The BULLETIN
OF THE
VANCOUVER MEDICAL ASSOCIATION

UNIVERSITY OF B.C.
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Vol. XII. JUNE, 1936 No. 9

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TUMOURS OF THE OVARY

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THE VANCOUVER MEDICAL ASSOCIATION

BULLETIN

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STATISTICS—APRIL, 1936

Total Population (Estimated)	247,558
Japanese Population (Estimated)	8,055
Chinese Population (Estimated)	7,895
Hindu Population (Estimated)	320

	Number	Rate per 1,000 Population
Total deaths	248	12.2
Japanese deaths	3	4.5
Chinese deaths	12	18.5
Deaths—residents only	217	10.7
Birth registrations: Male 175; Female 146	321	15.8

INFANTILE MORTALITY—	April, 1936	April, 1935
Deaths under one year of age	14	4
Death rate—per 1000 births	43.6	13.5
Stillbirths (not included in above)	7	4

CASES OF COMMUNICABLE DISEASES REPORTED IN THE CITY

	March, 1936		April, 1936		May 1st to 15th, 1936	
	Cases	Deaths	Cases	Deaths	Cases	Deaths
Smallpox	0	0	0	0	0	0
Scarlet Fever	41	0	31	0	12	0
Diphtheria	5	3	0	0	0	0
Chicken Pox	34	0	64	0	24	0
Measles	46	0	31	0	7	0
Rubella	1152	0	2422	0	841	0
Mumps	262	0	243	0	109	0
Whooping Cough	10	0	15	0	10	0
Typhoid Fever	0	0	1	0	0	0
Undulant Fever	0	0	0	0	0	0
Poliomyelitis	0	0	0	0	0	0
Tuberculosis	43	22	28	10	13	--
Meningitis (Epidemic)	0	0	0	0	0	0
Erysipelas	6	0	7	0	3	0
Encephalitis Lethargica	0	0	0	0	0	0
Paratyphoid Fever	0	0	0	0	0	0

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[We publish herewith the Programme of the Summer School of the Vancouver Meidcal Association, to be held on dates given below. The names of the lecturers and their subjects are a guarantee of an excellent and most profitable session. We will give more details later.—Ed.]

VANCOUVER MEDICAL ASSOCIATION

Summer School Programme

September 8, 9, 10, 11, 1936

1. Dr. Gordon B. New—*Department of Oral and Plastic Surgery, Mayo Clinic, Rochester, Minn.*
   1. Malignant diseases of the mouth and accessory structures.
   2. Tumours of the neck.
   3. Reconstructive surgery of the face.
   4. Tumours of the larynx.

2. Dr. W. McK. Marriott—*Department of Pædiatrics, Washington University, St. Louis, Mo.*
   1. Infant nutrition and gastrointestinal disturbances.
   2. Ear, nose and throat infections during infancy and childhood.
   3. Conditions associated with alterations in the chemical equilibrium of the body.
   4. Diagnosis and treatment of the more important blood disease of infancy.

3. Dr. Evarts A. Graham—*Surgeon, University of Washington, St. Louis, Mo.*
   1 and 2. Lectures on thoracic surgery.
   3. Certain phases of gallbladder disease.
   4. Surgery of the pancreas.

   Dr. Graham will also give one clinic.

4. Dr. J. McF. Bergland—*Lecturer in Clinical Obstetrics, Baltimore.*
   1 and 2. Complications in labor.
   3. Relief of pain.
   4. Infections in pregnancy.

5. Dr. C. B. Farrar, *Psychiatric Hospital, Toronto, Canada.*
   1. Evolution of a delusion.
   2. Psychoses which may simulate organic disease.
   3. Subject left to speaker's choice.

   Dr. Farrar will also give one clinic.

6. Dr. Rollin T. Woodyatt, *Chicago, Ill.*
   Subjects for lectures not yet available.

7. Dr. C. E. Dolman—*Provincial Health Laboratory, Vancouver, B. C.*
   Undulant Fever.

EDITOR'S PAGE

The forthcoming meeting of the Canadian Medical Association in the latter part of this month of June should receive a good deal more from us than the expression of a pious hope that as many medical men as possible will see fit to attend it.

"The time has come," the Walrus said. At the risk of identification with an animal who is hardly ever mentioned except in a rather derogatory way, we should like to say the same thing. Our profession has much to learn, and much to unlearn, and one can only hope that opportunity, who has only a forelock to catch as it fleets by, has not escaped us wholly.

We are, and it is very largely excusable in us, a very incoherent profession. We are isolated units of force to a great extent, and our influence in the community is very largely personal and not corporate. One sees this in the common experience that the same man who will accuse the medical profession of almost all the crimes in the calendar, will loyally, almost blindly, adhere to his own family doctor, submit himself and his loved ones willingly, if not altogether cheerfully, to the various forms of torture and discipline which the said family physician thinks wise to inflict, and will trust him through it all; so that the relation of a doctor to his patients carries with it satisfactions and friendships which are perhaps some of the happiest and deepest of any to be found.

Nothing must impair this relationship. More and more we should try to see that every family, every individual, shall have his own trusted medical friend and father confessor and physician. In what we may say of the need of change, we shall never lose sight of the fact that this to us is a wellnigh sacred obligation of ours to society. So much so that we agree cordially, and have always agreed, with the conclusions of the British Medical Association, who lay it down as an axiom in their Report on Proposed Medical Service for the Nation, that every family, indigent or working, poor or rich, should have its own family physician. There is something in this relationship that makes for loving service—in the sense that love is sometimes defined, as the "intense desire to help." Or as St. Paul would say, "Love is kind." There are kindness and unselfishness and devotion in this relationship—and neither we nor those we try to serve can do without it and fail to suffer loss.

But there is something more to be said, too. We must not continue to live in the shadow of an outworn tradition, and one which no longer fits the needs of either ourselves or society. Today the isolated unit is a very useless and helpless thing. He is useless to himself or others because he is helpless, and cannot do what he would, or what he knows he should. The medical man of today needs badly to learn that his duty to society entails, as one of its items, that he should be part of a firmly knit organism, which is efficient because of solidarity and flexibility, which knows its work and what it should be doing, and is able through unity and a clear knowledge of itself to impress these things upon society at large.

And it is just this that the Canadian Medical Association is aiming at, and gradually bringing to pass—and our provincial and local associations are gradually articulating their energies and powers with those of the larger body. The programme in Victoria is an amazing one—it is worth a week of any man's time; one cannot remember any programme as good. Victoria in June is apt to be a dream of loveliness, and its people are hospitality itself;

the week can and will be a thing to look back to for years, just for the pleasure and profit to be gained; but at this present juncture, most important of all,—and this means important to every man jack of us, not merely this section or that section—is the opportunity this meeting will give us to link ourselves together more closely than ever.

This has been said in various forms many, many times. But never has it been so true as now. Why are we so slow to grasp the truth that "no man liveth to himself," and only in so far as you and I and the other man does his or your or my share, can we ever hope for that measure of security and protection that should be ours and that are so important to the community at large—for, and we know it, the health and well-being and prosperity of the community at large will depend mainly, "under the providence of God" as the Prayer Book says of the British Navy, on the health and well-being and scientific achievement of the medical profession. There is too much of a tendency to divide ourselves into compartments—so that the right hand of therapeusis knows nothing of what the left hand of prevention is doing —and the leg of the orthopædist says to the stomach of the abdominal surgeon, "I have no need of thee." This is all wrong, of course. All our branches derive from the same tree, and draw their sap and strength from the same roots, and we forget this continually—so that the "health" department of medicine and the practising physician have not the understanding of each other's problems, and the consequent sympathy, that they should have for each other. Medicine, with its broad humanity, its freedom from international or racial or creedal barriers, should be the most united of all the professions, for our aims and interests are all one in reality.

So go to Victoria, for five days if you can, or for four or three or two or one, as you can afford time, and perhaps money, and add your essential bit to that of others, till in the sum we achieve a new and better order of things.

NEWS AND NOTES

The Health Insurance Committee of the College of Physicians and Surgeons had a meeting on May 28th, when they had a talk from Mr. E. M. Casey, of the Washington State Medical Bureau.

Mr. Casey gave us some very interesting and timely information. The Bureau was started some three or four years ago as a definite attempt on the part of the profession in Washington to give to the public a health service.

Today, in King County alone, they have 406 physicians, with some 28,000 beneficiaries, and the scheme is apparently growing.

At present, families are not included, but the wage-earner receives a large measure of medical service, including doctor, hospital, drugs, consultations, etc. Each patient has free choice of doctor. Payment is by the fee system for services rendered, and appears to be fairly satisfactory, working out at from 50% to 60% of the statutory fee list, with prospects of improvement.

We are gathering more data on this through Mr. Casey.

