest H. Gastric carcinoma; a clinical research. *South. M. J.*, Feb., 1935, *28*, 107–114.

An analysis of 245 operatively demonstrated gastric carcinomas emphasizes the need for a new conception of the symptomatology and for a new interpretation of the clinical findings in this disease. A persistent fallacy is that organic structural disease will cause continued and permanent symptoms. That organic malignant disease may present remittent or intermittent symptoms has been positively proved. The following points should be well borne in mind: (1)

local gastric symptoms, loss of appetite, cardialgia, eructation, pyrosis, nausea, vomiting, pain, distention and variable types of discomfort are no worse in beginning carcinomas than in other gastric diseases; (2) a latent stage is possible, during which the process advances very slowly with utter absence of symptoms; (3) a general marasmus, or a variable anemia, may occur, with the gastric symptoms so wholly in abeyance as to be quite unrecognizable; (4) a beginning carcinoma may progress without definite symptoms; again, it is marked by ulcer symptoms, or symptoms of chronic gastric catarrh. The outstanding symptoms in this series are fully discussed and the postoperative results of 25 cases are presented.—*W. R. Brooksher.*

MEUWISSEN, TH., and SLOOFF, J. Roentgen examination of the pyloric canal of infants with congenital hypertrophic pyloric stenosis. *Am. J. Dis. Child.*, 1934, *48*, 1304–1315.

The authors' method of examination of the pyloric canal in infants having congenital hypertrophic pyloric stenosis is based on measuring the length of the canal on the roentgenogram, taking into account the factor of magnification caused by the projection of the shadow of the canal on the film. The actual length of the pyloric canal differs only slightly from the length of the pyloric muscle.

In their study the length of the canal varied from 1.5 to 24 mm. as measured on the roentgenogram. They conclude that when the length exceeds 6 or 7 mm. the conditions that are present may cause the clinical picture of congenital hypertrophic pyloric stenosis.

Their technique is described in a previous article. Roentgenoscopy is important, as it indicates the location of the pylorus and its actual behavior. They expose a series of from six to twelve films to complete the examination. The paper is illustrated by roentgenograms showing variations in the length of the canal in various patients.

They multiply the length of the canal as measured on the film by a factor which is found in the equation: distance from focus of the tube to the pylorus divided by the distance from focus of the tube to the film.—*R. S. Bromer.*

GÂLDĂU, D., and POP, B. Leziunile caustice ale stomacului. (Caustic lesions of the stomach.) *Primul Congres Naţional de Radiol. şi Electrol. Med.*, Bucureşti, October 26–28, 1934, Comunicări, pp. 40–45.

The authors observed during the past six years 11 cases of suicidal attempts by the swallowing of caustic soda. Until recently it was the accepted opinion that esophageal stenosis represents the only sequelae in the later stages of such cases and that all the gastric symptoms must be attributed to this stenosis. By performing regular roentgenographic examinations of the entire gastrointestinal tract in all 11 cases the author was able to demonstrate that in 72 per cent of the cases pyloric stenosis and in 18 cases more superficial lesions (bilocular stomach) were present. It was observed that in the majority of the cases the first gastric symptoms appeared three to four weeks after the swallowing of the lye, usually at the time when the esophageal symptoms start to clear up and the patient is under the impression that he is entering the stage of convalescence. They consist chiefly of vomiting and gastric pain which is not relieved until the stomach contents are evacuated. In a few instances the stenosis develops slowly extending over a period of several years.

The authors explain the presence of these gastric signs as due to the fact that the stomach undergoes a spastic contraction as soon as the caustic agent starts to act on the pylorus, this then leading to a longer sojourn in the lower portion of the stomach. The esophagus and the cardiac end of the stomach in this respect are less active so that the caustic agent passes through them more quickly and the lesions thus appear of a more superficial nature. All gastric lesions provoked by caustic substances necessitate sooner or later surgical intervention.—*T. Leucutia.*

SKELETAL SYSTEM

HESS, JULIUS H., BRONSTEIN, I. P., and ABELSON, S. M. Atlanto-axial dislocations unassociated with trauma and secondary to inflammatory foci in the neck. *Am. J. Dis. Child.*, May, 1935, *49*, 1137–1147.

The authors report the finding of 22 cases in the literature of atlanto-axial dislocations in the absence of trauma, disease of the bone or congenital anomalies. In addition, they report 2 cases of their own. Cases reported have had various descriptive terms applied to the condition, such as malum suboccipitale rheumaticum, distention luxation of the atlanto-epistropheal joints, maladie de Grisel, Drehungsverrenkung des Atlas, spontaneous hyperemic dislocation of the atlas and nontraumatic atlanto-axial dislocation.

Several explanations have been advanced concerning the production of this dislocation. Thus Wittek presumed that it was due to an effusion into the joints with relaxation of the ligaments following an inflammatory focus in a nearby area. Another explanation is decalcification as a result of hyperemia of the upper cervical vertebrae secondary to inflammatory processes in and about the pharynx. Spasm and contraction of the prevertebral muscles, associated with lymphatic infection of the retropharyngeal space secondary to inflammatory conditions of the nasopharynx is also thought to be a cause. In the authors' opinion, the production of this dislocation involves a combination of factors, the sine qua non being weakening of the lateral ligaments. In addition, rotation of an excessive degree may also be a factor. Fixed rotation of the neck assumed in the treatment of suppurative lesions of the neck may be concerned in the production. They found no record of any injury of the spinal cord as a complication.

Prophylaxis is suggested by the following means: (*a*) early recognition of the condition by cognizance of its occurrence; (*b*) avoidance of overrotation of the head in exposing operative fields, as in operations on the mastoid and for suppurating glands, and (*c*) guarding against turning of the head in children with suppurative foci of the neck, necessitating the wearing of abundant dressings requiring frequent changes. Several cases were reported following mastoidectomy.—*R. S. Bromer.*

Root, J. Harold. Albers-Schönberg's disease. *Am. J. Dis. Child.*, 1935, *49*, 964–973.

Root collected 70 cases of Albers-Schönberg's disease in the literature and reports one additional case in detail. His patient was a female infant, aged six weeks when first seen, who showed on roentgen examination multiple fractures with greatly increased density of all the bones of the skeleton and with marked bands of lessened density near the ends of all the long bones. No transverse bands and no clubbing of the ends of the long bones could be demonstrated. Later at one year of age there was a more pronounced increase in density of all the long bones, with clubbing of their ends and the same marked bands of lessened density near their extremities.

The interesting points about the cases reported in the literature, the pathologic process and the symptomatology of the condition are reviewed. Opinions as to the etiology fall into the following groups: (1) faulty metabolism secondary to endocrine imbalance; (2) faulty phosphorus metabolism also secondary to endocrine imbalance; (3) infections; (4) a rachitic osteomalacic process, and (5) a leukemic condition.

Root's case showed some unique features, the outstanding ones being the huge callus formation at the site of the most recent fracture and the mildness of the secondary symptoms in comparison with the marked sclerosis of the bones. The degree of anemia, of enlargement of the liver and the hydrocephalus were comparatively slight.—*R. S. Bromer.*

Philips, Herman B. A lateral view of the clavicle; roentgenographic demonstration by a new technique. *J. Bone & Joint Surg.*, Jan., 1935, *17*, 202–203.

