The BULLETIN
OF THE
VANCOUVER MEDICAL ASSOCIATION

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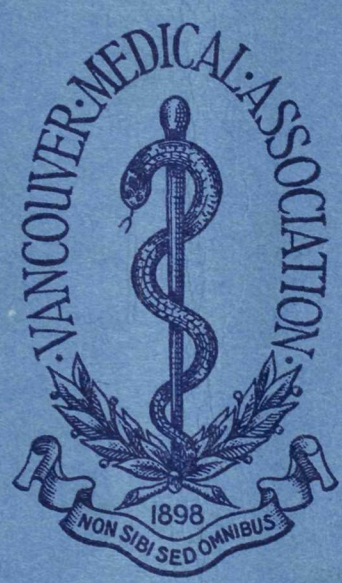

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NEWS AND NOTES

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THE VANCOUVER MEDICAL ASSOCIATION

BULLETIN

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In materia medica, Protamine Zinc Insulin supplements rather than supplants unmodified aqueous solutions of the specific anti-diabetic principle such as have been in common use since 1922. In some instances the use of unmodified Insulin alone is desirable; in others, Protamine Zinc Insulin alone is now indicated; while in others, the use of both preparations gives best results.

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VANCOUVER HEALTH DEPARTMENT

STATISTICS—JANUARY, 1937

Total Population—estimated	253,363
Japanese Population—estimated	8,522
Chinese Population—estimated	7,765
Hindu Population—estimated	352

	Number	Rate per 1,000 Population
Total deaths	285	13.3
Japanese deaths	9	12.4
Chinese deaths	12	17.9
Deaths—residents only	256	11.9
BIRTH REGISTRATIONS—		
Male, 153; Female, 137	290	13.5

INFANTILE MORTALITY—	January 1937	January 1936
Deaths under one year of age	16	14
Death rate—per 1,000 births	55.2	43.6
Stillbirths (not included in above)	3	7

CASES OF COMMUNICABLE DISEASES REPORTED IN CITY

	December, 1936		January, 1937		February 1st to 15th, 1937	
	Cases	Deaths	Cases	Deaths	Cases	Deaths
Smallpox	0	0	0	0	0	0
Scarlet Fever	28	0	25	1	23	0
Diphtheria	0	0	3	0	3	0
Chicken Pox	75	0	80	0	13	0
Measles	1593	5	1543	2	230	0
Rubella	7	0	0	0	2	0
Mumps	143	0	200	0	105	0
Whooping Cough	0	0	9	0	10	0
Typhoid Fever	0	0	3	0	0	0
Undulant Fever	0	0	0	0	1	0
Poliomyelitis	1	0	0	0	0	0
Tuberculosis	25	13	19	5	12	
Meningitis (Epidemic)	1	0	1	0	0	0
Erysipelas	9	0	7	0	7	1
Encephalitis Lethargica	0	0	0	0	0	0
Paratyphoid Fever	0	0	0	0	0	0

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VANCOUVER MEDICAL ASSOCIATION

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Programme of the 39th Annual Session

GENERAL MEETINGS will be held on the first Tuesday of the month at 8 p.m.

CLINICAL MEETINGS will be held on the third Tuesday of the month at 8 p.m.

Place of meeting will appear on the Agenda.

General Meetings will conform to the following order:

8:00 p.m.—Business as per Agenda.

9:00 p.m.—Papers of the evening.

1937

February 2nd—GENERAL MEETING.

DR. T. MCPHERSON AND

DR. J. D. BALFOUR: "Obstruction of the Small Bowel."

Discussion opened by Dr. L. H. Appleby.

February 16th—CLINICAL MEETING.

March 2nd—OSLER LECTURE.

March 16th—CLINICAL MEETING.

April 6th—GENERAL MEETING.

DR. WALTER TURNBULL AND STAFF: Symposium on "Pelvic Conditions."

April 20th—CLINICAL MEETING.

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EDITOR'S PAGE

A wise man of old, writing an essay on "The Philosophy of Times and Seasons," said:

"To every thing there is a season, and a time to every purpose under the heaven . . .

"A time to rend
and a time to sew,
A time to keep silence
and a time to speak."

It will be a very good exercise for any medical man to discover the origin of these remarks, and we will not spoil the pleasure of the chase by disclosing their source—but if we were inclined to preach a sermon, no better text could be found for us at the present juncture of affairs.

It is a difficult time: a time demanding of us cool and deliberate judgment, and sympathy and respectful consideration for those who may not agree with us, or see eye to eye with us in many regards. It is no time for destructive criticism only—but constructiveness, honest and sincere helpfulness toward the enhancement of the common good, must be our guiding motives. Just to rend is not only not enough, it would be unworthy of us; nor, as we well know, is there any desire to do that, except as preparation for the reconstruction, the sewing and stitching together of the unfinished stuff that will make of it a fabric that will endure, and be of real value.

And as regards speech. We are proud of the dignity and forbearance that have characterized what utterances have been made from our side—and we applaud the reserve and patience that have been shewn. One is tempted so often to speak, to explain, to argue, to retaliate—certain things have been written and said by persons who should know better, which were provocative and designed to hurt and anger us—but that is not argument, nor does it advance their cause; and there is a much deeper and more important consideration, that of what will, in the end, prove to be the best and fairest to all concerned, and will do most to alleviate suffering and hardship, and promote health and happiness. We are sure that the responsible leaders on both sides feel this equally, and will together work out a suitable *modus vivendi.* And we feel, too, that when it *is* time to speak, those who are leading our side can be trusted, as by their actions hitherto they have shown themselves pre-eminently worthy of our entire trust, to speak reasonably, fairly, honestly, yet with kindness and generosity, and sympathy for the real difficulties of the position. Till then, we again commend to our readers the little text with which we began, that they may "read, mark, learn and inwardly digest it," and continue as they have so well begun.

AMERICAN COLLEGE OF SURGEONS NORTHWEST SECTIONAL MEETING

The Northwest Sectional meeting of the American College of Surgeons will be held at the Olympic Hotel, Seattle, Wash., on March 31, April 1 and 2, with Dr. E. Weldon Young, Chairman, and Dr. Edwin A. Nixon, Secretary.

The following speakers are passing through Vancouver on March 28th and 29th: Dr. George Crile, Cleveland; Dr. C. L. Scudder, Boston; Dr. Perry Goldsmith, Toronto; Dr. G. A. B. Addy, Rothesay; Dr. C. C. Higgins,

Cleveland; Dr. P. B. Magnuson, Chicago; Dr. M. L. Mason, Chicago; Dr. G. B. New, Rochester; Dr. B. C. Crowell, Chicago.

A meeting is planned for Vancouver on the evening of March 29th. All members of the B. C. Medical Association are invited to attend. Further particulars as to programme later.