* * * *

The luncheon of the B. C. Medical Association on Health Insurance held on May 21st was a great success, and it is hoped to hold others.

* * * *

Dr. T. R. Whaley has just returned from a trip to Great Britain and the Eastern States.

Dr. A. C. Frost's second son, Jack, has just completed his medical course at McGill. His older son, Gardner, another graduate of McGill, is at present spending a holiday in Vancouver.

* * * *

Dr. Herman Robertson of Victoria, president of the Canadian Medical Association, also has a nephew who has just graduated in medicine at McGill, with very high honours: Dr. Rocke Robertson, son of Mr. Justice Robertson.

* * * *

Dr. Howard Spohn has gone to Vienna on a postgraduate trip.

* * * *

Dr. W. A. Kemp has recently opened an office in Vancouver, specializing in endocrinology.

* * * *

The Osler Club had their annual blow-out at Vancouver Golf and Country Club at Burquitlam on May 28th. It had rained heavily all morning, and some of the members shewed a lamentable lack of faith in the special divinity that looks after Thursday afternoons and golf and the medical profession, in their hesitation about going. But the deity aforesaid was on the job, and the afternoon was quite fine.

* * * *

The days of summer holidays are approaching. Perhaps the most ominous sign is that Dr. "Jimmy" Sutherland has missed several games of golf, in obedience to what he doubtless thinks is the higher law of family duty. He was last seen with "a hammer and two of his daughters" (sic!) disappearing in the direction of his summer cottage on the North Arm.

RECENT ADDITIONS TO THE LIBRARY

Ranson, S. W.—Anatomy of the Nervous System. 1935.
French, H.—Differential Diagnosis. 1936 (donated).
1936 Yearbook of Pædiatrics.
1936 Yearbook of Obstetrics and Gynæcology.
1936 Yearbook of General Therapeutics.
Keys and Cromwell—Management of Fractures. 1934.
Harrison, B. M. J.—Textbook of Roentgenology. 1935.
White, J. C.—Autonomic Nervous System. 1935.
Butlin, H.—Diseases of the Tongue. 1931.
Rehfuss, M. Z., and Belson, G. M.—Medical Treatment of Gallbladder Disease. 1936.
Mosenthal, H. O.—Variations in Blood Pressure and Nephritis. 1931.
Boyd, W.—Pathology of Internal Diseases. 1936.

FROM NICHOLSON FUND

Jennings, H. S.—Genetics.
Hirschfield, M.—Men and Women.
Yearsley, M.— Le roi est mort.
Marette, J. R.—Race, Sex, and Environment.
Hale-White, Sir W.—Great Doctors of the 19th Century.
Ballance, Sir Charles—History of Surgery of the Brain.
MacAlister, E.—Sir Donald MacAlister.
Reid, E. G.—The Great Physician (Sir Wm. Osler).
Williams, L.—Minor Medical Mysteries.
Munthe, A.—Story of San Michele.
Gosse, P.—Go to the Country.
Schleich, C. L.—Those Were Good Days.

OPEN LETTER TO THE MEMBERS OF THE B. C. MEDICAL ASSOCIATION

At this time, a little more than a month before our annual meeting, it seems fitting that a review of the happenings in the British Columbia Medical Association during the past few months be undertaken in order that the members generally have some understanding of our present position, particularly in regard to such important matters as our relationship with the Canadian Medical Association, and with the College of Physicians and Surgeons of this Province.

You will recall that at our last annual meeting a resolution was passed authorizing the present Executive of the British Columbia Medical Association so to change our Constitution that we be known as the Canadian Medical Association, British Columbia Division. Our Constitution and Bylaws Committee promptly undertook the study of this, conferred with the Council of the College of Physicians and Surgeons, and secured their hearty support. The Council in turn referred the whole matter to their legal advisor for his considered opinion as to how this could best be accomplished. After careful study on his part, he gave it as his opinion that the change could not be satisfactorily made without amending the Medical Act. Accordingly, at the request of your Executive, the Council had the necessary amendments to the Medical Act of British Columbia drafted and ready for introduction at the last session of the Legislature. As you are aware, Health Insurance became the dominant issue at that time and the relationship between our profession and the Government became so delicate that it was deemed inadvisable to attempt to introduce any amendments to the Medical Act for the time being. Hence, postponement of our becoming a Division of the Canadian Medical Association became imperative. Your Executive had hoped to have completed the change at its annual meeting this coming June, and had not these difficulties arisen would undoubtedly have done so, but now it will be another year, at least, before anything final can be accomplished in this regard. In the meantime the Canadian Medical Association has been kept acquainted with our difficulties and I am sure it is in full agreement with our action.

Despite some difficulties that occurred during the winter between the Canadian Medical Association, particularly the *Journal,* and our own Association, which I feel were very satisfactorily cleared by the excellent gesture of the Executive of the Canadian Medical Association itself in sending Doctors Bazin and Routley to the coast to assist us in any way they could, there still exists the happiest relationship between the Canadian Medical Association and the profession of British Columbia. The very frank and open way in which our problems were discussed could only lead to better understanding and ultimate good, not only to the medical organization in this Province, but to the profession in Canada as a whole. The *Journal* recognized the mistake it had made in publishing at a very inopportune time an article that was detrimental to our interests, and I feel confident that the policy of that publication will be altered in such manner as to give *some* leadership in solving the economic problems that are facing the profession today. I earnestly hope that in the near future Canadian Medicine will enjoy a much better solidarity than at present exists; it appears to me *that the greatest need facing Medicine in Canada is solidarity.* In that I include all branches of the profession, public health, hospital authorities, Universities

and those engaged in actual practice. We are far too divided at the moment. Why cannot we all unite under one banner, with one object in view, namely: collectively and *through our own purely Medical organization* to put Medicine on the highest plane possible in every particular that affects our relationship with the public we serve? Our primary allegiance should be to our own medical organization no matter in what department we happen to find ourselves.

Health Insurance has been of necessity the main concern of the profession this year, and your Executive has given its full support to the Council of the College of Physicians and Surgeons and the Health Insurance Committee in their struggle with the Government and the Legislature over this rather miserable legislative experiment. I am satisfied that everything possible was done to protect the public and the profession in combatting the Health Insurance Bill; the Government was apparently committed to Health Insurance in some form, no matter what its consequences to the medical men of the province might be. I feel that to protect the public and ourselves we would be fully justified in taking a very decided stand against anything that would tend to lower the standard of medical practice in British Columbia. The Health Insurance Committee is still gathering data, and studying all aspects of medical work here, in order to be ready when the occasion arises to protect the interests of the profession. It deserves our heartiest support. Our main efforts must be toward developing strong effective organization, and to that end your Executive, on recommendation from its Constitution and Bylaws Committee, has decided to incorporate under the Societies Act of the Province as the Scientific and Educational Section of the College of Physicians and Surgeons, still retaining its name. This will clearly define the functions of the two bodies, which have the same membership and the one fee. This should simplify and materially strengthen medical organization here in British Columbia. It will in no way interfere with our becoming a Division of the Canadian Medical Association when the time is opportune.

The appointment of an Executive Secretary of the two bodies in the person of Dr. M. W. Thomas, a man who knows first hand actual conditions of medical practice in B. C., has been a very wise move. A man with his knowledge and experience of medical life here, and devoting his full time to the work, should materially help in uniting the profession in B. C. and help us solve our many problems. This appointment fills a gap that has been staring at us for a long time. It is for us to give him our hearty support and the confidence that his position demands if he is to be of most value to us. He should be a key man with us and it is up to us to make him so.

There are many other activities of your Association during the year which I could cite, but space does not allow more at this time. These will be presented at our annual meeting in the form of reports. I sincerely hope that all who possibly can will be present at our annual meeting on June 23rd, which is held during the Canadian Medical Association Convention in Victoria.

The C. M. A. Convention has been very carefully arranged and should be well worth anyone's while attending. Health Insurance will likely again be a dominant issue at the annual meeting of the College of Physicians and Surgeons, and that alone should impel everyone to be present if at all possible. Kindly make every effort to be present in Victoria, June 22nd to 26th.

I wish to thank the members of the Executive and the various Committees for their hearty co-operation and support during the year.

Thanking you all very sincerely,

H. H. MILBURN, *President*,
B. C. Medical Association.

SERUM THERAPY

By C. E. DOLMAN, M.B., B.S., M.R.C.P., Ph.D.(Lond.), &c.

The following paper, read by Dr. Dolman before the Vancouver Medical Association on April 7th, 1936, suffers from the unavoidable omission of the illustrations which added so much to its interest. Dr. Dolman proposes to publish elsewhere, and at a later date, a more extended version of this paper, and meantime we appreciate the opportunity to give this to our readers.—EDITOR.