Philips describes a new technique for the roentgen examination of the clavicle. The usual procedure is a posteroanterior exposure with the film placed against the clavicle. The new lateral exposure, which he advocates, secures a view perpendicular to the conventional one just described. The film is placed slightly lower than in the posteroanterior projection and a small cone with a long target-film distance is utilized, affording a tangential view of the clavicular region. The target-film distance should be about 36 inches and the angle to the feet varies from 25 to 30 degrees. The position of the tube is several inches beyond the top of the patient's head. If the posteroanterior projection is made with the rays directed slightly toward the head, the second projection, just described, will afford a view perpendicular to the former. This will demonstrate whether or not the position of the fragments is satisfactory in two planes and also the new projection will eliminate the shadows of superimposed ribs, affording better definition of bony union. In the case of a patient who is in too much pain to be placed prone on the roentgen table or whose dressings prevent him from assuming this position, the same type of roentgenogram can be obtained by having him lean against a vertical plate holder and making corresponding changes in the angle of the rays, etc.—*R. S. Bromer.*

Howard, Nelson J. Epiphyseal fracture-dislocation at the elbow joint. *J. Bone & Joint Surg.*, Jan., 1935, *17*, 123–132.

Howard states that lower humeral epiphysiolysis with dislocation of the epiphysis (of the capitellum and trochlea, or of the capitellar portion alone) is a relatively common injury in the first decade of life, and that it is as truly a clinical entity as fracture-dislocation of the shoulder joint. It is followed by almost total loss of use of the elbow joint unless adequate treatment is employed. This is a compression injury and is sustained by direct violence, such as falling on the flexed elbow. As the epiphysis separates and the force continues, the capitellar epiphysis is forced through the anterior capsule and dislocation occurs. The capitellar epiphysis alone may separate, or the capitellum with the trochlear epiphysis may subluxate. Closed reduction may occasionally be successful. Reduction when incomplete is followed by extreme loss of function; therefore, operative reduction is warranted in every case in which reduction by manipulative methods is incomplete. The roentgenograms which are reproduced show very clearly the nature of the injury.

In cases of unrecognized or unreduced epiphyseal separation and dislocation, the radius and ulna may undergo secondary late posterior dislocation. This condition was shown in 2 of Howard's patients.—*R. S. Bromer.*

ROENTGEN AND RADIUM THERAPY

SCOTT, W. W. Primary carcinoma of the ureter. *Surg., Gynec. & Obst.*, Feb., 1934, *58*, 215–227.

To be regarded as a primary carcinoma of the ureter, the gross and microscopic descriptions of the tumor must be characteristic of carcinoma and the tumor must be primary in the ureter and not be a transplant from elsewhere in the urinary tract nor be an extension of metastasis from elsewhere. This is a relatively rare condition as evidenced by the fact that the author was able to collect only 59 cases from the literature and in addition presents 2 of his own.

A critical review of all of these cases showed metastases to have been demonstrated in 23, while in 8 others nearby structures were involved by direct extension. The relative frequency of involvement of the following organs by metastases was: retroperitoneal lymph glands, 17; liver, 9; lungs, 8; pancreas, 2; bladder, 2; opposite kidney, 2; and once each in the adrenal, spleen, pericardium, pleura, pelvis, vertebral column, and skin. It would seem that metastasis from primary carcinoma of the ureter occurs earlier and more frequently than from carcinoma of the bladder. The average age was 55.7 years.

Symptoms. The most common symptoms of primary carcinoma of the ureter are not characteristic of that disease alone. Hematuria is the most frequent symptom, occurring in 72 per cent of the cases. Pain was present in 65 per cent of the cases. Frequency of urination was noticed more often in those patients having tumors of the lower and middle portions of the ureter. There was involvement of the lower third of the ureter in 57 per cent of the cases.

In 40 per cent of the cases a palpable mass was present. In most instances this proved to be a dilated kidney. There were a few cases in which the primary growth was palpable on either abdominal, vaginal or rectal examination.

By cystoscopic examination occasionally tumor tissue is seen projecting from the ureteral orifice or a transplant is present on the bladder wall near the orifice. An obstruction is encountered which does not scratch the wax tipped catheter. A most suggestive feature is the persistent, rather copious, steady bleeding from the orifice on the involved side following ureteral manipulation with a catheter.

It is seldom that roentgen examinations yield conclusive proof of a primary carcinoma of the ureter; the findings are sometimes quite suggestive and tend to support the accumulated evidence in favor of such a diagnosis. In those cases in which ureteral calculus and traumatic stricture have been excluded, a pyelogram showing a partially obstructed ureter with dilatation above the point of obstruction and an enlarge kidney pelvis with no filling defects of the type seen in primary carcinoma of the renal pelvis or parenchyma, suggests the possibility of primary carcinoma of the ureter, especially if there has been a history of recurrent hematuria. There is usually marked distortion of the ureter as seen on the pyelogram.

Treatment. In a few cases deep roentgen and radium therapy were tried but were of rather questionable value except as a palliative measure. The character of the disease plus the usual advanced age of the patient makes the average operative risk rather poor. There was a primary operative mortality of 27 per cent. Of the cases reviewed, in which a follow-up was possible,

only 2 patients are living and well over a five year period.—*J. H. Vastine.*

Bugbee, Henry, G. Ureteral occlusion following radium implantation into the cervix. *J. Urol.*, Nov., 1934, *32*, 439–448.

The author reports 6 cases in which a functionless kidney due to pyonephrosis and secondary to ureteral occlusion was removed, the time elapsing between the cervical irradiation and the nephrectomy ranging from five months to nine years. Two additional cases, not operated upon, presenting ureteral occlusion were seen one month and five years following irradiation. The urinary tract should be routinely examined in the follow-up care of patients receiving cervical irradiation.—*W. R. Brooksher.*

Smith, Frank R. The incidence of vaginal fistulae in patients with carcinoma of the cervix. *Am. J. Cancer*, Sept., 1934, *22*, 52–58.

The records of 2,852 cases of proved carcinoma of the cervix were studied to answer the question, "How frequently does vaginal fistulae occur at Memorial Hospital following radiation therapy for carcinoma of the cervix?" This is statistical report from which it was deduced that (1) fistula is primarily a manifestation of advanced disease, (2) the incident of fistulae is increased by (*a*) interstitial radon irradiation, (*b*) lack of filtration, (*c*) re-treatments, (*d*) infection, (*e*) structural type of lesion, (*f*) hysterectomy before irradiation. There were 94 cases of vaginal fistulae during the period from 1916 to 1932.—*J. H. Harris.*

Binkley, George E., Technique of radiation therapy and colostomy in rectal cancer. *Am. J. Surg.*, Feb., 1935, *27*, 231–236.

In addition to producing clinical cures in properly selected operable cases, radiation therapy is capable of providing a valuable degree of palliation in many other cases. It should not be used routinely as a curative agent, being but one of several selective methods of dealing with this lesion. The most suitable form of interstitial irradiation is by the small, non-removable gold radon seed. This procedure is supplemented by externally applied irradiation with high voltage roentgen rays. Radiation therapy may be advantageously employed in (1) favorable and operable cases, in which this procedure alone may be curative; (2) operable cases wherein preoperative radiation therapy offers an advantage in promoting clinical cure, and (3) advanced cases, in which irradiation alone, or combined with colostomy, offers the highest degree of palliation. Technical details of radiation therapy and colostomy are fully discussed.—*W. R. Brooksher.*

Herger, Charles C., and Thibaudeau, A. A. Tertatoma of testis. *Am. J. Cancer*, Nov., 1934, *22*, 525–535.