A. W. HUNTER, *Chairman.*

ANOTHER "BOOK AGENT" WARNING

Medical men are warned against paying any money to book salesmen until they are satisfied with their credentials. A certain company seems to be unfortunate in its representatives, as no less than three men claiming to represent this company have been found unreliable in the matter of collections in the last three months. Recently a number of doctors in Vancouver are alleged to have been victimized by a man calling himself "A. J. Shefford," who is taking subscriptions for Mosby journals. In spite of the fact that a letter was received by the Secretary of the Vancouver Medical Association from the Circulation Manager of the C. V. Mosby Company stating that this man was honest and reliable, the Credit Manager of the same company has now written letters to several doctors in the city stating that "A. J. Shefford" has no authority to collect subscriptions and that the company will not be responsible for any payments made to "Mr. Shefford." The police have been asked to try and locate "Mr. Shefford," but it is feared that he has left Vancouver.

VANCOUVER MEDICAL ASSOCIATION SUMMER SCHOOL

The Summer School will be held this year in June, from the 22nd to the 25th inclusive. Lectures will be held as usual in the Hotel Vancouver.

The Committee are happy to announce that the following men have promised to lecture this year:

Dr. Leonard Rowntree, of the Philadelphia Institute for Medical Research.
Dr. Wm. Boyd, Pathologist, of Winnipeg.
Dr. Paul B. Magnuson, of Chicago.
Dr. Harold Brunn, of San Francisco.
Dr. Donald V. Trueblood, of Seattle.

Details of the programme are practically complete and a tentative outline will be published in next month's issue.

NEWS AND NOTES

The Osler Lecture will be given at a dinner to be held in the Aztec Room of the Hotel Georgia, on Tuesday, March 2nd. Dinner will commence at 7 p.m. and the lecture at 8 p.m. sharp. Tickets for the dinner at $1.00 each may be obtained from members of the Executive Committee or at the Library. Dr. W. A. Whitelaw will be the lecturer this year.

* * * *

Dr. A. B. Nash of Victoria spent two or three days in Vancouver. He came over to attend the lectures given by Dr. Walter Schiller.

Dr. B. J. Hallows of Parksville came over to Vancouver to hear the lectures given by Dr. Walter Schiller.

* * * *

The members of the Eye, Ear, Nose and Throat Section who attended the mid-winter Clinical Course in Los Angeles have now returned, and all report a very interesting session and most enjoyable visit in the south.

* * * *

Word has been received in Vancouver that Dr. Howard Caple, who has been working in hospitals in London, Sheffield and Glasgow for the past two years, has taken the degree of M.C.G.O. This degree, instituted five years ago, is held by only three Canadians, as far as can be ascertained. It is "Master of the College of Obstetricians and Gynæcologists." Dr. Caple is on the staff of Queen Charlotte Hospital, in London. After the Coronation he will return to Vancouver with Mrs. Caple.

* * * *

Dr. W. N. Moray Girling of Vancouver will leave, with his wife and family, at the end of February to take up residence in the United States. Dr. Girling will join the Bute Clinic at Bute, Montana. His many friends will wish him the very best of luck in his new undertaking.

* * * *

Dr. A. E. Davidson, of the Provincial Mental Hospital at Essondale, has returned after spending four months at the Psychopathic Hospital at Denver, Col.

* * * *

We regret to note the death of Dr. G. A. E. Kelman of Fernie, B. C. Dr. Kelman came to Fernie in 1923, and was one of Fernie's most popular citizens. Our sympathy is extended to his wife and family.

THE PROBLEM OF VENEREAL DISEASE AND THE PROGRAMME FOR ITS CONTROL

Address given by Dr. S. C. Peterson, *Director of the Venereal Disease Department of the Provincial Board of Health.*

Mr. Chairman: Members of the B. C. Medical Association:—"In the beginning God created the Heaven and the earth, man and venereal disease." In these words Ricord, the famous French venereologist, facetiously expressed the generally accepted conviction that the venereal diseases enjoy an antiquity probably as old as Man. There is indisputable evidence which shows that the Chinese were acquainted with gonorrhœa more than 5,000 years ago. Syphilis, however, as we know it, is a relatively modern disease. If it was known to the ancients it must have been in some other form. Syphilis produces highly characteristic lesions and these have not been described in the older writings. Likewise the bones of those who died in Europe and Asia previous to the beginning of the sixteenth century do not seem to show the easily recognized signs of this disease.

Syphilis seems to have been recognized first in Europe late in the fifteenth century at the siege of Naples, when it broke out in the army of Charles VIII. Most students believe that it was contracted from the native women by the sailors who accompanied Columbus when he discovered America.

Spreading rapidly from the army of Charles VIII, it soon became epidemic in Europe, spread like wildfire, and created much havoc. It was variously known as the Spanish Plague or the French Disease. In fact, it was credited to almost every nation. A friend of mine used to remark, however,

that they never accused the Scotch of its origin. The disease, then, is only about 400 years old, but scientific knowledge of it is even more recent. Early in the present century progress in the understanding of syphilis became rapid. In 1903 Metchnikoff and Roux first succeeded in inoculating the disease into animals, thereby opening the subject to experimental study. In 1906 Schaudinn and Hoffman found and described the germ. In 1907 Wasserman perfected his blood test for the disease. In 1909, after thirty years of effort, Ehrlich discovered salvarsan. In 1911 Noguchi cultivated the germ artificially. Since these fundamental discoveries, enough progress has been made in the study of the disease to wipe it out entirely in a generation or two if the medical knowledge available could be properly applied.

It is entirely probable that a great step would be taken toward the ultimate solution of the problem of venereal disease control if it were possible to arrive at some reasonable agreement between health authorities and specialists on the one hand and the medical profession and the general public on the other as to the incidence and prevalence of syphilis and gonorrhœa in the population as a whole. The general acceptance of the extent of its widespread ravages would compel immediate attention. Those in authority who have seriously and scientifically studied the situation are of one mind and in general agreement in respect to these matters. The casual individual, governed only by general impressions,—and might I say prejudices?—unsupported by any statistics, is as a rule disinclined to credit the findings of the first group. Carefully conducted surveys by responsible health authorities in connection with other diseases and conditions are accepted without much controversy, but there seems to be a marked aversion or disinclination to accept the findings in regard to the incidence and prevalence of syphilis. There is perhaps a very natural and commendable excuse for this opposition. It is not pleasant to contemplate the statement that such a large number of people in our midst are the victims of the worst plague in history, that half of them do not know they are infected, that at least a third of them are entirely innocent of any wrong-doing, and that the disease ranks at least fourth among causes of death.

If some agreement between the groups mentioned could be arrived at by compromise, even at a much lower figure than official estimates demonstrate is the case, a start could be made from that point in a joint effort toward better judgment of the situation. If the argument be continued endlessly no progress will be made. It would be more profitable to discount every statement in the estimate by half, look at the problem frankly, and judge whether it is not even then serious enough to lend every effort towards its solution.

While we do not have exact statistical knowledge of any disease, accurate figures on the venereal diseases are even more limited for various reasons. Half or more of the persons found to have syphilis during routine physical examination or blood test surveys do not know they are infected. The female gonococcus-carrier is usually unaware of her condition. Still other persons, while knowing of their infection, through shame or ignorance attempt self-treatment or go to "quacks" or drug stores for treatment. But despite these handicaps a body of useful information has been accumulated as to the size of the venereal disease problem.