DEFINITION: Serum Therapy may be broadly defined as the transference of a specific humoral antibody from an animal known to have a high concentration of this antibody in its blood, to another animal which it is desired to endow temporarily with an increased supply of the same antibody.

The advantage of so broad a definition is that while it emphasizes the basic principle of serum therapy, yet all the proper applications of the term appear to be covered. Thus the antivenins come within the scope of our definition; the possible use of a species other than equine as donor, or other than human as recipient, is not precluded; hyperimmunization of the donor is not made an essential prerequisite; and recognition is given to both the prophylactic and the remedial aspects of serum therapy.

Time will not permit any attempt to cover, this evening, the whole subject of serum therapy as above defined. I must not discuss its past history, nor speculate as to its possible future. Neither the antivenins, for instance, nor the applications of serum therapy to veterinary practice, can be considered. I propose to confine attention to the principles and problems involved in the use of certain specific antitoxic and antibacterial substances (obtained from the blood serum of hyperimmunized horses) for the prophylaxis and treatment of human infections.

CLASSIFICATION: Hyperimmunized horse serums are customarily classified into two main groups, *antitoxic* and *antibacterial*.

Antitoxic serums, or antitoxins, are prepared from horses which have received a series of injections of a bacterial filtrate containing either crude exotoxin, or formalinized exotoxin (toxoid); and are assayed by determination of their specific neutralizing power for the corresponding toxin. The antitoxic serums currently available, with their approximate dates of introduction to the medical profession, will neutralize in vitro the toxins of the following micro-organisms:

C. Diphtheriae (1890); Cl. Tetani (1892); Cl. botulinum (1897); Bact. Shigae (1904); Cl. welchii, Cl. septique, Cl. œdematiens (1918); Str. scarlatinæ (1924); Staphylococcus (1934); N. meningitidis (1935)

Antibacterial serums, on the other hand, are prepared from horses which have received a series of injections of a suspension containing either dead or living bacteria; and are assayed in terms of either their agglutinating power against suspensions of the homologous micro-organisms, or—more satisfactorily—their power to protect a laboratory animal against the lethal effects of a measured dose of this micro-organism. Serums of this type were

introduced, at the approximate dates shown, for use against the following micro-organisms:

1. B. anthracis (1895); 2. N. meningitidis (1906); 3. Str. pneumoniæ (1910).

Other less well-known anti-bacterial serums have been prepared and their clinical use reported, against:

Bact. flexneri (1902); H. influenzæ (1911); Bact. typhosum (1935); Br. abortus (1935).

I shall first give consideration to certain general principles and difficulties underlying successful application of serum therapy, illustrating my remarks by reference to some of the foregoing antitoxic and antibacterial serums.

Principles of Serum Therapy: The first principle of serum therapy is *Specificity*. That is, the antibodies which the patient receives must be specific for the toxæmia, or the infection, or both, from which he is suffering, or against which it is desired to protect him. This principle clearly presupposes *correct diagnosis*. An acute pharyngitis due to staphylococcus will not be benefitted by diphtheria antitoxin; nor an acute tuberculous broncho-pneumonia by anti-pneumococcus serum; nor a streptococcal osteomyelitis by staphylococcus antitoxin; nor a meningitis due to H. influenzæ (Pfeiffer's bacillus) by anti-meningococcus serum. When no laboratory facilities are available for an immediate attempt to identify the casual micro-organism in severe cases of acute pharyngitis simulating diphtheria, of pneumonia, of osteomyelitis, or of cerebro-spinal meningitis, it is justifiable to administer, without delay, the serum homologous with the micro-organism most commonly responsible for the disease in question. But a definite proportion of failures of serum therapy will be attributable to this source of error.

Apart from *species* specificity, there must be considered *type* specificity. Type specificity should be particularly kept in mind in pneumonia. Type 1 anti-pneumococcus serum is of no avail to a patient with pneumonia due to Type 2 pneumococcus. To take another example, Cl. botulinum occurs as two types, A and B, which produce antigenically distinct toxins. A case of botulism, fortunately a rare disease, due to Type A would derive no benefit from antitoxin prepared from Cl. botulinum Type B. As more is learned of the relationship of antigenic structure to pathogenic effects, the importance of type specificity as an important factor in other varieties of serum therapy may become increasingly recognized.

The second principle of serum therapy is *Potency*. That is, the desired antibodies must be present in high concentration in the serum, so that they may be available to the patient in a minimum bulk of alien protein. Satisfactory observance of this principle depends upon the acceptance of units, the imposition of *standards*, and distribution under *licence*. International units of potency have been proposed and accepted for the majority of the antitoxic and antibacterial serums already listed. It is interesting and gratifying to note that the investigation and control of these units has latterly been conducted under the aegis of the League of Nations (Committee on Standardization of the Health Organization of the League). Most of these units involve, officially, determination of the highest dilution of the respective serums which will protect some small laboratory animal (usually guinea-pig or mouse) against a stated number of minimal lethal doses of the corresponding toxin or live culture. Various other methods of determining potency are practised.

The production of high potency serum depends upon the operation of several factors, among which are the following: the selection of suitable horses; the use of a satisfactory antigen; correct volume, time, and route of doses; careful checking of the fluctuations in circulating antibody by frequent trial bleeds of the horse; prompt exsanguination when the trial bleed shows an appropriately high titre of antibody; efficient methods of concentration and refinement. While the aim of every ethical manufacturer of serums is to increase the potency of the products, a definite limitation is set by a regulation which prohibits a content of more than 20% of total solids in therapeutic serums.

The licensing authorities on the North American continent are the National Institute of Health, Washington, and the Laboratory of Hygiene, Ottawa (operating under the Department of Pensions and National Health). Connaught Laboratories, the only serum institute in Canada licensed to manufacture biological products by both Washington and Ottawa, is subject to inspection by their representatives, and must observe the standards they impose. The United States regulations require the potency of every serum to be printed on the outside of the package as well as on the label of the vial. Where no official unit has been accepted, the words "No U.S. standard of potency" must appear. Substandard serums have undoubtedly been distributed in the past in certain countries, but increasingly stringent regulations are now being applied.

The third principle of serum therapy is *Early Administration*. That is, given a supply of specific, high-potency serum, its efficacy will diminish rapidly with delay before administration, till a time is reached in the progress of the disease when no amount of serum, however specific and potent, will exert any apparent beneficial effect. This principle presupposes a prompt diagnosis, the knowledge that serum therapy is indicated, and availability of the requisite serum. To defer the diagnosis of diphtheria, for example, until a case of presumed broncho-pneumonia has come to autopsy, will not help anybody; and one has encountered many examples of staphylococcal septicæmia, particularly in adults, which remained undiagnosed until the disease had progressed to a hopeless stage. One man, I recall, had an appendectomy performed at a large teaching hospital for staphylococcus septicæmia. Another got infected after a prostatectomy, and ran an intermittent fever for three weeks before a blood culture was done and a septicæmia found. Make good use, therefore, of your laboratories.

Then there are many instances of the diagnosis having been made early enough but serum therapy being delayed until the patient was moribund. The doctor does not know there is a serum, or else he decides to hope the patient will get well without it. Moreover, it is regrettable that serums are not always as readily available as they should be. They are costly, and while some provincial or municipal governments make provision for the supply of certain types of serum to those who cannot afford to pay for them, there is no doubt the expense of serum therapy is often regarded as prohibitive. But a greater demand for serum would permit a lesser price. When there is a very rare demand for a serum, the manufacturers will tend to be less interested in its production than in the improvement of a serum which is widely used. If you encounter tomorrow a case of botulism, for instance, you would certainly experience some delay before obtaining a supply of the appropriate serum.

The importance of this principle of early administration derives from the fact that the deleterious effects of pathogenic micro-organisms upon the

animal body are attributable to a process akin, in certain respects, to chemical union between the animal cells and the toxic substances derived from the micro-organisms. This chemical union is to some extent irreversible. The final firmness of the union may vary with the different micro-organisms concerned, and for every bacterial toxæmia there is possibly a period of definite duration in which the union between cell and toxin is relatively loose. The local blanching of the scarlet fever erythema following the early injection of the specific antitoxin into the skin (Schulz-Charlton reaction) is possibly an instance of a relatively loose cell-toxin union. In gas gangrene infections, again, the toxins appear to form a looser type of union with the body cells than in diphtheria, tetanus, or botulism, where the union appears to be almost completely irreversible. In these latter diseases, indeed, once symptoms have appeared, our resort to serum therapy is founded on the hope that widespread toxin-cell union has not already occurred to an extent not yet manifest clinically, and on the assumption that all newly-formed toxin will henceforward be neutralized.