A statistical study of the 63 cases of testicular tumor seen at the State Institute for the Study of Malignant Disease is given. The pathology is given in some detail. They divided the cases into five groups: (1) Malignant teratoma with adult features. In these tumors were found definite adult structures, cartilage, fat cells, adult squamous epithelium, glandular epithelium, smooth muscle fibers, etc. All their cases of this type showed metastasis when first seen and all died within two to eight months. (2) Embryonal carcinoma (seminoma) were those made up of large, round or polyhedral cells with vesicular hyperchromatic nuclei characteristically growing in large sheets of alveoli. Only one case of the 20 of this group had no metastasis when first seen. One patient was alive ten years after treatment but the majority died in less than one year. (3) In embryonal carcinoma with lymphoid stroma, the presence of a large number of lymphocytes was characteristic. Of the 9 patients in this group who had no demonstrable metastasis when first seen, all are alive and well without recurrences following surgery and irradiation. (4) Embryonal adenocarcinoma is a tumor made up of alveoli lined with large cuboidal or low columnar cells with hyperchromatic nuclei. Ten of the 11 cases in this group died within two to eight months. (5) The chorioepithelioma of the testis which is similar in pathology to that seen in the uterus was not encountered in this series.

The treatment consisted of simple orchidectomy followed by radiation therapy of the lymph-bearing areas. The authors prefer to give the irradiation immediately after operation.

Their experience with the Aschheim-Zondek test has been limited to 12 cases but they belive it to be of value as a diagnostic procedure and as an aid in the conduct of treatment.—*J. H. Harris.*

Moscariello, Alfredo. Gravidanza eparto normale in utero carcinomatoso curato col radium e clinicamente guarito. (Pregnancy and normal delivery in a carcinomatous uterus treated with radium and cured clinically.) *Radiol. med.*, Feb., 1935, *22*, 121–124.

A women thirty-three years of age had had four children all living and well. In December, 1931, she began to have a bloody discharge outside the menstrual periods and in February a diagnosis of carcinoma of the uterus was made. Histological examination showed pavement epithelioma of the cervix. On Feb. 23, 1932, she was treated with 30 mg. radium, the dose being 14.5 mcd. On March 30 she was given a second application of the same kind. On March 30, 1933, the ulceration was almost completely healed but another application of the same kind was given, making a total dosage of 43.5 mcd. The patient improved rapidly and in June was apparently completely cured. On Aug. 26 she returned complaining of a pulling feeling in the lower part of the abdomen and increased size of the abdomen. An irradiation of 21.7 mcd. was given. The uterus continued to increase in size and soon it became evident that she was pregnant. Pregnancy normal. Labor began with the fetus in a transverse position on June 30, 1934. Version was performed but the fetus died of asphyxia. Puerperium normal. The woman was seen three months later in excellent health and the genital findings the same as before the delivery.

In such cases the author thinks Caesarean section should not be decided on in advance but the patient kept under observation and labor allowed to proceed normally unless the cicatrization seems to be such that normal delivery would be impossible.—*Audrey G. Morgan.*

Russum, B. Carl. Important lines of attack upon the cancer problem. *Nebraska M. J.*, April, 1935, *20*, 123–125.

Russum is of the opinion that the most pressing needs in the present-day attack upon cancer are: (1) well-directed research by properly qualified investigators; (2) realization by the physician that we must and can diagnose cancer early, and (3) realization that the proper handling of cancer patients is a cooperative procedure among members of the profession.—*W. R. Brooksher.*

Galifi, Liborio. Sul trattamento Röntgen dell'ulcera perforante del piede. (Roentgen treatment of perforating ulcer of the foot.) *Radiol. med.*, Feb., 1935, *22*, 164–167.

A man aged forty-five had a very deep perforating ulcer of the plantar surface of the great toe which had grown worse under all the usual treatments. He denied alcoholism and syphilis and his Wassermann reaction was negative. He refused surgical treatment on account of fear of recurrence. On the theory that perforating ulcer is an angiotrophoneuritic disease he was given roentgen irradiation of the dorsolumbar spinal column. He was given four series of irradiations by Busi's technique. The first day two fields beside the lower dorsal column were irradiated, the tube being inclined 40°; 140 kv., 2 ma., one-third of an erythema dose or 115 r on a field 9×12 cm.; focal distance 30 cm. The same treatment was given the next day over the lumbar spinal column. This treatment was repeated three more times at intervals of twenty to thirty days. Local ultraviolet irradiations were given in the intervals. The ulcer began to improve after the first series of irradiations and is now practically entirely healed.

This method is suggested as a preliminary treatment even in cases in which surgical operation seems necessary as it will probably prevent recurrences which are the greatest danger in surgical treatment.—*Audrey G. Morgan.*

Coley, Bradley L. The treatment of osteogenic sarcoma by irradiation. *Am. J. Surg.*, Jan., 1935, *27*, 43–47.

Seventy cases of osteogenic sarcoma treated by irradiation without amputation were studied; 64 are now dead. Of the 6 living, 4 have fibrosarcomas, 1 a sarcoma developing on an old osteitis fibrosa cystica, and 1 is apparently a sclerosing osteogenic sarcoma. Only 1 has survived for more than five years. Irradiation is preferable to amputation only: (1) when of doubtful operability, (2) when the histologic picture suggests definite radiosensitivity, (3) when a small periosteal lesion affords opportunity for combined external and interstitial irradiation, and (4) in medullary osteogenic fibrosarcomas of low malignancy. All inoperable cases and those refusing amputation should receive thorough irradiation. Prolonged fractional dose therapy is favored.—*W. R. Brooksher.*

Holst, L., Schaal, G., and Negovskij, N. Die Roentgentherapie des Ulcus ventriculi et duodeni. (Roentgen therapy of gastric and duodenal ulcer.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, Oct., 1934, *50*, 360–367.

The authors report a group of 29 cases (17 with gastric ulcer, 8 with duodenal, 2 with hyperacid gastritis, 1 with hypacid gastritis and 1 with jejunal ulcer) which were treated with the following roentgen technique: A front and back field over the stomach was treated at two or three day intervals with 15 to 20 per cent S.E.D. with 0.5 mm. Cu+3 mm. Al, 23 cm. skin target distance, 165 kv. No special diet or other treatment was given the patients. Of this group 17 received definite benefit from treatment up to six months after treatment in cases, but in none was a permanent result achieved. The results are explainable as a direct effect of roentgen rays on the inflammatory focus and an indirect effect on the vagus. —*E. T. Leddy.*

Williams, John T. Primary carcinoma of the vagina. *New England J. M.*, Jan. 24, 1935, *212*, 156–157.

The literature is reviewed and 2 cases of primary carcinoma of the vagina are reported in detail. The symptoms are identical with those of carcinoma of the cervix. Diagnosis is by inspection and biopsy. Radium therapy, followed by roentgen irradiation, is the treatment of choice.—*W. R. Brooksher.*

Desjardins, Arthur U., and Gianturco, Cesare. Results of treatment in tumors of the testis. *Am. J. Surg.*, Jan., 1935, *27*, 71–78.