For both syphilis and gonorrhœa the consensus of cases under treatment on a given day have provided the most comprehensive picture of prevalence. These studies in the United States have demonstrated that at any time there may be found at least 683,000 cases of syphilis and 493,000 cases of gonorrhœa under treatment or observation by licensed physicians, including both

new and old infections. The incidence-records of fresh infections occurring annually show 4 per thousand for syphilis and 8 per thousand for gonorrhœa. Based on these findings it can be said that in the United States approximately 1,500,000 persons each year seek treatment for either early syphilis or acute gonorrhœa. These figures do not include infected persons not under the care of doctors. Data collected by the American Social Hygiene Association reveal at least double this number buying remedies in drug stores or going to unqualified and illegal practitioners. In addition to these, the group of infected persons not receiving any treatment at all cannot be estimated, but is admittedly large.

Knowledge of the actual number of syphilis cases in the population is obtained chiefly through routine blood testing of large numbers of individuals. Many of the supposedly healthy groups have been so tested in connection with obtaining licenses, or routine medical examinations for health services of one kind or another. These groups have included food handlers, drivers of public conveyances, barbers, domestic servants, farmers, coal miners, chemical workers, high school and college students, and applicants for marriage licenses. The rates recorded have ranged all the way from less than one per cent to as high as twenty-five per cent. The obvious observation here is, of course, that when one speaks of one in ten or one in twenty in respect to the prevalence of syphilis, one does not necessarily mean or imply one in every ten or one in every twenty. The figure naturally is an average and refers to the mass.

The wide variation in figures are the effect of many social, economic and other factors. For example, there is no doubt that a higher disease rate prevails among the class of people who attend clinics; these clinic cases constitute about 40% of all venereal disease cases under known treatment. Among negroes the incidence of syphilis is said to be four to six times what it is among the other racial groups as a whole. There is a higher rate in cities than in rural communities. About one and a half times as many men as women are infected. The peak age of infection occurs in young adulthood, between the ages of 20 and 25 years. Estimates of congenital syphilis in the population differ according to the experience of the observers. Stokes believes that from 3% to 5% of the whole child population has congenital syphilis. Jeans and Cooke found in St. Louis that 5% of the children born into families of the poor had syphilis, while children of the well-to-do exhibited a rate of less than 1%. On this basis 2% was estimated as a conservative figure for congenital syphilis in the general population.

Allowing for the relative proportions of these various groups, it is estimated that 5% is a conservative measure of syphilis among men, women and children in the whole population. Some public health authorities, on a different basis, have placed the figure considerably higher. Dr. Thomas Parran, Surgeon General of the United States Public Health Service, recently made the statement that one adult in ten is infected by syphilis at some time during his or her lifetime.

In regard to gonorrhœa, our figures are not so satisfactory or definite. Unlike syphilis with its blood and spinal fluid tests, there are no comparatively simple and positive ways to discover the presence of gonococcal infection in large sample groups of the population. Where opportunity exists for adequate examinations and follow-up of large bodies of men, gonorrhœa is found to be far more prevalent than syphilis. In the United States Navy, for example, there are three cases of gonorrhœa to one of syphilis, and among the younger men the ratio is over six to one.

It is unfortunate that I am compelled to use figures compiled in the

United States, but there are no official estimates available for Canada. I believe the American estimates are at least approximated here for the following reasons:

1. British Columbia is a seacoast province.
2. It has a large nomadic population.
3. Diagnostic and treatment facilities are unavailable to a large proportion of the population.
4. Even in the cities facilities have been inadequate, and no attempt at case-finding or follow-up has been made.
5. Only a small fraction of those afflicted with syphilis in the last twenty or thirty years have received anything approaching modern standards of treatment requirements.
6. Adequate tests of cure have not been generally carried out in the past. The number of routine spinal punctures done has been negligible. It is hard to get them done even now, due to lack of hospital facilities.

Now why do I stress the importance of these estimates of incidence and prevalence? Simply because the facts are not generally known, even to the medical profession. The public are quickly becoming aware of them through wide publicity in the Eastern press, and in popular magazines. The large life insurance companies also are busy disseminating knowledge as to the prevalence and seriousness of syphilis and gonorrhœa. Recent actuarial studies show a ratio of approximately 140 to 100 between actual deaths and expected deaths among syphilitics. February 10th has been designated as Social Hygiene Day all over the United States, and public education of the facts in regard to syphilis and gonorrhœa will be carried on by means of the radio, movies, exhibits and lectures in thousands of communities. A similar campaign of education is contemplated here at a later date as part of the programme of the Provincial Board of Health. It is therefore obvious that the members of the profession most vitally concerned should have a clear idea of the extent of the problem.

To stress its importance is but to labour the obvious. Venereal disease is undoubtedly the community's most urgent public health problem. It is without question a far greater menace to human life, efficiency and happiness than any other communicable disease. Syphilis is still the killer of the race, and as a misery producer gonorrhœa remains unrivalled. Parran states that automobile accidents in the United States in 1934 resulted in 107,000 cases of permanent disability. Yet in that same year syphilis alone attacked and disabled more than half a million persons. Fifteen per cent of the blind have syphilis of the eyes and many more are blind because of gonorrhœa; 10% of admissions to mental hospitals have syphilis of the central nervous system; 18% of all serious heart and blood vessel conditions are due to syphilis. Approximately 100,000 deaths annually in the United States are attributed to syphilis alone.

What can we do about it?

What shall we attempt in British Columbia?

To answer the first question we must know what can be accomplished by the treatment of the diseases themselves, and in order to estimate what can be done in this Province we must study what has been done in regard to their control in other places. We shall study these things particularly in regard to syphilis, because although progress is being made in the study of gonorrhœa its treatment is only now in the process of standardization. There is no disease that offers a more hopeful prognosis than does syphilis. There is no branch of preventive medicine that offers such promise. Listen to Stokes:

"Given a co-operative patient in the sero-negative primary stage of syphilis, we can promise almost a 100% chance of cure.

"Practically any infectious case can be temporarily sterilized in 3 to 4 days. It can be kept non-infectious by enough arsenicals and by continuous uninterrupted treatment.

"The number of injections, the preferable drug, the preferable dose, is now known for every situation involving infectiousness.

"The precise risk of infection for the child is known, for each period of pregnancy, for each amount of treatment.

"Conditions for stopping, starting and prolongation of treatment are known.

"Systems for early and latent syphilis, all phases, with proportions of curative results, exact number of injections, drug, total dose, can be read off like motor oil charts.

"Nine-tenths of the reactions, complications and troubles of treatment can be prevented.

"The chief cause, and prevention, of fixed positive blood tests in early cases is known.

"How to cure 80% or more of previously incurable neuro-syphilis is now known.

"How to lengthen instead of shorten the life of the heart case is now known.

"How to cure symptomatic cure in 40 to 100% of stomach and liver syphilis, 90 to 100% of skin and bone syphilis, is known.

"How to save one eye and prevent involvement of the other in interstitial keratitis, the nemesis of the syphilitic child, is known.