It is interesting to contrast the small amounts of circulating antibody which suffice to *protect* from an infection, with the relatively enormous amounts which may be got into the blood stream in serum therapy, to no advantage if they get there too late. The presence of $\frac{1}{100}$ unit of diphtheria per c.c. of serum generally suffices to ensure protection against the disease; yet a patient treated with antitoxin at a late stage may die despite the presence of 10 units or more of antitoxin. Again, the prophylactic dose of 1500 units of tetanus antitoxin will usually result in a circulating titre of about $\frac{1}{5}$ unit of antitoxin a few days later, and this will protect against the disease. Yet one hundred times this titre of antitoxin acquired through late serum therapy may prove absolutely useless. Patients who recover from lobar pneumonia rarely develop a sufficient amount of antibody in their serum to protect mice against more than 100 lethal doses of homologous pnemococci per c.c. After late administration of anti-pneumococcus serum, on the other hand, 1 c.c. of a patient's blood may be able to protect mice against 1,000,000 lethal doses of homologous culture, and yet the patient may die. The very small amount of measles antibody which can reach the blood of a measles contact, following injection of 10 c.c. of convalescent serum, is almost always sufficient to prevent the development of the disease if given during the first five days after exposure, but no amount of convalescent serum has any apparent effect upon the disease once manifest. Antivaccine virus serum injected intradermally into a rabbit *before* injection of vaccinia virus into the same site, will prevent the characteristic reaction. Given one minute *after* the virus, the serum will have no inhibiting effect. Anti-Rous sarcoma serum given to a fowl *before* injection of a sarcoma filtrate will confer temporary immunity; given *after* the injection will not prevent development of the tumour. Examples of the operation of this principle might be multiplied; and I have gone into it at some length because it is of such fundamental importance, and is on the whole ill-appreciated.

Closely related to the third, are the fourth and fifth principles of serum therapy, namely, those of *optimal route* and *adequate dosage*. Bearing in mind what has been already stated, it is clearly of paramount importance that, once the disease is diagnosed, a decision to resort to serum therapy reached, and a supply of specific serum at hand, our main object must be to bring a large quantity of the antibody into as intimate a contact as possible with those parts of the body where extensive cell-toxin union has

occurred, in an attempt to break up this union; with those foci where toxin is still being produced, in order that neutralization *in situ* may take place; and with those tissues which have so far resisted the effects of the toxin, with a view to protecting them therefrom. In generall all this is best achieved by the *intravenous* route of administration. Given by this route, all the serum injected is at once distributed throughout the body, and the maximum concentration of circulating antibody will be reached just after completion of the injection. The delayed absorption of antibody from the muscles is not sufficiently realized. Following an intramuscular injection of a serum, *e.g.*, diphtheria, scarlet fever, or staphylococcus antitoxins, from 48 to 72 hours must elapse before the maximum titre of antibody is detected in the blood stream. Such a delay may be literally fatal in a disease of rapid course, such as lobar pneumonia; and little or nothing is gained by administering antipneumococcus serum by any route other than the intravenous. Indeed, with few exceptions, all serums should, both in theory and in practice, be given intravenously, although this route undoubtedly entails more trouble to the doctor, and constitutes a greater reaction hazard to the patient. Meningitis is one exception to this rule. In the serum therapy of meningitis —whether meningococcic, influenzal, pneumococcal, streptococcal or staphylococcal—the intrathecal route must be adopted, since very little antitoxin permeates from the blood stream, through what Friedemann has called the "blood-brain barrier," into the cerebrospinal fluid. On the other hand, intravenous serum should also be given when there is a concomitant septicæmia. There are occasions when direct application of serum to an exposed infected surface would seem to be indicated; as, for instance, in a pneumococcal empyema drainage wound, an osteomyelitis, or a carbuncle.

Again, in the *prophylactic* use of serums, the intramuscular route, if resorted to very soon after exposure to infection, usually permits sufficiently rapid absorption to ensure protection. The same route will serve in the ordinary case of uncomplicated, well-localized carbuncle. But, in general, therapeutic serums should be given intravenously, if possible.

So much for the principle of *optimal route*. The principle of *adequate dosage* is self-explanatory, though in actual practice far too seldom observed. The general tendency is to give too little serum, and to this fact many of the failures of serum therapy are undoubtedly due. There is no fixed treatment dose of serum, although direction sheets usually state some figure as a guide. In prophylaxis, a definite dose may be fairly safely recommended; but in treatment, each case presents a special problem. The age and general condition of the patient, the type and severity of the infection and toxæmia, the presence of complications, and especially the duration of the illness, and the response to the first doses of serum, must all be taken into consideration. The longer the time since onset, the more serum will be necessary. More must be given by the intramuscular route than by the intravenous route. And it is important to be especially liberal in dosage when there has been a blood stream infection, with multiple foci, as *e.g.* in staphylococcal septicæmia. In such conditions, the blood stream may become sterile and the patient appear much better, so that serum is withheld; the circulating antitoxin is excreted, or at any rate diminishes in titre; and then, a few days later (this has happened so often) a relapse occurs, and staphylococci reappear in the blood stream. The principle of adequate dosage really involves, in fact, that a high titre of circulating antibodies should be maintained until the infection is well localized, and toxæmia satisfactorily abated.

The sixth and final principle is that of *accessory treatment*. Serum

therapy is too frequently the last resort of the harassed practitioner. All else may have been done for the unfortunate patient—quite commonly under a mistaken diagnosis; and then, with the patient moribund, recourse is had to serum therapy. I hope from what I have said, and shall say tonight, to make clear to you that recourse to serum therapy at this stage of a disease is tantamount to the requisition of a miracle. In other instances, serum may be given comparatively early in the infection, but is expected to eliminate the disease without any other treatment except for rest in bed, an attractive nurse, and a reasonably digestible diet. In the pyogenic infections particularly, pus can be expected to form, and should be considered of favourable portent, provided it be *drained*. The letting out and mopping up of pus is, after all, one of the surgeon's chief functions; but one has been continually surprised to find a reluctance to perform this very important accessory treatment.

Difficulties in Serum Therapy. Some of the main difficulties militating against successful serum therapy may be considered under the heading *Complications*. These complications may occur during the course of any relatively simple infection, just as a satisfactory outcome appears in sight. First, one may mention *secondary infection*. This has occurred several times in my own experience: *e.g.*, a patient being given staphylococcus antitoxin for severe osteomyelitis and septicæmia, and doing well, takes a grave turn, and dies of streptococcal pericarditis; another, making a most gratifying recovery with the help of serum therapy from staphylococcal meningitis, developed a double secondary infection of the meninges with a hæmolytic streptococcus and a diphtheroid bacillus, which proved fatal; yet another, having turned the corner in a staphylococcal septicæmia, in the course of which it was necessary to resect a rib to drain an abscess, developed a pneumococcal empyema. Full use should therefore be made of the laboratory at all stages of severe infections of this type. The reports will not only add inestimably to the value of case records, but will indicate eventualities of the foregoing order.

More common types of complication are those attributable to the peculiar habits or habitats of the micro-organisms involved. Abscess formation may occur, for instance, in remote and vital parts of the body, such as the brain, kidneys and lungs. Serum has no power to cause absorption of an abscess any more than the therapeutic serums in common use can act like an *in vitro* antiseptic and directly kill their homologous micro-organisms. Again, infection may settle in certain foci inaccessible to the blood stream and there prove comparatively unamenable to serum therapy. Hence an osteomyelitic focus may be expected to discharge pus and micro-organisms long after the patient is convalescent from septicæmia. An ear may discharge following streptococcal otitis media, for weeks after the patient has overcome, with the help of scarlet fever antitoxin, a severe attack of scarlatina. Or pneumococcal pus may continue to discharge from an empyema drainage tube during convalescence from pneumonia successfully treated with pneumococcus antitoxin. In other words, the value of a high titre of specific circulating antibody to any one part of the body infected with a micro-organism, will depend upon the extent to which the blood fluids gain access to that part.

Reactions constitute another serious difficulty rather frequently encountered in serum therapy. These reactions are of different ætiology and character, and may be considered as of three main types, the *Allergic*, the *Thermal*, and *Serum Sickness*

The *allergic reactions* arise from parenteral injection of certain substances peculiar to the horse and highly toxic to certain human beings, which it has not yet proved possible to separate from the desired specific antibodies. Dyspnœa, cyanosis, rapid weak pulse, flushing of face, pain in abdomen and in lumbar or substernal regions, apprehension, and collapse, may all be present in varying degree, and their onset is usually within one-half hour of the first injection of serum. In its most severe manifestation, this reaction may prove almost immediately fatal; but this acute shock-like form is fortunately rare. In other less severe types of allergic reaction, the above syndrome may be complicated by urticaria or an acute asthmatic attack. The treatment of allergic reaction is by epinephrine, one-half to one cc. of the 1:1000 solution, given subcutaneously, intramuscularly, or in severe cases intravenously. Repeated doses may need to be given. While mild degrees of allergic reaction are no contra-indication to further administration of serum, provided they prove controllable by epinephrine, in the more severe types of reaction—particularly those accompanied by urticaria or asthma—no more serum should be given.