The authors comprehensively discuss the results of treatment in 155 pathologically proved cases of tumors of the testis. The greatest incidence was in the third and sixth decades. The relation of trauma and of undescended testis could not be ascertained. In nearly every case of embryonal carcinoma and teratoid tumor, metastasis first occurs in the group of retroperitoneal lymph nodes surrounding the abdominal aorta in the vicinity of the celiac axis on the same side as the affected testis, and remains confined to this group for a long period. Such metastasis occurs much earlier than is generally supposed and may be presumptively quoted by careful attention to clinical symptoms referable to the gastrointestinal tract. Pulmonary metastasis is generally a late complication. The recognition of metastasis is an important factor in therapy. Permanent cure is considered a criterion of surgical rather than of radiological treatment. In many cases irradiation is employed because surgical procedures cannot be considered. Too, in cases not receiving permanent cure by radiotherapy, there is much, even prolonged, benefit. Postoperative irradiation yields results that cannot be obtained by simple orchidectomy in the attainment of prolonged arrest of the malignant process, even in the presence of obvious metastasis. Roentgen therapy alone appears preferable for the embryonal carcinoma; for the teratoid tumor, surgical removal combined with thorough postoperative irradiation is indicated.—*W. R. Brooksher.*

Jugenburg, A., Peretz, L., and Mostowa, R. Neue Ergebnisse zur Pathogenese des Röntgenkaters. (Some recent investigations of the cause of roentgen sickness.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, 1934, *49*, 632–640.

Following some investigations of Peretz the view was put forward by Jugenburg that roentgen sickness is due to an imbalance of conditions in the bacteriology of the colon and the resorption of products of decomposition. Investigations of the microflora of 18 cases who had large doses of roentgen rays on the abdomen and the results of the investigation confirm the hypothesis. In the majority of cases after roentgen treatment there is a decrease in the number of *B. coli* and an increase in other bacteria. The treatment of roentgen sickness by colon bacilli therefore seems indicated. The results of this treatment will be discussed in a later paper.—*E. T. Leddy.*

Nicolescu, V. Contribuţiuni la tratamentul tromboflebitelor prin roentgenterapie. (Contribution to the treatment of thrombophlebitis by roentgen therapy.) *Primul Congres Naţional de Radiol. şi Electrol. Med.*, Bucureşti, October 26–28, 1934, Comunicări, pp. 100–104.

Fourteen cases of thrombophlebitis occurring in 12 individuals (2 bilateral) were treated by the author by means of roentgen therapy, 12 being acute and 2 chronic at the time of the treatment. Of the acute, a complete healing was obtained in 10 cases, one died from septicemia

and in the last amelioration was obtained. In the 2 chronic cases likewise amelioration occurred. In all acute cases a disappearance of the pain was observed within five to seven hours after the irradiation, the diminution in the size of the swelling occurring shortly after. Within five to ten days a complete disappearance of the swelling and of all clinical signs was noted, patients being able to get up after the fifth day and leave the hospital walking on their own feet on the tenth day. The technique employed was as follows: two seances of 150 r each were applied to the regions along the thrombosed veins with 170 kv., 0.5 mm. Cu and 1.0 mm. Al as filter, 30 cm. skin target distance, 4 ma., 10×15 cm. field. In one single case, in which the pain failed to disappear, the treatment was repeated the next day with 100 r over each field. In the chronic cases the dose of 150 r was repeated three times during a period of seven days. The careful transportation of the patient to the roentgen therapy room is of the utmost importance so as not to produce a breaking through of the thrombus. The general conclusion is reached that roentgen therapy constitutes an ideal method in the treatment of thrombophlebitis by greatly shortening the evolution of the disease, by alleviating the painful symptoms and by forestalling more serious complications.—*T. Leucutia.*

BENETATO-MODVAL, MARIA, and RUSU, VIOREL. Influenta razelor röntgen asupra paratiroidelor, calcemia şi fosfatemia. (The influence of roentgen rays on parathyroids, calcemia and phosphatemia.) *Cancerul*, April–June, 1934, *2*, 84–89.

In a normal state the parathyroid hormone destroys daily a certain quantity of calcium phosphate of the skeleton; on the other side, it permits an osseous deposit of an equivalent quantity of exogen calcium phosphate. The result of this double process is a mineral elimination equivalent to assimilation, that is, a balanced mineral state, the phosphatemia and the calcemia remaining constant and there being a constant relation between them (Ca+P=K). In hypoparathyroidism the calcium balance becomes positive, that is, the assimilation exceeds the elimination, whereas in hyperparathyroidism the calcium balance is negative, this being associated with hypercalcemia due to increased mobilization of the osseous calcium and inhibition of compensatory ossification of the bone. The phosphorus of the blood in this case is diminished.

The authors studied the effect of irradiation on the parathyroid glands in 23 cases, 10 of which were irradiated for Basedow's disease and the remainder for cervical adenitis. In the Basedow cases, ⅓ S.U.D., that is, 200 r with 4 mm. Al and 120 kv., 2 ma., 30 cm. skin target distance, was administered through one field, whereas in the inflammatory adenitis the dose was ½ S.U.D., and in a few malignancies 1 S.U.D. The calcium and phosphorus were determined before irradiation and twenty-four hours later. The following results were obtained: (1) The calcemia and phosphatemia are within normal limits in cases suffering from Basedow's disease or cervical adenitis, whereas in cachectic cancerous patients the calcemia is lower and the phosphatemia increased. (2) Following irradiation with roentgen rays of the thyreoparathyroid glands, the calcemia decreased without reaching the subnormal limits, whereas the phosphatemia presented insignificant variation regardless of the dose and quality of the roentgen rays. (3) The roentgen rays applied to the cervical region produced an inconstant hypofunction of the parathyroid glands manifesting itself in hypocalcemia.—*T. Leucutia.*

SCHENCK, SAMUEL G. Roentgen therapy for acute cervical adenitis. *Am. J. Dis. Child.*, June, 1935, *49*, 1472–1486.

Schenck treated 105 patients with acute cervical adenitis with minimal doses of roentgen rays. He divided his patients into two groups. For the first group, consisting of patients two years of age or younger, lower voltage and less filtration were employed; for the second group, comprising those over two years of age, higher voltage and filtration were used. The field exposed comprised not only the normal tissues surrounding the swelling but the entire area of the neck on the affected side. His purpose was to irradiate the entire chain of lymph nodes, some of which might be draining the source of infection. His factors used were 100 to 140 kv. (peak) with a filter of from 3 to 5 mm. of aluminum, at a target skin distance of 30 cm. With this method, he states, 25 per cent of an erythema dose amounted to from 125 to 140 r, measured in air with backscattering.

Of his patients, 85.7 per cent were cured, and

in 14.3 per cent the glandular lesion terminated in suppuration. In the 85.7 per cent of the patients who were cured, all subjective symptoms, including the temperature, were relieved within forty-eight hours, and the swelling subsided within one week. The age of the patient, the cause and duration of the symptoms, the height of the temperature and the size of the swelling are not contraindications to this form of treatment, and have apparently no effect on the results. The roentgen rays act by shortening the stages of the acute inflammation in the lymph nodes, resulting in rapid resolution of the pathologic process. Whether the rays have a direct bactericidal action is still unsettled. Roentgen therapy is the treatment of choice for acute cervical adenitis and should be so recognized. When administered under proper supervision, it has demonstrated its value in the management of a protracted and annoying condition such as this. The cases which have a mild course with little or no fever, a cervical swelling of small or medium size and little discomfort will probably not need roentgen therapy. Duration of the adenitis for longer than two weeks is, however, an indication for irradiation.—*R. S. Bromer.*

Popp, L. Despre sacralisare şi efectul radioterapiei asupra acesteia. (Sacralization and the effect of radiotherapy upon it.) *Cluj. med.*, March, 1935, *16*, 130–134.