"The superiority of treatment over non-treatment; of modern treatment over old-fashioned treatment, is now established. Modern methods are fully justified, are superior to the old, second to none, and have negligible disadvantages when properly used. Simplification is bringing them increasingly within reach of any doctor who can read English, examine a patient, obey or profit by instructions, clean his hands and tools, use a needle, stop when he meets a danger sign and seek advice instead of blundering ahead."

Let us now look at what has been accomplished elsewhere. It has been recognized for a long time that signal success has attended the efforts of venereal disease control in certain European countries, particularly the Scandinavian countries and Great Britain. In contrast, it has been evident that no such diminution in the incidence of venereal disease has occurred on this continent. In fact it is probable that both gonorrhœa and syphilis are increasing, not decreasing. It is commonly reported that Denmark has unusual control of the venereal diseases, especially syphilis, and has practically succeeded in eliminating this disease from the kingdom.

In July of last year a commission was appointed in New York to visit and study conditions in regard to venereal disease in the three Scandinavian countries and in Great Britain.

Their investigation shows that syphilis has declined markedly since 1920 in each of the four countries studied. In the Scandinavian countries it has become almost a rare disease. In these three countries, with a total population of 13,700,000, health authorities were notified of less than 1600 cases in 1933. Careful inquiries and corroborative evidence convinced the Commission of the accuracy and relative completeness of the reports. In Great Britain the recorded prevalence, as indicated by clinic admissions, is now one-half of that recorded in 1920. In contrast, the prevalence of gonorrhœa continues high and has not declined proportionately.

In all these countries, in law and practise, the control of venereal disease is a public responsibility, the cost of which is borne generally by the central government. In the Scandinavian countries, the system by which health officers are notified of all cases, and the requirement that all infected persons take treatment, are the chief factors in the control. In Great Britain no legal control over the patient is exercised, entire dependence being placed upon free clinic treatment for all. Significant success has attended the Swedish requirement that all sources of infection be ascertained and brought under treatment.

In all of the countries studied, generous provisions are made for free clinic and hospital services, readily available at suitable hours, to all comers, irrespective of their financial status, by competent, well-paid physicians. This service is in connection with established poly-clinics and hospitals.

Throughout the Scandinavian countries and Great Britain the relationship between the medical profession and public health authorities is close and cordial. The Scandinavian system seems particularly conducive toward stimulating a reciprocal interest on the part of the physician toward public health. In Great Britain the general physicians' apparent lack of desire to treat venereal diseases undoubtedly tends toward greater use of the clinics of that country. This is further increased by the inability of a large part of the population to pay the relatively high fee of specialists, and the treatment of syphilis and gonorrhœa, both in the male and female, has been segregated into one specialty in Great Britain. Special venereal disease clinics have been established, replacing services formerly in departments of dermatology, urology and gynæcology. Appointments to positions in venereal disease clinics are made only from those who are proved to be well qualified.

Adequate laboratory facilities for diagnosis are available in each country, and some form of government supervision of service is maintained. In Denmark the work of the diagnostic laboratory serving the whole country is integrated with the system of notification, with outstanding success. Both a complement fixation and a precipitation test for syphilis are the usual routine in a given case. In Great Britain much reliance is placed upon the complement fixation test for gonorrhœa.

The reduction in syphilis prevalence seems to have been due to medical measures rather than to the exercise of moral restraints, as evidenced by the continued high prevalence of gonorrhœa. In the Scandinavian countries public education concerning the venereal diseases is not now an important phase of the programme, although the public is well informed concerning treatment facilities. In Great Britain education of the public is still considered important. The venereal diseases are discussed in Denmark with exceptional frankness.

Prophylaxis by chemical or mechanical means is not officially promoted in any of the countries. In each country the regulation of commercial prostitution has long been abandoned in favor of repressive measures of varying degrees of severity.

Among the other factors which have enabled the Scandinavian countries particularly, and, to a lesser degree, Great Britain, to make encouraging progress toward the conquest of syphilis, the following are especially important:

1. A homogeneous population united to a large degree in language, race, customs and moral standards.
2. A mature civilization in which respect for law and constituted authority is almost universal.
3. A general high level of education and almost total absence of illiter-

acy. Especially high standards of education in medical and other professions.

4. Quack, cultist, and drug-store diagnosis and treatment of syphilis and gonorrhœa are at a minimum in these countries, and the practice of the healing arts is limited, at least in the Scandinavian countries, to regularly licensed physicians. A fully developed social legislation in the Scandinavian countries supports and supplements the public health and medical laws.

What is the programme for British Columbia?

I shall merely outline it briefly and tell you what has been done and what our plans are for future developments. I want to state quite emphatically here that I fully realize the fact that no comprehensive plan of venereal disease control can succeed here or elsewhere without the wholehearted support and the actual co-operation of the medical profession.

We have expanded the facilities and services of this division by the addition of a consulting staff of experts at the local clinic. We have increased laboratory services through the co-operation of the Provincial Laboratory. We have modernized treatment methods and technique, and have added a competent social service department. It is our hope that the profession will acquaint themselves with and utilize all these services; they are all free and at their command for both pay and part pay patients.

The programme is a result of a conference on venereal disease held in Vancouver in May, 1936, composed of representatives of the Government, the medical profession and Health Officers, including, I believe, your President, and embodied in a report with recommendations to the Department of the Provincial Secretary.

Specific recommendations for this Province follow, and include:

1. The establishment of a Division of Venereal Disease Control, similar to the Division of Tuberculosis Control, to develop and integrate the venereal disease work of the Province.
2. The appointment of a Director to develop, direct, and administer the programme; to direct the work of the central office and to render service at the Vancouver Clinic.
3. A central office to be established at Vancouver in connection with the clinic there. In the central office records of all the work throughout the Province would be kept, and private physicians would report their cases to this office.
4. It was felt desirable to appoint an advisory council upon which would sit the Provincial Health Officer, the Director and some members of his staff, one or two other Departmental officials, some medical men and social workers. The function of the Council would be to advise on policy administration.
5. *Staff.*—Several part-time physicians would be required at the Vancouver Clinic and one at Victoria. Part-time assistants might be appointed to maintain treatment centres at a few other points in the Province. Several medical-social workers, nurses, technicians and office workers would also be required.
6. It would be desirable as soon as possible to obtain new and modern quarters for the Vancouver Clinic. The problem of the Victoria Clinic should be canvassed with particular reference to the value of its being transferred to the Jubilee Hospital.
7. There should be established a central records system, based on reports from the various clinics, from private physicians, laboratories' reports, and reports of the case-finding programme. With

these records statistics could be devised to show the incidence of venereal disease. Central records would provide an indispensable basis of knowledge for the development of the work.