Most, though not all, allergic serum reactions may be avoided by doing eye and skin sensitivity tests on every prospective recipient of horse serum. In the *eye,* or ophthalmic, test, a drop or two of normal horse serum, diluted 1 in 10, is placed in the conjunctival sac. A positive reaction is marked by erythema, lachrymation, and reddening of the eye, within 20 minutes after instillation of the serum. In the *skin,* or intradermal test, 0.1 cc. of normal horse serum, diluted 1 in 10, is injected intradermally into the flexor surface of the forearm. A positive reaction will be indicated within 5 to 20 minutes by the formation of an urticarial wheal at the site of injection, surrounded by a zone of erythema which may show irregular, pseudopodia-like extensions.

Positive sensitivity reactions to horse serum will usually be given by the following individuals:

1. Those who are spontaneously sensitive to horse dander. A history of such sensitivity signifies that serum therapy would be very hazardous, and is best avoided.
2. A certain proportion of persons who are subject to asthma, hay fever, and similar allergic conditions. Even if the sensitivity tests are negative, it is advisable to precede the injection of serum, in patients of this type, by an injection of epinephrine; while, if the intravenous route is to be used, a smaller initial dose than usual is indicated, and the injection must be given with extreme slowness.
3. Patients who have had an injection of horse serum within a period of from 7 to 10 days up to a few months previously, or who are still suffering from serum sickness (*vide infra*). Sensitivity to horse serum acquired from previous parenteral administration is not commonly very acute after a few months have elapsed; but the precautions stated in the preceding paragraph should be observed.
4. Positive sensitivity tests will be given in some instances where there is no history of either allergy or a previous injection of serum. The existence of such individuals alone makes the performance of the sensitivity tests a desirable routine procedure.

Desensitization may be attempted in individuals who give a positive eye or skin reaction. No one method is prescribed for this, but in severe cases of sensitivity, a commencing dose of the serum to be used as small as $\frac{1}{40}$ cc., subcutaneously, is advocated. Successive doses should be given by the same

route at intervals of 10 to 15 minutes, each dose being double the preceding dose, provided that no undue reaction has occurred in the meantime. When 1 to 2 c.c is well tolerated by the subcutaneous route, intravenous administration may be commenced. The rate should be *very slow*. Anti-pneumococcus serum, for instance, which is usually injected from a syringe directly into the vein, should be given at a rate not faster than 1 cc. per minute; while other serums are perhaps best given intravenously by a slow continuous drip method, diluted in saline, so that the first 1 cc. may take 1 hour.

While the allergic reaction hazard is greatest when serum is given intravenously, it should be emphasized that severe reactions of this type may occur following the intramuscular or any other route of administration, if due precautions be not taken to guard against them.

Thermal or *chill* reactions are not due to allergic sensitivity, as this is ordinarily understood, but to some factor peculiar to the serum, to the patient, to the disease, or to the interaction of these three variables. Between 20 minutes and 1½ hours after the first injection of serum, a general rigor will occur, lasting up to ½ hour, accompanied by cyanosis, dyspnœa, rapid pulse, low blood pressure, and apprehension. The temperature may rise several degrees, and subsequently falls, with profuse sweating. Milder reactions of this type need give rise to no alarm; but if severe, further serum should be withheld for a few hours. In pneumonia, or septicæmic conditions where the temperature is usually already high, alarming degrees of hyperthermia may result, accompanied by pronounced cyanosis, almost uncountable pulse, delirium, convulsions and collapse. When this occurs, no further serum should be given. In the presence of pre-existing obstruction to the pulmonary circulation, severe myocarditis or hyperpyrexia, a fatal issue may occur in consequence of a superimposed thermal reaction.

Liability to thermal reactions is not indicated by tests for serum sensitivity. Certain batches of serum seem more prone to contain the reaction-producing factor than others, but in general concentrated and refined products are less liable than crude serums to produce thermal reactions.

Epinephrine has little or no effect upon this type of reaction, and the treatment is symptomatic. Precautions to be taken to minimize their incidence include very slow administration of the serum, warming serum to body temperature prior to administration, and rejection of all serums containing a precipitate.

Serum sickness is a fairly common type of delayed reaction to horse serum therapy, with onset characteristically on the 7th to 10th day after the first injection. Urticaria (which may be troublesome for a day or so), joint pains and swelling, generalized glandular enlargement, œdematous foci, with mild fever, are the most common features. Epinephrine and ephedrine may prove useful, but for the most part treatment is symptomatic. The condition is never dangerous and is transitory.

A further difficulty of serum therapy may be defined as that of the unknown extent of *irreparable antecedent damage to vital cells and tissues.* The patient may, in other words, have already suffered fatal, but not clinically apparent, damage before any attempt is made to give specific serum therapy. Such patients are to all intents already dead. A toxic myocarditis, metastatic abscesses in the lung, or thrombosis of a cerebral vein, may be present but undiagnosed at the time the decision is made to give serum. This difficulty is, in fact, a restatement (from a somewhat different viewpoint) of Principle 3, viz. *early administration.*

The final difficulty, to which only brief allusion will here be made, arises

from the *incompleteness of available specific antibodies*. This incompleteness derives, in turn, from our comparative ignorance of the parts played by various bacterial antigens in furthering the progress of any one infection. Diphtheria, tetanus, and botulism represent true toxæmias; that is, the respective micro-organisms have no invasive powers, and all the outstanding signs and symptoms of these diseases are attributable to toxins disseminated throughout the body from a localized focus of multiplying bacteria. The situation is very different in many of the other diseases for which serum therapy is advocated. In streptococcal and staphylococcal septicæmias, for instance, our problem is not only to neutralize toxins, but also to aid destruction of the infecting micro-organisms.

None of the antitoxic serums at present in use are actively bactericidal, but certain of them are believed to promote phagocytosis by neutralizing specific leucocidic substances liberated by the homologous micro-organisms. One of the outstanding problems in serum therapy is the production of specific antibodies to combat those factors which bestow the property of *invasiveness* upon certain micro-organisms. There has recently been a considerable revival of interest in the analysis of the mechanism of bacterial invasiveness, and this is yielding promising results.

GRANULOSA CELL CARCINOMA OF THE OVARY, WITH REPORT OF A CASE

By H. H. Pitts, M.D.

(Read before the Osler Club, April 22, 1936.)

These tumours are said by same authorities to be relatively rare and by others to be relatively common, and the fact that I have seen, probably I should say recognized, only this one case, which serves as the excuse for this paper, in well over 50,000 surgical specimens of all types examined in the past fifteen years, would seem to point to their rarity, at least as far as one's own experience is concerned. These tumours vary greatly in size, many being extremely minute and others seen only on microscopic examination, and this fact may account for the relatively small number reported in the literature until fairly recently, when previous reports have stimulated interest in them and probably caused observers to be more watchful for them.

Up to the present time approximately 245 cases have been reported, and these have been admirably reviewed by Bland and Goldstein in the August, 1935, number of *Surgery, Gynæcology and Obstetrics*. Novak and Brawner, in the November, 1934, number of the *American Journal of Obstetrics and Gynæcology*, present an excellent clinical and pathological study of 36 cases coming under their own observation, and present details of historical interest, histogenesis, diagnosis and treatment. They begin their paper with the two following paragraphs:

"A striking illustration of the slowness with which new knowledge permeates the medical profession is to be seen in the case of the granulosa cell tumours of the ovary. Within the past few years this group of neoplasms has been so much discussed by gynæcologic pathologists that one might get the impression that they constitute a newly described type of growth. As a matter of fact, the pathologic characteristics of these tumours were fully described more than twenty years ago, while during many years before and after this a considerable group of more or less clearly defined instances of

the lesion had been reported, though often under other names. The present common designation of these tumours as 'granulosa cell carcinoma' was applied more than a score of years ago.

"The present-day interest in tumours of this variety is due, first, to a realization of the fact that they are not nearly as rare as was once believed; and, second, to the fact that they possess interesting biological properties not shared by most other ovarian tumours. It is this latter characteristic especially which, in this day of feverish interest in gynæcological endocrinology, has stimulated the study of granulosa cell tumours of the ovary."