After discussing in detail the pathologic and roentgenologic appearance, as well as the technical procedure for its roentgenography, the author reports 2 cases of sacralization with active clinical symptoms which were treated successfully by roentgen therapy. The method employed was as follows: One single field of irradiation, including the two last lumbar vertebrae and the first three sacral vertebrae; 600 r were given in two fractions of 300 r each, focal skin distance 30 cm., 2 ma., 180 kv. A little later 550 r, divided into two fractions each, was administered over Valleix's points (point of exit of the sciatic nerve, tibial nerve and peroneal nerve) on both sides. A few days following the treatment amelioration of the pain started in. In four weeks the series of treatments was repeated. In the first case a complete cessation of the symptoms was obtained five months, and in the second three months after the treatment. Roentgenograms taken preliminary to treatment and after the cessation of all symptoms revealed no change whatever in the sacralization. The good radiotherapeutic effect is explained on the basis that in both instances the appearance of pain was the result of traumatic contusion which probably provoked an exudative inflammatory process with pressure on the nerve and that the radiation therapy helped to bring about a resolution of this inflammation.—*T. Leucutia.*

Delario, A. J., and Meyers, F. R. Deep roentgen-ray therapy in the treatment of disturbances of the autonomic system. *J. Med. Soc. N. Jersey*, May, 1935, *32*, 287–297.

Deep roentgen therapy appears indicated in angina pectoris because its depressant action on the sympathetic ganglia should prevent coronary spasm and the threshold of nervous conduction would be raised to prevent the painful stimuli from reaching the central nervous system. Excellent results were obtained in these cases, one of which is detailed. Similar relief of pain was obtained by irradiation of the sympathetics in Raynaud's disease, Berger's disease, and in endarteritis of other origin. The treatment was also found useful in the so-called essential hypertension cases. Other conditions in which roentgen irradiation may prove of value are peptic ulcer, diabetes and allergic diseases. A number of case reports accompany the article.—*W. R. Brooksher.*

MacKenzie, A. R. Acute septic throat; treatment with roentgen-ray. *West Virginia M. J.*, May, 1935, *31*, 196–198.

The author discusses his results in the treatment of 32 consecutive cases of severe septic sore throat, of whom 30 recovered without apparent heart, kidney or bone damage. The 2 fatal cases were seen late in the disease after blood stream infection had supervened. The technical factors are not given.—*W. R. Brooksher.*

Leucutia, T. Irradiation in lymphosarcoma, Hodgkin's disease and leukemia. *Am. J. M. Sc.*, Nov., 1934, *188*, 612–622.

Leucutia analyzed 2,425 cases from the literature and 129 personally observed cases in this study. Irradiation is considered the method of choice in all three lesions. In lymphosarcoma there results an increase in the life expectancy from $2\frac{1}{2}$ to $3\frac{1}{2}$ years with cures in 10–15 per cent of the cases. The immediate results may be termed "spectacular." Irradiation should be

by penetrating rays with as much of the lymphatic system covered as is possible. Careful management of the patient is vital.

In Hodgkin's disease there is great symptomatic improvement, with an increase in life expectancy from 2 to about 3½ years and a 5-year survival of from 15 per cent to 33 per cent of the cases. In some cases the symptom-free period is prolonged beyond the 10-year period and may be considered a cure. Penetrating rays are also employed in this disease but favorable results have been reported from the use of the radium pack. Irradiation must extend over a period of years for survival.

The acute and chronic forms of the disease must be distinguished in any study of the irradiation effects on leukemia. No cures occur and prolongation of life is not materially increased. Symptomatic improvement may, however, be remarkable.—*W. R. Brooksher.*

Cathcart, J. W. The radiologist and the goiter problem. *Texas State J. Med.*, March, 1935, *30*, 703–706.

Radiologists should accept for treatment, so far as is possible, only those cases conforming to the classical picture: tachycardia, fine tremor, loss of weight and strength with anorexia, tolerance to cold, intolerance to heat, enlargement of the thyroid gland, exophthalmos (in 10 per cent), and, in advanced cases, vomiting and diarrhea, a high basal metabolic rate and short duration of voluntary apnea. Patients not conforming to the classical clinical picture should be repeatedly examined and observed over an extended period.

The adolescent and the moderately enlarged toxic goiters are distinctly a radiological problem. To surgery belong the large adenomatous and colloid types. Distinct advantages of irradiation are the absence of mortality, freedom from pain, and general convenience and availability of the method. While the heart must be considered in any mode of therapy, it presents fewer terrors to the radiologist than to the surgeon.

The author considers roentgen rays and radium of equal value and employs them interchangeably. The technique is detailed and a brief review of 84 treated cases is presented. The importance of the internist in the management of the case is emphasized.—*W. R. Brooksher.*

Negru, D. Röntgenterapia în cancerul mamelei. (Roentgen therapy in cancer of the breast.) *Primul Congres Naţional de Radiol. şi Electrol. Med.*, Bucureşti, Oct. 26–28, 1934, Festivităţi, Rapoarte, pp. 253–269.

The relatively superficial location of breast cancer has incited roentgenologists from the beginning to try irradiation as a method of treatment. It was soon found, however, that the problem presents considerably greater difficulty than carcinomas in other locations, as for instance, carcinoma of the uterus, because of the peculiar extension of the carcinoma of the breast by lymphatic permeation. Therefore, with time a combination of radical surgical excision and pre- and postoperative irradiation of large areas around the breast and of the regional glands has become more and more a standard method. In this report the author gives a detailed résumé of the literature of the various roentgen therapeutic methods and the results obtained thereby in the treatment of cancer of the breast. The Steinthal division into three groups is made the basis of classification when considering the five year results.

The following general conclusions are reached: (1) Mammary cancer represents a lesion which is very difficult to treat by roentgen rays alone. (2) Every operable cancer of the breast should be operated upon by extending the intervention to the supraclavicular fossa whenever necessary. (3) Postoperative irradiation is indicated with moderate, spaced and repeated doses. (4) In every instance irradiation must include the supraclavicular region, even if no enlargement of the lymph nodes is demonstrable. (5) Preoperative irradiation does not appear to be necessary. (6) In inoperable cases and in recurrences roentgen therapy either alone or in association with radium therapy forms the method of choice. Temporary amelioration is obtained as a rule and in many instances inoperable tumors become operable. A permanent cure by radiation therapy of an inoperable cancer is observed only very rarely. (7) In Paget's disease of the breast deep irradiation must be used. (8) The personal results of the 100 cases treated by the author during the past ten years coincide with the statistics of other investigators.—*T. Leucutia.*

Severeanu, G. Radiumterapia cancerului mamelei. (Radium therapy of cancer of the

breast.) *Primul Congres Naţional de Radiol. şi Electrol. Med.*, Bucureşti, Oct. 26–28, 1934, Festivităţi, Rapoarte, pp. 271–294.