8. Outlines the development of the social service and follow-up programme by collaboration with the Welfare Field Service, private social agencies, public health nurses, police, etc. The follow-up of patients to induce them to attend regularly for treatment would be the first part of this programme to be stressed. Arrangements should be made by means of notification of patients, outside physisicians and outside clinics for treatment of those who move away from the main centres of Vancouver and Victoria. This work will lay the basis for the use of compulsory treatment among patients, and families will be sorted out and referred to collaborating agencies for attention.
9. The development of the case finding programme includes examination of contacts, school medical examinations, examination of hospital patients, certain industrial or trade groups, etc.
10. It is very desirable that the clinics in Vancouver and Victoria function as teaching centres. Internes from the hospitals should gain knowledge and experience in these clinics. The clinics should be in close touch with the consulting staffs of the general hospitals in Vancouver and Victoria. Through the clinics, education of the medical profession in the most modern methods of dealing with venereal disease would take place. There should be cross reference of cases between the Vancouver clinic and the Outpatient Department of the Vancouver General Hospital, and close collaboration between the two. Physicians should be encouraged to report on all cases drawn to their attention. Close collaboration with various other agencies, including Municipal Health Departments, the Provincial Laboratory, mental hospitals and other health and welfare agencies is most important. The Division of Venereal Disease Control should have close relations with the Health Insurance Commission and the Indigent Medical Service, both of which will certainly bring to light many cases of venereal disease. With arrangements for adequate service perfected, the Division of Venereal Disease Control will be in a position to use the compulsory provisions of the Act. It is urged that careful study of the act be made by physicians, health agencies, etc.
11. And lastly, that an extensive programme of dignified publicity and education will probably prove to be essential. It has been proposed that the Vancouver Health League could give great assistance in this connection.

These, then, are the details of the programme as recommended. I am sure you will agree that they are quite comprehensive and practical. The Government is determined to carry the programme through. The brilliant results obtained in other places are a challenge to any progressive community to lend every effort possible in this campaign to lessen the ravages of the venereal diseases. Enlightened public opinion will very soon force the issue if health bodies and the medical profession do not take the initiative in collaborative measures against the world's greatest plague.

Let me close with an extract from an editorial in the Journal of the American Medical Association of July 18. "The conquest of syphilis is the next great objective in public health—sufficient reliable information indicates that it is probably the most prevalent of all communicable diseases

except measles in epidemic years. The history of medicine shows instance after instance in which the combined forces of medicine and public health have conquered disease as far as public co-operation could be procured. With the combined efforts of physicians, public health officials, educators, and the public, syphilis can be conquered next."

TWO LECTURES ON PRACTICAL GYNÆCOLOGICAL ENDOCRINOLOGY

By Dr. Walter Schiller, *Vienna.*

The Vancouver Medical Association was very fortunate to have a return visit from Dr. Schiller, whose lecture on Early Diagnosis of Carcinoma of the Cervix was abstracted in the December, 1936, number of the Bulletin. Dr. Schiller's ability as a lecturer is due not only to his monumental knowledge of his subject, but to his clear and logical method of building up a connected and coherent picture, and his habit of summarizing and digesting as he goes—so that one can follow him without difficulty, assimilate his offering, and leave with a feeling of satisfaction rather than the repletion that leads to indigestion afterwards.

Dr. Schiller dealt with the sex hormones, taking those of woman as the particular ones of which he wished to treat. He spoke at length, and we summarize his remarks as follows:

Whenever we prescribe sex hormones, in the treatment of illness or dyscrasia due to their insufficiency or absence, we are prescribing physiological substances, familiar to the organism. They are not like drugs which we commonly use, e.g., quinine and digitalis, designed to introduce new factors and new stimulations or actions. We can only, in our use of these hormones, reinforce insufficiency, or supply the lack of substances that should be in the body.

So we must have *exact* knowledge of the physiological properties of the glands we are reinforcing or replacing. There is no place for hit-or-miss therapy; we can only obtain results from accurate application of our remedy.

With regard to the sex hormones, the first thing we note is that female sex functions are performed rhythmically, in a definite recurring cycle; these functions are thus rhythmic or cyclic.

The menstrual cycle is the basis of female sex function—and follows a definite order.

The second thing that we note is that this female sex function is performed in three different groups of organs, or three stations, as it were, in three strata. The lowest station is controlled only by the one above, which in turn is controlled by the highest station. But the top station cannot control the bottom *except through the middle station.*

We may compare our female system to a house with a basement, a ground floor and an upper floor.

The basement contains the uterus and is open to inspection and palpation.

Its activities are directed by the ground floor, where the ovaries are. These control the uterus directly, and govern the menstrual cycle.

In the top floor we have the pituitary gland which controls the ovary.

In a well-regulated administration authority works along defined channels. So the top floor can only influence the basement through the ground floor.

Thus *we never give anterior pituitary to control the uterus when the ovary is absent or not functioning.*

The menstrual cycle may be defined as the sum of the changes that take place in the ovaries and uterus (the endometrium of the latter, and to a lesser but very important extent the myometrium) in cyclic manner, roughly once a month, the process extending over and being completed in that time, and ending with the "menstrual flow" unless pregnancy supervenes.

Let us consider the endometrium in the first phase (about 2 weeks) of the cycle. At first as we examine post-menstruation the glands of the endometrium, we find small glands, straight, short, empty of secretion.

For two weeks these enlarge, but remain straight and empty.

This is the *stage of proliferation*: the first 2 weeks of the cycle.

During the second phase (third and fourth weeks) the glands become tortuous, and are seen to be full of a mucin-like secretion.

This is the *stage of secretion* (in humans) and *of transformation* in *animals*. These two phases are fundamentally different.

So our first conclusion is that there must be at least two different hormones responsible for these two different phases—one directing proliferation, the other directing secretion and transformation.

So there must be two phases of ovarian function to correspond—since the ovary directs the uterus.

As we examine the ovary, its actions and secretions, we find confirmation of this double function.

At the beginning of the cycle, the adult ovary shews anywhere from 5 to 15 Graafian follicles, 3 to 5 mm. in diameter. During the first half of the cycle one of these enlarges to 8 to 10 mm.and bursts. This process takes roughly two weeks. This bursting is known as ovulation. An ovum is discharged.

After ovulation (note: only one follicle as a rule ripens and discharges) the follicle collapses, but in a few hours refills with fluid. There is an enormous increase in granulosa cells, not only in number but in size. These cells are filled with thread-like granules (the lutein hormone or luteo-hormone). We have the familiar *corpus luteum*.

Luteinization continues for two to four days; this corpus luteum carries on the work of *preparing the endometrium for the embedding and growth of the ovum*. This is its only function, that of preparing the endometrium for a fertilised ovum. Fertilisation commonly takes place in this two to four days after ovulation. If it does, the corpus luteum persists, as we know, for reasons to be described later. If fertilisation has not taken place, the corpus luteum lives 8 to 10 days only, then degenerates, ceases the production of lutein and collapses. The mucosa of the endometrium which was supported and stimulated by the luteal hormone is *suddenly* cut off, degenerates, and we have menstruation.

This is what menstruation is, the sloughing off of a mucosa, engorged, with large, tortuous glands full of mucin, all of which were prepared with only one object in view, the provision of a bed for the growing organism, the fertilised ovum.