We are indebted chiefly to Robert Meyer and Von Werdt for the present-day knowledge of these tumours—to Von Werdt for the name and thorough pathologic study, and to Meyer for the theory of histogenesis; *i.e.*, origin from granulosa cell rests, which is now generally accepted. Von Kahlden reported the first case in 1895 under the name of "adenoma of the Graafian follicle," and soon many other reports followed with, also, the coinage of many new terms. Meyer's theory is that these tumours arise from granulosa cell rests remaining froh the early oophorogenetic phase of ovarian development and he offers as support for this theory the histological characteristics of the cells, their frequent arrangement in folliculoid fashion and the effect on the endometrium. Embryonal cell rests have been found in theovaries of the newborn and with the findings reported by Te Linde and Geist from the microscopic study of very early granulosa cell tumours, still further support is given to the probable origin in embryonic rests of the ovarian parenchyma in the ovarian medulla.

The tumours vary from millimetre or even microscopic size to 15 or 20 cm. in diameter, but some have occupied almost the entire abdominal cavity. The shape varies, but, generally speaking, they assume a more or less ovoid form, frequently somewhat lobulated, usually unilateral but quite frequently bilateral. On section they present a more or less solid pinkish-white cut surface but, especially in the larger ones, there may be considerable degeneration or cystic change. They are generally fairly well circumscribed. Histologically, the tumours can be subdivided into three fairly well defined sub-groups according to the predominating arrangements of their cells: (1) the *folliculoid,* in which the cells show a tendency to follicle reproduction or simple rosette formation; (2) the *cylindromatoid,* where the cells are arranged more in column-like masses or alveolar aggregations without definite follicle formation. This type is said by some to be the most common and they are frequently diagnosed, even microscopically, as carcinoma solidum, medullary carcinoma and endothelioma. (3) The diffuse or *sarcomatoid* group. Here the epithelial cells assume a much more atypical appearance and both cylindroid and folliculoid characteristics are seen, as well as diffuse sarcomatous-appearing masses and nests of cells, or the whole picture may be sarcomatous in appearance.

The clinical aspects of these tumours are even more interesting than their rather complex and varied histological structure, due to the definitely established fact of the secretion of ovarian follicular hormone by them with resultant very remarkable manifestations, more especially during what might be termed the "latent" period of ovarian activity, *i.e.*, before puberty and postmenopausal. Children show well marked sexual precocity with hyperplastic and hypertrophic mammary changes even in 5 and 9-year-old girls, secretion of colostrum, development of pubic and axillary hair and vaginal bleeding. In old women, there occurs what might be termed a rejuvenation manifested by hypertrophy of the breasts, either regular or

irregular menstruation, enlargement of the uterus to the size of the normal uterus of the childbearing years and hyperplastic changes in the endometrium.

A more confusing picture is presented during active sexual life, but where there is a long history of metrorrhagia not responding to the usual endocrine therapy, it should suggest the presence of a granulosa cell tumour, especially so if either unilateral or bilateral ovarian enlargement can be detected. Then, again, amenorhœa may be the prominent feature, or it may alternate with profuse and prolonged bleeding, which array of symptoms in the presence of a unilateral pelvic mass, breast changes, etc., may make the diagnosis of an ectopic pregnancy a very plausible one. Margaret Schulze of the University of California Department of Obstetrics and Gynæcology, in a paper on these tumours, notes the possibility of sterility being dependent upon endocrine influences of the tumour, one of their patients who had been sterile for five years having had a child two years after the removal of one of these tumours and this without any further treatment. In this same paper Schulze further states, "The tumour may arise at any age, but is relatively rare before puberty and relatively common in old age. Of 80 cases which Klaften collected, 7, or 8.7%, occurred before or at the beginning of puberty; 34, or 42.5%, after the menopause. Two cases occurred at 5 years, and 8 between 70 and 80 years."

Pain and evidence of pressure may occur at any time and age. Abdominal enlargement is not particularly common, as generally speaking the tumours are small, but occasionally there may be ascites. There may be evidence of anæmia only, due to continued hæmorrhage, but generally their physical condition is good. Klaften reported that two of his cases had BMR's of plus 18 and plus 24 respectively, which returned to normal following extirpation of the tumour. Estimations of follicular hormone in urine and stool have been made and are found to be much increased when the tumours are present, and gradually diminished after their removal. Besides folliculin, progestin has also been found to be secreted. The folliculin effect has been demonstrated by the production of œstrous effects in castrated mice. Novak and Brawner state as follows, in a recent paper: "It is of interest to note that the Aschheim-Zondek reaction has been positive in a number of instances, through this mild response is not, of course, conclusive. In Pahl's case, however, both the second and third degrees of reaction were positive. This is significant in view of what has been said as to the possibility of lutein-like changes in the tumour cells. Just how these are to be explained we can only speculate. The frequent finding of prolan A in the urine of these patients suggests that there must be some interaction between the ovary and the anterior lobe, and that the luteinizing factor of the latter brings about the occasional transformation of granulosal into lutein or lutein-like cells. After all, the normal lutein cell of the corpus luteum is only a modified granulosa cell, and for that matter it is possible, as some believe, that progestin is only a modification of folliculin. If this is true, it is not difficult to understand the occasional transforation occurring in the granulosal tumour, while the effects of the tumour hormones are in conformity with what we know of these effects upon the genital mucosa and sex character development generally."

In this same paper these two authors make the following statement, which might be accepted as a diagnostic criterion for these tumours: "It is in childhood and in the postmenstrual years that the preoperative diagnosis of the nature of the tumour can most often be made, at least presumptively.

This is because of the physiological and biological effects produced by the growth, which stand out sharply in patients at these ages, as already emphasized in a previous paragraph. If an ovarian tumour is demonstrable in a child with precocious menstruation and puberty, it is very likely to be of the granulosa cell type. Again, if a tumour is found in a patient well beyond the menopause, associated with periodic and perhaps pseudomenstrual bleeding, it is almost sure to be a granulosa cell cancer. The likelihood is converted into almost absolute certainty if a diagnostic curettage yields a frankly hyperplastic endometrium. In both of these groups, hormone studies are of even greater value that in the case of tumours encountered in patients during reproductive life."

The following case is reported through the kindness of Drs. J. J. Mason and J. W. Lang of West Vancouver.

Mrs. N. D. R., age 68 years.

Past history essentially negative except for radical amputation of breast, V. G. H., November, 1934. Typhoid fever at age of 40.

Menses began at age of 12, regular 5-6 days every 28 to age 52. Has had 7 full term pregnancies, no miscarriages. Children all alive and well, the youngest 36 years of age. Between the ages of 52 and 64 had no menstrual flow either regular or irregular but for past four years has had regular menstrual flow lasting 10 days every three weeks. Complained of dyspnœa during past summer but did not see her doctor. For the past few weeks has had some pain in right lower quadrant. Bowels regular until she went to bed 10 days ago. Vomiting past two days. A mass is palpable in lower abdomen to right of uterus and slightly movable. Has cystocele and rectocele. Catheter urine shows trace of albumen and moderate number of pus cells. Nocturia 1. Has been gaining weight.

Operation on March 11, 1936, by Dr. J. J. Mason. On opening the abdomen much thin, bloody fluid was found free in the abdominal cavity. Liver, etc., normal. Left ovary was occupied by a tumour mass which was to the right of the uterus and attached to right pelvis by thin adhesions and in one place to the bowel, where capsule of the tumour had split and a hæmatoma the size of a golf ball was present here. Tumour delivered and resected. Right tube and ovary normal. Uterus well developed, not menopausal type, and was not removed. No diagnostic curettage was done but probably would have shown a hyperplastic endometrium. The tumour measured 20x12x10 cm. A diagnosis of possible granulosa cell carcinoma was made by Dr. Mason.

Pathological Findings

Macroscopic examination.—Specimen consists of a large, roughly ovoid but slightly lobulated or nodular tumour mass weighing 153 gm., and measuring 20x12x10 cm., replacing the left ovary. A Fallopian tube stretched over it shows nothing of particular note beyond two small parovarian cysts in its mesentery. The surface of the mass is smooth and dilated blood vessels course over it. On section it presents, generally, the appearance of a markedly enlarged ovary, the various structures of gigantic proportion. One pole is replaced by a simple cyst the size of an orange, smooth lined and filled with bloody fluid. The central portion is extremely hæmorrhagic, containing masses of blood clot arranged within cystic structures, and here and there small yellowish masses indicate luteal tissue. The most characteristic feature, however, consists of smaller and larger nodules of greyish, smooth, brainlike tissue probably arising from the stratum granulosum, as would certainly be suggested by the history. These bodies, for the most part, appear fairly well circumscribed, but the tissue itself is so cellular as to suggest a malignant process. Numerous other small simple cysts are encountered throughout the mass, the actual size of which is largely due to them. They are interspersed throughout, scattered amongst the tumour tissue. The supporting structure in some fairly large areas, however, has a somewhat cellular appearance.