Radium therapy as a sole agent of treatment of carcinoma of the breast is superior to the surgical method, as demonstrated by the statistics of Keynes, Lee and Pack, Soiland, and 185 cases treated by the author. The results are in direct relation with the anatomo-pathologic character of the tumor, this indicating the size of the area which must be irradiated. It is the author's contention that by following the radium therapeutic method, biopsy becomes unnecessary. The technique employed consists in the interstitial application of standardized radium needles with high filtration so as to eliminate the beta rays and the soft gamma rays. In addition to the primary lesion, all those zones are irradiated by external irradiation (either gamma rays or roentgen rays) which are known to form seats of predilection for the lymphatic extension of the carcinoma. The author recommends a dose of 50 to 70 mc-hr. per cm.^{3} to the tumor tissue of the primary lesion. The areas treated by external irradiation include (1) the axilla, (2) the infra- and supraclavicular regions and (3) the internal mammary region. The superiority of the radium therapy is due to the fact that it produces a disappearance of the neoplastic cells by conserving at the same time the normal tissues of the surrounding structures.

The five year cures in the cases treated by the author are presented as follows: Group I (Steinthal)—47 cases with 10 cures and 8 untraced; Group II—64 cases with 7 cured and 14 untraced; Group III—43 cases with 5 cures and 11 untraced, and Group IV—31 cases with no cures.—*T. Leucutia.*

Smith, George Gilbert. The treatment of bladder tumors. *Pennsylvania M. J.*, May, 1935, *38*, 569–576.

One hundred and fifty cases in the author's personal practice are analyzed and among other questions discussed is: What is the value of radium in the treatment of vesical neoplasms? Radon seeds were implanted through the cystoscope into ulcerated, sessile, single tumors in 2 cases with apparent control of both at eight and fifteen months' intervals. No other treatment seemed advisable and the results, even if temporary, are highly satisfactory. Radium was implanted by the suprapubic route in 28 cases, of whom 5 have lived for periods of from three to fifteen years, respectively. Twenty-one per cent of this group may be said to have been materially benefited, perhaps cured, by radium therapy. While radium is of value in a limited group of cases, resection, when possible, gives better results.—*W. R. Brooksher.*

Morton, Daniel G. Cervical cancer: an autopsy study of women dying with cervical cancer after radiation. *Calif. & Western Med.*, May, 1935, *42*, 345–348.

A study of 36 autopsies on women treated for cervical cancer by radium, roentgen rays, or a combination of both, revealed that 22 died from the local growth, 8 from distant or metastatic cancer, and 6 from accident or complication. Death from local spread was usually due to ureteral blocking with consequent hydroureter, hydronephrosis and uremia. Death due to metastatic malignancy was no different from that seen in the usual case of widespread malignancy. In but one case was total absence of local cancer demonstrated, implying that in all other cases insufficient radiation had been employed. For the purposes of this analysis, radium dosage was considered adequate if it exceeded 4,500 mc-hr., or, if particularly well distributed in and about the cervix, even if slightly less in amount. Cases which were advanced when first observed usually died from local extension with frequent absence of metastases. With adequate treatment there was longer life for the patient with death due more often to metastatic lesions. Of 11 patients graded 1 or 2, 5 died from accident or complication—treatment mortality.—*W. R. Brooksher.*

MISCELLANEOUS

Bischoff, Fritz; Maxwell, L. C., and Ullmann, H. J. Hormones in cancer. VIII. Influence of the hypophysis. *Am. J. Cancer*, June, 1934, *21*, 329–345.

This paper is a summation of results obtained leading to the conclusion that the pituitary gland may be concerned in neoplastic extension.

Transplantable rat sarcoma R10, mouse sarcoma 180, rat carcinoma 256, and a spontaneous mammary mouse carcinoma were used in demonstrating the influence of the following experimental procedures upon the growth behavior of the neoplasm:

(1) Pituitary irradiation.

(2) Parenteral administration of standardized growth-promoting pituitary extracts, of standardized gonad-stimulating extracts of the pituitary, or of standardized urine of pregnancy preparations.

(3) Pituitary irradiation combined with the administration of the extracts described above.

The results of the experiments using proper controls are as follows:

1. Irradiation of the pituitary with sublethal doses, which bring about a temporary cessation of body growth, significantly retard the growth rate of rat sarcoma R10, rat carcinoma 256, and a mouse carcinoma (spontaneous mammary) if the tumor appears at the period of maximum body weight retardation.

2. In the case of rat carcinoma 256, the above effects were abolished by simultaneous dosage of pituitary extracts with standardized growth-promoting powers.

3. A cessation of body weight growth produced by various poisons, equivalent to that following pituitary irradiation, failed to retard tumor growth significantly.

4. In older rats dosage with standardized growth-promoting preparations of the pituitary significantly accelerate the rate of growth of carcinoma 256. In younger animals, and with mouse sarcoma 180 and rat sarcoma 10, the effect was less significant.

5. Dosage of urine of pregnancy augmented the effect of pituitary irradiation upon the rate of growth of mouse sarcoma 180. The effect was less significant for rat carcinoma 256 and rat sarcoma 10.

6. Attempts to abolish permanently the function of the anterior lobe of rats or of mice through pituitary irradiation were unsuccessful.—*Wendell C. Hall.*

Cooke, H. Hamilton. Hepatolienography; experimental study of the elimination of the contrast medium. *Arch. Surg.*, July, 1934, *29*, 29–41.

This study presents a review of the literature on the use of thorium dioxide in hepatolienography and a series of experiments designed to investigate the rate of elimination of thorium dioxide from the body.

A review of the literature discloses a difference of opinion as to the rapidity of elimination of the dye from the body. Most writers indicate, however, that it is eliminated very slowly, if at all. The author notes that no quantitative studies have been reported of actual adequate elimination by any organ.

A group of rabbits, injected with 2.5 c.c. of colloidal thorium dioxide per kilogram of body weight, failed to show any evidence of elimination of thorium, either by roentgen or histologic method of examination. The animals were observed for as long as forty-five days after injection. The author also found that it was impossible to affect the rate of elimination by any means used in this experiment. The material used consisted of 14 consecutive daily injections of 100 c.c. of 0.9 per cent saline solution, a 10 per cent solution of dextrose, a 5 per cent solution of calcium chloride, 0.2 c.c. of combined typhoid vaccine, or 0.25 c.c. of epinephrine.

The author concludes that the thorium is removed from the circulation by the phagocytic reticulo-endothelial cells located principally in the liver, spleen, suprarenal glands, kidneys, lungs, bone marrow, and ovaries. The results of this study indicate that once the thorium is phagocytosed by the reticulo-endothelia cells it is apparently permanently fixed in the body.—*G. W. Chamberlin.*

Segenidse, G. A., and Solotuchin, A. S. Über Röntgendiagnostik entzündlicher Herde im Knochengewebe mittels geringer "Thorotrast"—Dosen. (The roentgen diagnosis of inflammatory foci in bones by means of small quantities of "Thorotrast"; an experimental study.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, Dec., 1934, *50*, 556–562.