But we note certain things. Out of the 5 to 15 follicles apparent in the ovary at the beginning of the menstrual cycle, one one as a rule (occasionally two) enlarges, ripens and ruptures. Why is this so? (in humans at least —some animals have litters).

There are two answers probable: (1) This follicle as it grows produces a *depressant* substance or hormone, which affects other follicles which might

have grown and inhibits them (an anti-ovulating hormone). This is an interesting theory—as if we could find and produce this anti-ovulating hormone in sufficient quantities, we could use it as a contraceptive. This would be the ideal functional way of contraception. So physiologists have spent years in its search—so far without any result, probably because the hormone does not exist.

The second explanation is that this follicle grows and bursts because of stimulation which it gets from the secretion of the anterior pituitary (prolan), and that there is only enough secretion for one follicle to ripen. Today we accept this theory.

In mice we see double uteri, and an ovary attached to each. There are four maturing follicles in each ovary at a time. If we extirpate one ovary, we get eight maturing follicles in the other. There is enough prolan A for eight follicles.

In twin pregnancies (non-identical twins) there is an excess of prolan A. This has been shewn by certain cases where twin pregnancies occurred while prolan A was being administered.

So the first phase of ovarian action is the follicular phase, the second phase the phase of luteinization.

The first phase is *preparation for estrus,* so the hormone is known as *folliculin* or *estrogen.* It has other names, e.g., theelin. This hormone, folliculin, is isolated from the fluid in the growing follicle: hence the name folliculin.

The second phase is *preparation for the embedding of the ovum;* of the endometrium. This is luteinization, and is effected by *luteo-hormone* or *lutein. Another* name given is *progestin* or progesterol.

The Pituitary

The anterior lobe of the pituitary produces two gonadotropic hormones: (1) Prolan A, which stimulates the follicle up to bursting, during which time the follicle elaborates folliculin; (2) Prolan B, which stimulates the corpus lutein, to produce lutein, and carry on luteinization.

Antuitrin is the sum of these two prolans, A and B.

They have never been satisfactorily separated, and there is no commercially pure prolan A or prolan B.

Folliculin.—As with all hormones, we follow certain rules in regard to this substance. We must have (1) *qualitative* tests of its presence, i.e., criteria of its physiological action which shew whether it is present or not; (2) *quantitative* tests by which we can measure the amount present. This latter we estimate by biological means.

What is the test for folliculin (qualitative)? Its work, we know, is to prepare for ovulation and estrus, and *this is its only function.* We cannot imitate the menstrual cycle by giving folliculin alone in any amount. We can only produce proliferation of mucosal glands in the endometrium, and ripening of a follicle; we cannot obtain secretion or lead to menstruation. So if ovarian function is deficient, folliculin alone will not replace it. Lutein must also be given. (In humans only, the corpus luteum produces a small amount of folliculin as well as lutein, its chief product.)

We may give folliculin harmlessly all through the menstrual cycle, but we must never give progesterol, or lutein, before the second phase (third and fourth week).

The qualitative test of folliculin is obtained from the fact that it produces estrus, a general hyperæmia of the sex organs. Also in rats the vaginal mucosa shews definite changes. Examination of this, however, by section,

ruins the whole vagina, which is very flimsy and thin and so cannot be practically used.

Smears from the mucosa shew the changed cells cast off, and this method is of value. Injection of folliculin into castrated adult female mice will shew changes in the vaginal smears, squamous cells, instead of columnar.

The *quantitative test*. Here the unit is the smallest amount which will produce estrus in a castrated adult rat or mouse (rat-unit, or mouse-unit, as the case may be—these are by no means identical).

This equals 1 rat-unit of folliculin.

But folliculin has been isolated in the pure form, and now we use as a standard that 1 mg. pure theelin (folliculin) equals 3,000 rat-units (Dorsy) or 10,000 international units (I.U.).

Where do we find folliculin?

(1) In liquor folliculi, and, in lesser amounts, in human corpus luteum also; (2) in the blood serum of pregnant women in considerable quantities; (3) in placenta in very large quantities; (4) in the urine of pregnant women (3,000 to 4,000 units daily); (5) in mares' urine we get as high as 50,000 to 200,000 units per day.

This gives us a cheap, plentiful source, in a watery medium, easy to isolate.

It has been found that male urine also contains folliculin: hence folliculin *is not a sex hormone*. It is also found in the blossoms of trees, even in the roots and leaves.

So folliculin is not a sex hormone at all, but the proliferation hormone. It is the hormone of growth and is found even in the oil from oil wells.

In animals it is concentrated in the sex glands, especially in the female; but wherever the process of proliferation is concerned, we find folliculin.

What is the practical use of folilculin? Why do pregnant women have so much? Its function is to stimulate and support the growth of the fœtus; and we know that it is essential to this. Babies, otherwise healthy, born at seven or eight months, will die, because they are cut off from the supply of folliculin, the growth hormone.

The full-term baby actually excretes folliculin, and gets more from the mother's milk.

Schiller was able, by giving folliculin to premature babies, to raise the number of those surviving to three times the usual number.

Where twins have been born, one smaller than the other, by giving folliculin to the smaller, we can increase its growth to be larger than the other.

But, if we are going to give folliculin to the premature child to save it, we must give it *within ten hours after birth*, or the interruption is fatal.

We give it in small quantities, 80-100 units per diem, divided in two doses, and given intramuscularly; keep it up for two to three months only. Then we stop it, and if curve of growth continues, cut it off completely; if the curve stops we resume its use.

So its first use is in prematurity.

We can give folliculin wherever there is impaired ovarian function, e.g., dysmenorrhœa, deficient, insufficient ovarian function.

Thus *for dysmenorrhœa* it is given.

Also, *for sterility*: it is given to ensure development of follicle and ripening of ovary, and to prepare the way for lutein (see below). We must give large doses, for the first two to three weeks of phase, for two to three months.

The oral administration is very wasteful, and one unit by hypo equals about 15 units by mouth.

Usually we give 5,000 units three times a week, or 10,000 twice or 50,000 once. It may be given in rectal suppositories, but not in vaginal.

There is no danger in overdoses.

A *third use* is derived from the fact that folliculin makes the vaginal epithelium thicker, higher, and more resistant to disease, in all mammalia.

Thus a pregnant woman never develops vaginitis, or gonorrhœa.

It can be used thus in g.c. infection, and in the g.c. vaginitis of children. We must carry on the treatment for months in children; but in the adult, we can get rid of g.c. in 10 days in a simple vaginitis by raising the resistance.

We give small doses at first, 100-200 units per diem, not massive doses.

Dr. Schiller gave some warnings about the use of folliculin—or rather about the dangers of its abuse.

In the first place, it must *never* be given where cancer is present. It causes rapid growth of cancer—especially cancer of the breast or uterus.

Secondly, there is a danger of addiction. Patients find it gives them energy and strength, and not only come to rely on it, but become very helpless without it. This is a very serious danger.

It can only be avoided by regular intermissions of the use of the drug, and these intermissions are essential.