Microscopic examination.—A great many sections were taken through various portions of the tumour mass and show a very variable type of structure. For the most part, the cells are relatively closely packed, rather ovoid or somewhat spindle-shaped, almost of sarcomatous appearance, of fairly large size and showing a moderately large, fairly deeply staining nucleus. Occasional mitotic figures are seen as well. The cells are supported by a relatively sparse stroma. Sometimes in these masses of cells there are smaller and larger spaces that may be immature follicles and very poorly defined as such. In still other areas there is a somewhat glandular or pseudo-rosette type of arrangement, but these are very scarce, and the whole structure is very well vascularized with some areas of quite extensive hæmorrhagic extravasation and a rather cystic or œdematous degenration. This is, appar-

ently, a definite granulosa cell carcinoma of the ovary and evidently of the so-called mixed type.

Prognosis.—The general consensus of opinion is that these tumours are less malignant than ovarian carcinoma generally, but they should not be considered so relatively benign as some writers claim. While those that recur do so locally or in the peritoneum, a number of cases in which osseous metastases have occurred have been reported. Novak and Brawner in their cases report a percentage of 28.1 clinical malignancy as against the 5 to 10% rate as an average or mean in the general literature of reported cases.

Treatment.—This is primarily surgical, and the extent of the surgical intervention naturally varies according to the operator's idea of the degree of malignancy of these tumours. Novak and Brawner hold the view that in the young patient removal of the adnexa on the affected side alone, with careful, fairly frequent, periodic check-up postoperatively, will be sufficient; while in the patient who has borne children, or in the postmenopausal case, it is probably the wiser procedure to do a panhysterectomy. Deep x-ray therapy is probably a useful adjunct both pre- and postoperatively, especially in view of the radio-sensitivity of granulosal tissue.

In conclusion, I might make a plea, at least from a pathologist's standpoint, for closer co-operation between surgeon and pathologist in the matter of history in those cases presenting such symptoms as have been enumerated in this paper, since this might serve as a lead in establishing more accurate diagnoses by putting the pathologist on the *qui vive* for the existence of these tumours. I feel sure that I have overlooked a goodly number in the past and so will endeavour to burden the surgeon with a measure of the blame due for my sins of omission.

HEALTH INSURANCE IN ENGLAND

R. G. Leland, M.D.
Chicago
(Bureau of Medical Economics, American Medical Association)

(Concluded from May issue)

There is no question but Sir Henry approves health insurance. No one disputes that position, but this restatement and emphasis of the official statement of the British Medical Association to the Royal Commission are of especial significance to us in the United States. In his opinion, "the organization of a national health insurance scheme is not necessarily, or even probably, the best means of utilizing limited resources for the promotion of national health." The United States is just now ready to discuss the question of "the best means."

In the twenty-one years that the British system has been in operation, about two billion dollars have been spent under the national health insurance scheme. If we are to enter on the spending of the much larger sum which would be necessary in this country, is it not well to consider the "other directions" in which such an "expenditure would produce an even more satisfactory return." These quotations of Sir Henry's may be interpreted to mean that however much he may now believe it is necessary to develop and expand national health insurance as the only line of advance open in England, he would not advise a nation that had not entered upon this plan so to utilize its "limited resources." This is the important phase of the question that interests us in the United States.

That the British Medical Association recognizes that in many ways the

existence of a national health insurance system has rendered more difficult the problem of a proper organization of all medical facilities is shown in the "Memorandum of Evidence by the Association's Scottish Committee" on "The Scottish Health Services." This appears as a Supplement to the *British Medical Journal* of July 7, 1934. Paragraph 164, page 15, of this memorandum says:

> With all its imperfections, the present system of national health insurance has become an accepted and valued part of the national life, and preserves what the Association regards as essential factors in the relationship between patient and doctor. It would appear, therefore, to be the wiser course to provide a national medical service by the extension of the present compulsory contributory system rather than to scrap the whole of the existing machinery and proceed to build on an entirely new foundation.

In other words, it is evidently still a debatable question whether if it were possible it would be desirable "to scrap the whole of the existing machinery and proceed to build on an entirely new foundation." Too much stress should not be laid on this quotation, which may be to some extent rhetorical. The previous paragraph indicates that the choice is now between the extension, development and adjustment of the national insurance system to meet the larger problems of medical service and "a salaried state service." Concerning the latter, the report says, "There can be no doubt that the great majority of the profession is strongly opposed to this." It would seem to be a fair interpretation of the entire report to say that because the "present system of National Health Insurance has become an accepted and valued part of the national life" that now only two alternatives are left for the British Medical Association to consider. One of these is the salaried state service and the other an effort to patch up and co-ordinate the present system of national health insurance with other forms of medical service.

Sensing the opportunity to make some changes in the methods of administering medical care to persons with low incomes, without following the European pattern of health insurance, several county medical societies in the United States have placed in operation plans which are worthy of notice.

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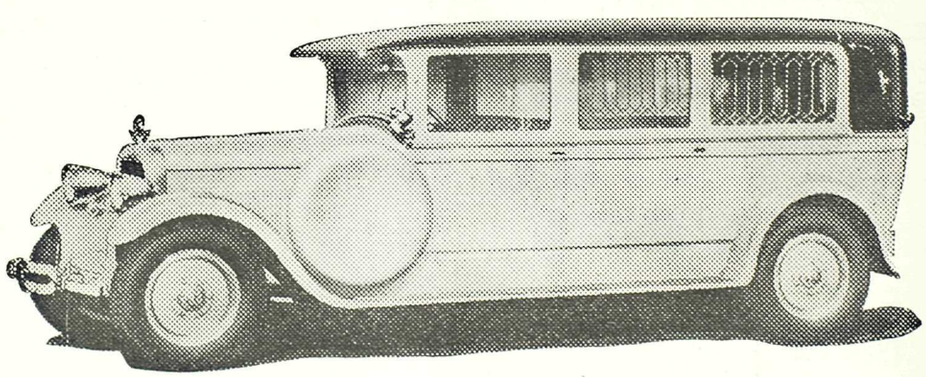

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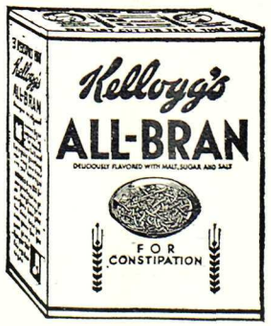

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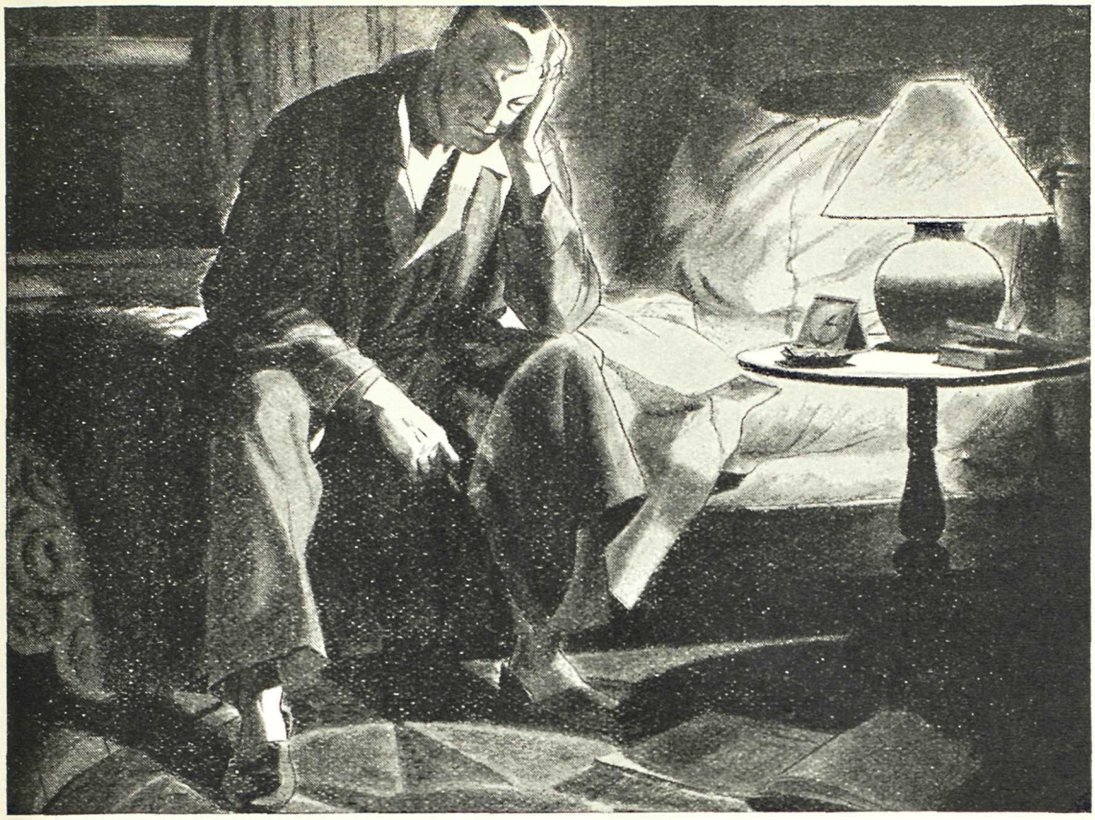