The authors made puncture wounds in the femurs of dogs, and three days later injected thorotrast into the femoral artery or vein. Thorotrast was found to be deposited around the wound in the bone due to the fact that the reticulo-endothelial cells collect there in the early stages of inflammation. Histologic findings are described in detail. The advantage of this technique according to the authors is that it uses only small quantities of thorotrast, an amount insufficient to cause any injury to the liver or spleen.—*E. T. Leddy.*

Brunschwig, Alexander, and Harmon, Paul H. Studies in bone sarcoma. I. Malignant osteoblastomata as evidence for the existence of true osteoblasts. *Surg., Gynec. & Obst*, Dec., 1933, *57*, 711–718.

Bone-producing metastasis from osteogenic sarcomata exhibiting much new bone formation

in the primary growth occurs much more frequently than is generally recorded. The authors offer the fact that metastases from osteogenic sarcoma contain calcium as conclusive evidence that deposition of bone is a specific cell activity of the osteoblast, a specialized form of the bibroblast, rather than a biochemical phenomenon in the interstitial or humoral spaces independent of cell participation.

Osteogenic sarcoma must be regarded as a malignant degeneration of a specific bone-forming cell—the osteoblast.—*J. H. Vastine.*

Brunschwig, Alexander, and Harmon, Paul H. Studies in bone sarcoma. II. Is new bone formation in osteogenic sarcoma the result of a local supersaturation of tissue fluids with calcium? *Am. J. Cancer*, Oct., 1934, *22*, 342–346.

The authors report the results of some experiments made to test the humoral hypothesis of osteogenesis as stated by Leriche and Policard, who believe that new bone formation in osteosarcoma is merely a reprecipitation of calcium absorbed locally by the growing tumor from normal bone.

In the reported experiments calcium in large amounts was made available in the immediate vicinity of transplantable sarcoma, composed of spindle and round cells. Other animals were given large amounts of viosterol over a period of weeks before the tumors were transplanted.

In none of the animals was any evidence of new bone formation found in the necrotic or living portions of the tumor, and the authors conclude that calcium in itself is incapable of rapidly bringing forth osteoblastic properties in malignant mesoblastic cells that do not under usual circumstances of growth exhibit such properties.—*J. H. Harris.*

Taylor, F. H. L., and Jackson, Henry. The carbohydrate tolerance in cancer patients and the effect upon it of roentgen ray radiation. *Am. J. Cancer*, Nov., 1934, *22*, 536–547.

This is a report of the experimental work undertaken to determine the incidence of a lowered carbohydrate metabolism in cancer and to study the relationship, if any, of the blood calcium to the carbohydrate tolerance in cancer patients. Blood sugar determinations were made upon a number of cancer patients, both before and after radiation therapy. No direct relationship was found between a decreased tolerance and cancer per se. About one-third of the patients studied showed a lowered tolerance for glucose, the presence of which was not inconsistent with the malnutrition accompanying the malignant state. Irradiation by roentgen rays did not produce any marked changes in the carbohydrate metabolism. In patients who originally showed a normal tolerance for carbohydrate, the development of a progressively decreasing tolerance strongly indicated an unfavorable prognosis. It was also found impossible to show any relationship between the decreased sugar tolerance found in some cases of cancer and the total serum calcium.—*J. H. Harris.*

Reinhard, M. C., Thibaudeau, A. A., and Candee, C. F. The development of multiple tumors in tarred and radiated mice: Part II. *Am. J. Cancer*, Nov., 1934, *22*, 590–596.

The final results of experimentation to study the effect of irradiation on the subsequent development of tar tumor is presented. A group of mice with a known rate of spontaneous cancer occurrence was used. One-half was irradiated after the application of tar for varying periods of time and the other half was used as control. Short wave length radiation to the extent of eight times the sterilizing dose and one-half the lethal dose was used. They concluded that there was no evidence that this type of irradiation changed the susceptibility of mice to tar tumors nor that it altered the carcinogenic power of the tar used.—*J. H. Harris.*

Franks, W. R., and Shaw, M. M. Effect of radiation, lactate, and iodoacetic acid on tumors. *Am. J. Cancer*, Nov., 1934, *22*, 601–605.

The glycolysis of tumor cells was interfered with at a time when cell respiration had been minimized by exposure to radiation. Sodium lactate was used to inhibit fermentation and iodoacetic acid was used to damage the glycolytic mechanism of the cell. These experiments were in vitro with transplantable mouse carcinoma and sarcoma. It was found that sublethal doses of sodium lactate showed little inhibition of the tumor growth. Sodium lactate injected two days after irradiation did not increase the effectiveness of the irradiation. Maximal doses of iodoacetic acid injected into one of the tumors appeared to inhibit its growth and the effectiveness of this drug was increased by previous irradiation.—*J. H. Harris.*

Flinn, F. B., Victor, J., Stillman, N., and MacDonald, D. Action of radium on tissue cultures. *Am. J. Cancer*, Oct., 1934, *22*, 351–358.

This article reports the results of some experiments undertaken to determine whether or not radioactive materials have a direct stimulating action on embryonic tissue in vitro. A solution of radium was added directly to a hanging drop or flask culture and thus the results obtained were due to the combined effect of the alpha, beta and gamma rays. From these experiments no evidence was observed of direct stimulation by the amounts of radium to which the cultures were exposed, nor did the oxygen consumption as measured give any indication of a direct stimulation. It was noted that cultures exposed to radium seemed more susceptible than the control culture to small variations inherent in tissue culture methods, namely, the temperature of the incubator and the difference in the fowl plasma used in the work. It was noted that the smaller the amount of radium used, the longer the time needed to bring about a lethal effect.—*J. H. Harris.*

Reinhard, M. C., and Goltz, H. L. Intensities from carious radium packs. *Am. J. Cancer*, Oct., 1934, *22*, 359–362.

A report is made of the calibration in roentgens of the radium packs used at the New York State Institute for the Study of Malignant Diseases. The calibration was made with a Victoreen condenser r-meter and measurements were made in air and with a wax phantom. Intrinsic filtration is discussed. By this is meant of filtration of the radium salt itself, the lower layers absorbing some radiation from the upper layers and at the same time hardening the resultant beam. They conclude that the variation in intensity of the different packs is due to differences in radiating areas and the intrinsic filtration. The size of the field has little or no influence upon the intensity. They emphasize the advisability of accurate calibration in roentgens rather than in milligram-hours, distance and filtration.—*J. H. Harris.*

Ziegler, Paul F., and Clark, George L. The x-ray in the study of the catgut ligature. *Surg., Gynec. & Obst.*, March, 1934, *58*, 578–589.

The authors obtain the diffraction pattern of suture material by passing a beam of roentgen rays defined by small pin-holes (about 0.025 inch in diameter) through a ligature specimen perpendicular to the fiber axis. A photographic plate is adjusted at a fixed distance behind the specimen, usually 5 cm. After development of the film the characteristic diffraction pattern appears which can be measured and interpreted in terms of constitution and structure of the material being tested.—*J. H. Vastine.*

Neeff, Th. C. Über Strahlendosen bei der Röntgenkymographie in der Schwangerschaft. (Roentgen doses in roentgen kymography in pregnancy.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, July, 1934, *50*, 86–90.