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SECOND LECTURE

Folliculin (*Continued*)

This is a very stable substance: can be boiled for hours without any chemical disturbance; can be boiled in 5% acid or alkaline solutions without damage. Thus it can be sterilised for use by boiling.

Its stability is also shewn by the fact that it is found in oil as it comes from wells. This means that it must have remained unchanged under very severe conditions of heat for thousands of centuries—coming originally from wood.

Progesterol or Progestin

This is the hormone that prepares the uterus for the embedding of the ovum, for placentation: it does the progravid or progestational preparation, hence the name. It is the luteo-hormone, derived from the corpus luteum which remains after ovulation.

Ascheim and Zondek, especially the latter, did the classical work on folliculin. They worked out the qualitative tests for this substance through its effect on the sex organs of the mouse and other animals.

But Zondek, who did so much work on folliculin, missed progestin entirely, because he did his work entirely on mice and rate, examining the vaginal changes.

The vagina of mice indicates only the estrus phase, i.e., folliculin action, but it does not in any way reflect the action of progestin.

Progestin affects the uterus: and we find it does this in two ways: (1) It affects the *endometrium,* producing tortuous cells, full of secretion, with hyperæmia and œdema of the whole endometrium (Corner and Clauberg); (2) it affects the *myometrium,* producing certain effects, to be detailed later.

Our qualitative tests for progestin are derived from the first of these. Corner and Clauberg worked not on the vagina of mice, but on the uterus of rabbits, choosing the *infantile female* rabbit. The endometrium here shews folds with simple tubules.

As the rabbit grows older the tubules enlarge, but remain straight and

are non-secreting. There is simple proliferation, due to the presence of folliculin, developing in the ovaries.

But as lutein appears we see great enlargement and tortuosity of tubules (pro-gravid phase) serving for the embedding of the ovum.

The three stages of the endometrium are: (1) infantile—pre-menstruation; (2) proliferation—adult; (3) secretion—pro-gravid.

Clauberg first gave large doses of folliculin to the infantile rabbit and secured proliferation, but even with such doses as eight to nine hundred thousand units he did not obtain any secretion phase. But when he gave progesterol, he obtained a secreting phase, exactly analogous to the changes in the human.

So we prove the presence of progesterol by giving first folliculin to the castrated infantile female rabbit (folliculin must be given to prepare the uterus by proliferation), then the substance we wish to test. If progesterol is present we get pro-gravid changes.

Quantitatively, the minimum amount necessary to produce pre-gravid changes in the castrated infantile female rabbit is one rabbit unit.

Clauberg found further—and this is important clinically—that luteal hormone has no influence unless folliculin has been first given—luteo-hormone does not act on a pre-proliferative endometrium.

So we never give luteal hormone without having first given a sufficient dose of folliculin.

Luteal hormone has the function of preparing the uterus for pregnancy—and nothing else. If the ovum is not fertilised, the corpus luteum collapses suddenly, and this causes menstruation, degeneration of the mucus membrane.

The corpus luteum does not prepare for menstruation, but for pregnancy. This is a very important distinction. *Menstruation only occurs after its collapse.* In 16 cases of laparotomy where a corpus luteum was found to be present and removed, 14 menstruated in three to four days.

If the corpus luteum remains there will be no menstruation.

So when we given lutein following folliculin, we cannot expect menstruation as long as we keep up the luteo-hormone administration. Stop it *suddenly,* and we get menstruation.

As a converse action, we can postpone menstruation by giving daily doses of luteal hormone. This was done during the Olympic games, where women athletes whose menstrual period was due to occur on or about the date on which they were to compete, were treated with luteo-hormone in large doses during the third and fourth weeks of their cycle, menstruation was postponed for three or four days, and they were enabled to appear in their events.

Myometrium

Next we have a test for the effect of luteo-hormone, or progesterol, on the myometrium. This was discovered by Knaus, who started 15 years ago a series of studies on the contractibility of the uterine muscle.

He found that the uterus of normal women shews regular contractions occurring every minute or two; minimual in amount, but definite. The uterine muscle thus engages in rhythmic contractions as does the heart, but these are at a different rate and very slight in comparison with cardiac contractions.

This was in itself a very interesting discovery—but he discovered something else, even more significant. These rhythmic contractions are only found in the first two weeks of the cycle; after which, in the third and fourth weeks, they disappear entirely, and the uterus is completely relaxed.

Why is this? The answer is not far to seek. The uterus has to get ready for the embedding of a fertilised ovum. This could not occur in a wrinkled, contracting mucosa. There must be a smoothed-out, relaxed bed prepared for the ovum, and there must be peace and quiet for it to grow.

As to the mechanism of this process of relaxation, Knaus discovered that progesterol paralyses uterine muscle.

Thus we see that progestin has at least two functions: (1) It is responsible for secretion in the glands of the endometrium, for a great increase in size, and tortuosity; (2) it paralyses the uterine muscle, and so prepares a quiet, restful bed in which the fertilised ovum may grow in peace.

So from this Knaus developed a *quantitative* test for progestin: namely, the minimum quantity necessary to paralyse the uterine muscle within 24 hours against the largest amount of pituitrin (post-pituitary secretion). This amount is one Knaus unit.

Biochemists have produced crystalline progestin, and we may measure it quantitatively as follows: 1 mg. progesterol or progestin equals 1 Corner unit, or 2 Clauberg units, or 6 clinical units.

Generally, British and American firms equate one rabbit unit to one Corner unit.

Progestin is a neutral white substance, soluble in ether, esterol, or olive oil, but not to any extent in water, hence "watery" solutions are not reliable, and are far too weak.

Oily solutions may be given intramuscularly, but are useless by mouth.

It is a fairly stable substance, somewhat affected by light and heat, so must be kept at a low temperature in the dark. It deteriorates at a fairly rapid rate, and preparations older than one year should be discarded, as of uncertain titre.

For what purposes may we use progesterol? A careful consideration of its action will suggest certain of them, and some of them have been described, e.g., to postpone menstruation, and in cases of amenorrhœa which are due to insufficient progesterol. In this latter, if we give progesterol, we must do so only for a definite time, then stop its use suddenly; this brings on the flow (the stoppage, remember, not the luteo-hormone, which will postpone it). Again, we must not forget that folliculin must always be given first, to prepare the endometrium by proliferation for the action of progesterol.

Sterility.—Where the husband is normal, with normal potent spermatozoa, the uterus and tubes are normal and patent in the wife, but pregnancy does not occur. Many of these patients are sterile because of insufficient corpus luteum; the uterus cannot be paralysed—the ovum cannot find a restful bed in which to grow: it cannot be embedded.

Most of these women have a longer menstrual cycle than usual and it is painful. We give luteal hormone (first, of course, giving folliculin in first two weeks) in the third and fourth weeks of the cycle, and they will become pregnant.

We give folliculin on, say, the 4th, 7th, 11th and 14th day in good-sized doses. This promotes estrus, ovulation, and gives enlarged glands. Then on the 18th, 19th, 20th, 21st, 22nd, 23rd and 24th day we give luteo-hormone, then stop. If fertilisation has taken place, there will be no menstruation; but we must give menstruation a chance to occur, in case fertilisation has not taken place. So we stop suddenly—and wait three days or so. If no menstruation occurs, we resume progesterol, and give it on the 27th and 30th days as an extra safeguard.