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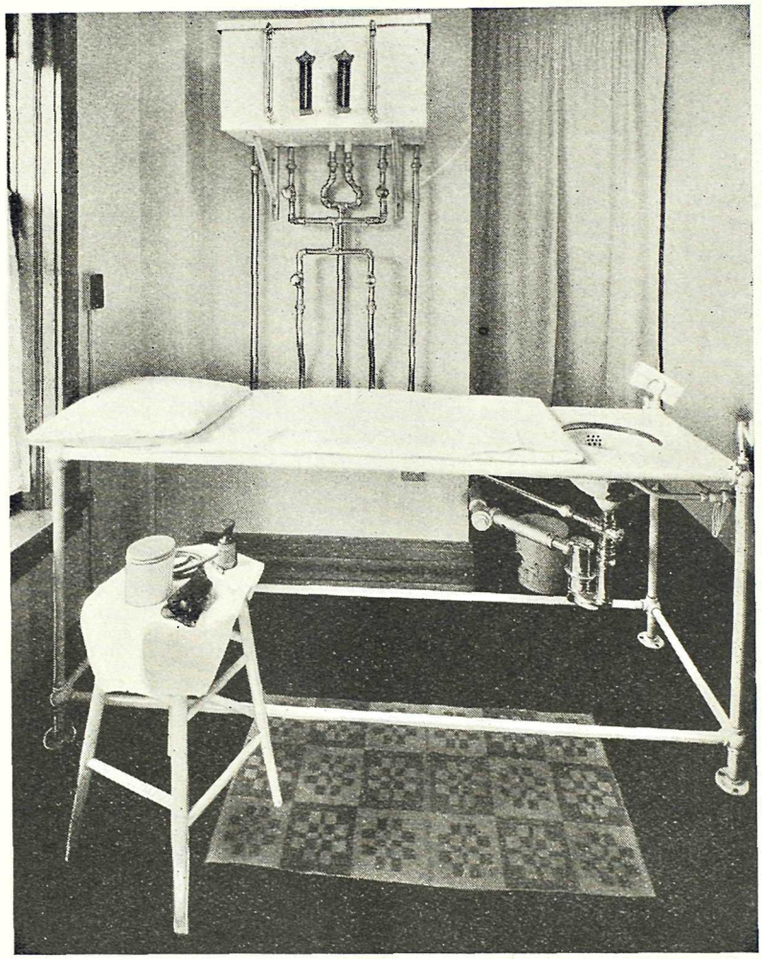

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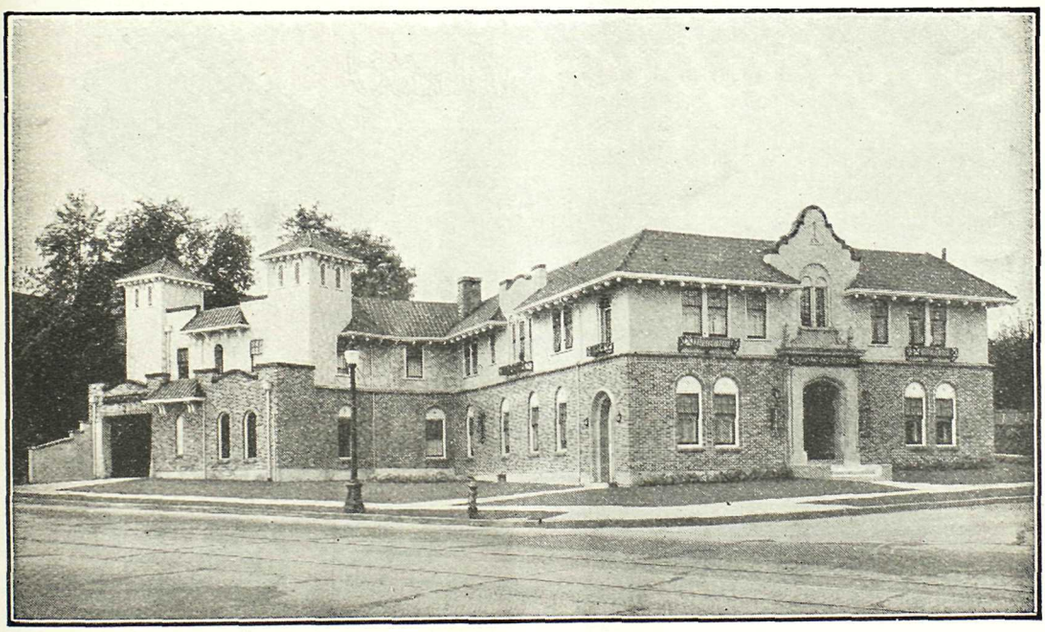

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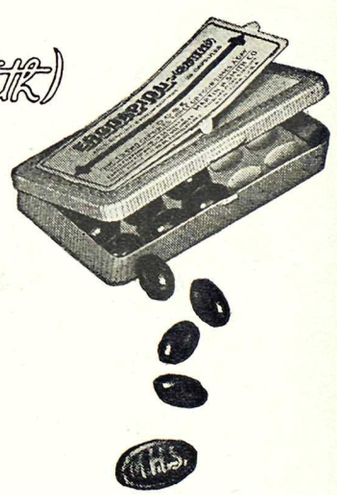

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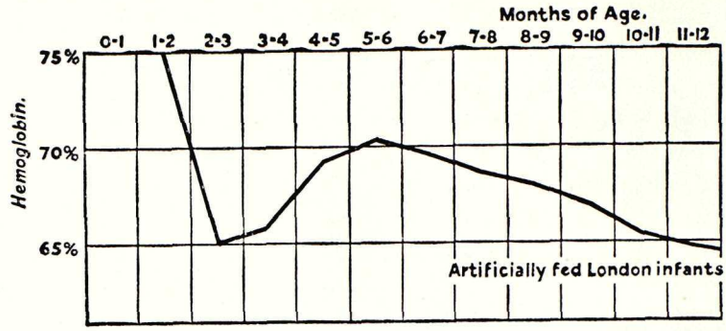

Hemoglobin level in the blood of infants of various ages. Note fall in hemoglobin, which is closely parallel to that of diminishing iron reserve in liver of average infant. Chart adapted from Mackay. It is possible to increase significantly the iron intake of the bottle-fed from birth by feeding Dextri-Maltose With Vitamin B in the milk formula. After the third month Pablum offers substantial amounts of iron for both breast- and bottle-fed babies.

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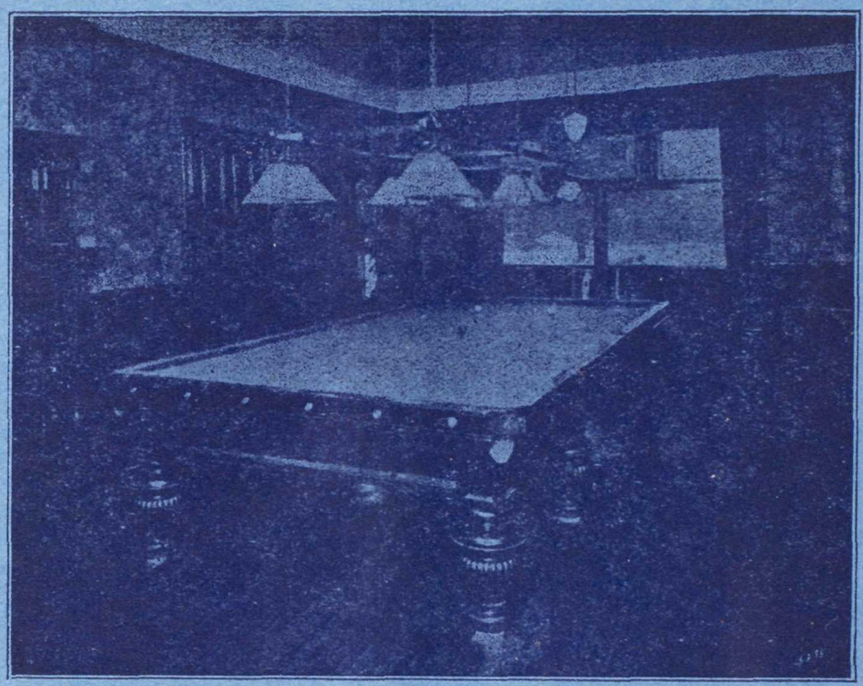

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