In kymographic studies made in pregnancy it is very necessary that the doses of roentgen rays applied to the fetus and the ovary be well within safe limits. Neeff gives some figures of the roentgen intensities applied to the skin and to the ovary during various kymographic investigations and points out that these doses can be decreased by improvements in tubes and films. At any rate, the doses in the usual kymographic studies are very small and yet are intense enough for diagnositc purposes.—*E. T. Leddy.*

Reinhard, M. C., and Goltz, H. L. Interpretation of dosage in roentgens. *Am. J. Cancer*, June, 1934, *21*, 380–383.

Dosages as reported in the literature, in the international unit of roentgen-ray quantity, the roentgen, are frequently guilty of one or more of the following omissions. (1) the beam is not defined in terms of its penetration or absorption; in other words, no qualitative estimation in terms of effective wave length or half-value layer is given; (2) the time over which the treatment is extended is not given; (3) the statement is not made as to whether or not the dosage, as reported, includes back-scattering.

For several reasons, it would seem preferable to report all doses as with air-scattering only. It has been shown by Packard that the increase in intensity with tissue-scattering is dependent on the type of ionization chamber which is used in measuring, and that there are large differences in the results reported by the various workers, due to the type of chamber used. It has also been shown by Hunt that the amount of back-scattering depends not only on the area irradiated, but also on the location of the par-

ticular area. Obviously, if we take the relation of air-scattering to tissue-scattering with one instrument, the back-scattering intensity will depend on the characteristics of the instrument as well as on the body area irradiated, and even though the air-scattering measurements are correct, the true intensity with tissue-scattering will not necessarily be obtained.

It is well known that when a beam of radiation is measured with back-scattering from an organic material such as animal tissue, the intensity is dependent on the area and the volume irradiated. Curves or tables showing the relationship between field size and intensity for beams of different qualities have been published by several authors. By using such curves the authors have found that the relation between air and wax-scattering as determined with a 20×20 cm. field, using a wax block 25×25×20 cm. is such that 800 r in air is the equivalent of 1,130 r with back-scattering from wax. Measurements were made with their thimble ionization chamber, which was calibrated in roentgens with air. They used a beam of roentgen rays generated by 200 kv (peak), 30 ma., and filtered through 0.5 mm. copper and 1.0 mm. aluminum. The resulting beam had an effective wave length of 0.16 Å.—*Wendell C. Hall.*

Reinhard, M. C. A radium safe. *Am. J. Cancer* July, 1934, *21*, 612–615.

In designing a safe for 1,750 milligrams of radium the following points were observed: (1) isolation from the personnel of the hospital for their protection; (2) protection against theft and against the radiation by lead; (3) accessibility for removing radium; (4) speed and ease of inventory.

For protection against theft an ordinary commercial steel safe with combination lock was used. Within this safe a lead box was fitted having sides 1 3/16 inches thick, a bottom 1 inch thick, and a top 1 5/8 and 2 inches thick. In addition there was ½ inch lead on the floor of the safe. This hollow lead box was then fitted with brass drawers filled with lead blocks in which small depressions were cut for the various forms of radium containers. The radium was so distributed in the drawers that the strongest radium containers were in the central portion of the chest.

In the same isolated room with the radium safe is a make-up table with lead protecting screens made of brass with 1 inch of lead in the horizontal part and 2 inches of lead in the base of the upright part, all work being carried on behind this screen.

With the type of safe described above a glanc into each opened drawer will reveal the number of tubes present when inventory is taken.

The author has found that a technician receives abour 1–2000 s. e. d. in one week as determined by the blackness of a dental film.—*Wendell C. Hall.*

Taylor, Hermon. Osteitis fibrosa: an experimental study. *Brit. J. Surg.*, Jan., 1935, *22*, 561–588.

This experimental study is so replete with important observations that any attempt to abstract it must fall short of doing its author justice.

Investigations planned to reveal the function of phosphatase showed that: (1) Phosphatase of itself did not produce bone changes. (2) Phosphatase was present in disease as the result of the bone involvement. (3) Phosphatase was rapidly destroyed in the body, very little being excreted by the kidneys. (4) Increased plasma phosphatase was indicative of a constant source of phosphatase because of its rapid destruction. (5) Phosphatase concentration was highest where bone proliferation was greatest.

With these data available the author developed a theory of ossification which stated that: The connective tissue cells responded to a continuous strain by the formation of phosphatase whereby bone was laid down in the matrix round the cells, thus becoming typical osteoblasts. The calcifying power of the phosphatase in the osteoblasts depended upon phosphate formation which precipitated calcium around the cells high in phosphatase. In other words, the calcifying power of phosphatase depended upon its local concentration and its ability to produce phosphate ions at that site. Using this same line of reasoning, the author concluded that decalcification associated with hyperemia was not so much a case of decalcification as it was a hindrance of recalcification because of excessive removal of phosphatase due to hyperemia.

Parathormone had an entirely different action which was manifested early by decalcification. This decalcification usually started in the sternal ends of the ribs becoming generalized

later. When decalcification became excessive, and hemorrhages into the marrow occurred as the result of the toxic effects of hypercalcemia, definite bone changes became evident. The damaged marrow was replaced by connective tissue cells with active phagocytosis of the hemopoietic elements becoming evident. At this stage the giant cells made their appearance which were indistinguishable from the ordinary osteoclasts. The giant cells appeared where there was real osteoclastic work to be done and damaged bone remolded. From these histological appearances, therefore, which were obtained by injecting large quantities of parathormone, it seemed that the extreme decalcification, marrow fibrosis, cysts, and giant cell tumors found in osteitis fibrosa were the result of a powerful decalcifying agent, probably due to parathyroidism.—*P. J. Hodes.*

Benetato-Modval, M., and Pop, Leonida. Influenţa razelor röntgen asupra colesterinemiei la canceroşi. (The influence of roentgen rays on cholesterinemia in cancerous patients.) *Cancerul*, Oct.–Dec., 1933, *1*, 346–355.

The authors have carried out a series of experiments in determining the effect of roentgen rays on increased cholesterin content of the blood of cancerous patients. The following conclusions were reached: (1) A hypercholesterinemia is observed in the blood of cancerous patients, regardless of the localization and state of evolution of the cancer. (2) Following application of roentgen rays a drop in the amount of cholesterin of the blood, that is, a negative curve, was obtained in most of the cases. (3) The cholesterinemic curve following irradiation has no diagnostic value. (4) The phenomena of roentgen sickness are in close relation and in direct dependence on the hypocholesterinemia following irradiation with roentgen rays.—*T. Leucutia.*

Hyde, Burton E. Observations in the use of irradiated blood in connection with cancer. *Ohio State M. J.*, May, 1935, *31*, 349–357.

The author's treatment calls for the irradiation (quartz mercury vapor lamp and roentgen rays) of autogenous blood and its return to the patient by intravenous injection. The factors employed for irradiation are not given. No reactions follow if the patient has a malignancy, but in the absence of malignancy, there is a moderate reaction to the injection. Injections are given at intervals of from five to seven days until a reaction does take place. The treatment is then suspended, to be subsequently repeated with the view to keeping that patient under control. The reaction is thought to occur when the malignant process is inactive. The beneficial results of the treatment are discussed. No harmful results have been observed in a series of over 4,000 injections. The observation is made that the non-malignant patient has a reaction following the injection while the malignant patient has none is suggestive that radiation has produced a chemical change in the blood. This change has been demonstrated by spectroscopic examination, detailed in the article. The possibility of cancer being a deficiency condition is mentioned.—*W. R. Brooksher.*