Dysmenorrhœa: prolonged and painful menstruations, due to deficient ovarian function, are remedied to a great extent or entirely by progestin.

Habitual abortion.—The function of the corpus luteum of pregnancy is to ensure perfect rest for the embedded ovum. This is why the corpus luteum persists after fecundation and embedding of the ovum. But if the corpus luteum of pregnancy is insufficiently strong or degenerates too soon, we get casting out of the ovum—abortion.

This may be habitual and occur in consecutive pregnancies. It is probably due to some insufficiency of support by the B factor of anterior lobe secretion of the pituitary (antuitrin) or prolan B, that the corpus luteum degenerates far too soon.

The posterior lobe secretion, pituitrin, is antagonistic to luteo-hormone, and if it is in excess, pregnancy terminates, and the corpus luteum extract will fail if it is not stimulated by prolan B.

So in habitual abortion, 17 or 18 days after menstrual period has been missed, due to pregnancy, we give progesterol (2 or 3 injections per week and carry on for 6 or 7 months).

In two years, Schiller has seen 14 such cases of habitual abortion cured by progesterol.

Fourthly.—We often see, especially in young girls, a condition in which the ovary does not produce enough progesterol to give a thorough progravid phase. We do not see the whole endometrium half transformed; we see half the endometrium shewing increase of tortuosity, œdema, secretion, etc.—the characteristic progravid changes—and the other half resting. It occurs in patches, and we have a jagged surface, as part of the surface degenerates and is cast off—and severe juvenile menorrhagias. These are accompanying signs of hypoplasia and sexual infantilism—scant pubic hair, small breasts, etc.

In these cases marvellous results are obtained by giving progesterol in heavy doses, following some doses of folliculin.

Schiller has seen cases where hæmoglobin has dropped to 25%; where hysterectomy or vaginal extirpation appeared the only hope for saving life, saved by giving progesterol, which stopped the menorrhagia completely.

Progestin is the characteristic female sexual hormone, found only in females. Folliculin cannot replace the deficient function of the ovary—it is merely a proliferating hormone.

Frigidity, neurasthenia, any condition of insufficient function, must be treated by progestin (following folliculin).

Progestin is found mainly in the corpus luteum. Commercially, the corpora lutea of pigs are used; but these are small, and the preparation is very expensive, so that in Europe an ampoule of 20 units strength costs $10.00, and 20 units is not a large dose.

We are now at the stage with progestin at which we were with folliculin some years ago; folliculin is now produced much more cheaply, and no doubt ways will be found in the case of progesterol also.

There are two ways in which it may be more cheaply produced: (1) A synthetic progestin may be obtained—and its production is claimed by certain German and American firms; (2) we may find a source of larger corpora lutea, e.g., the whale, where the corpus luteum is the size of a football.

In sterility and habitual abortion we must give as large doses as possible, at least 20 units to the dose. When one remembers that in habitual abortion two to three doses a week must be given for months, one can readily see that cost may be prohibitive. We shall see later, in discussing anterior lobe secretion of the pituitary, that in many cases the use of the latter, which is much cheaper, may obviate the necessity for using progesterol.

Why does the onset of labour occur when it does? The answer to this

is found in the relative amounts present in the blood of progestin on the one hand, and pituitrin, or posterior lobe of pituitary extract, at any given time. Making quantitative tests during pregnancy, we find that the amount of progestin in the blood is maximal at the time of conception, and declines steadily; while the amount of pituitrin is at a minimum at the beginning of pregnancy, and steadily increases during pregnancy; when it overtakes the declining progestin, and the lines cross, labour occurs. The placenta contributes a small amount of progestin, but not much. The reason for this onset at this point is obvious: as long as progesterol predominates, the uterus is at rest, and the ovum is also at rest; but a powerful stimulant of contractions, namely pituitrin, is gradually increasing in quantity, till it overtakes and neutralises the depressant progestin; then it is present in many times its usual amount, and induces powerful contractions of the uterus.

Pituitary Hormones

We are dealing now with those of the anterior lobe, which control the ovary in its two phases of activity.

The secretion of the anterior lobe was discovered first by Zondek, who called it *prolan*. It is also called *antuitrin*. It has only one effect, it stimulates ovarian function.

Thus: (1) it is responsible for the waking-up of the ovary at puberty—it is the puberty hormone, the gonado-tropic hormone. (2) It stimulates the follicle, its growth, and so the production of folliculin. Only part of the antuitrin does this, the fraction known as prolan A. (3) It stimulates the luteinizing function of the ovary. It stimulates and supports the corpus luteum, and is so indirectly responsible for the growth of the fœtus, for its continuance at peace, and so on. This action of antuitrin is due to its other fraction, known as prolan B.

So we use antuitrin A in sexual infantilism, late developments, deficient puberty, undescended testicle, etc.

We give injections of antuitrin for these purposes, but we must not expect immediate results; we must expect to have to go on giving it for three or four months before we get a response. The amount of hormone in the preparation is small.

B.—We use it to stimulate the development of the corpus luteum. In women who are sterile, the lack of progestin may be due to lack of prolan B; and so antuitrin should be given first, before we give progestin. It is much cheaper, and the pituitary lack is the cause in the majority of sterilities.

Prolan is neither readily soluble nor stable; it is prepared in slightly alkaline solutions, and deteriorates very rapidly; so it is generally dispensed in two ampoules, one containing progestin crystals, the other solvent. This is the best method. Some firms sell a solution, guaranteeing that it will be at least half the recorded strength at the end of six months.

It is standardised in mice and rat units—the rat unit equals one-eighth one mouse unit.

Prolan is found in both male and female pituitary glands, not in pregnant women, but in large quantities in placenta. In hydatidiform mole or chorion epithelioma we find it in amounts 30 to 40 times normal, and this is a diagnostic sign.

Urine of normal women contains traces of prolan; of pregnant women 8 to 10 or 15 units per day; in hydatidiform mole or chorion epithelioma 30 to 50 times as much, i.e., 300 to 500 or more units per diem.

This to summarise the four hormones:

1. *Prolan*, produced by anterior pituitary, influencing ovary only; has no effect on castrated individual; contains two fractions: prolan A, controlling follicle, and production of folliculin and stimulating ovulation, and prolan B, controlling corpus luteum, production of luteo-hormone, and supporting the corpus luteum of pregnancy.
2. *Folliculin*, produced by ovary (*inter alia*) in follicle growth, controlling œstrus, stimulating proliferation and ovulation.
3. *Progestin*, produced by ovary (corpus luteum); influences *myometrium*, causing paralysis and allowing embedding of ovum at rest, and *endometrium*, causing secretion, œdema, tortuosity, and preparing for embedding of ovum—later ensuring rest for ovum growth, till overtaken and neutralised by
4. *Pituitrin* (post-pituitary lobe secretion), stimulates myometrium, causing contractions; opposed by lutein or progestin.

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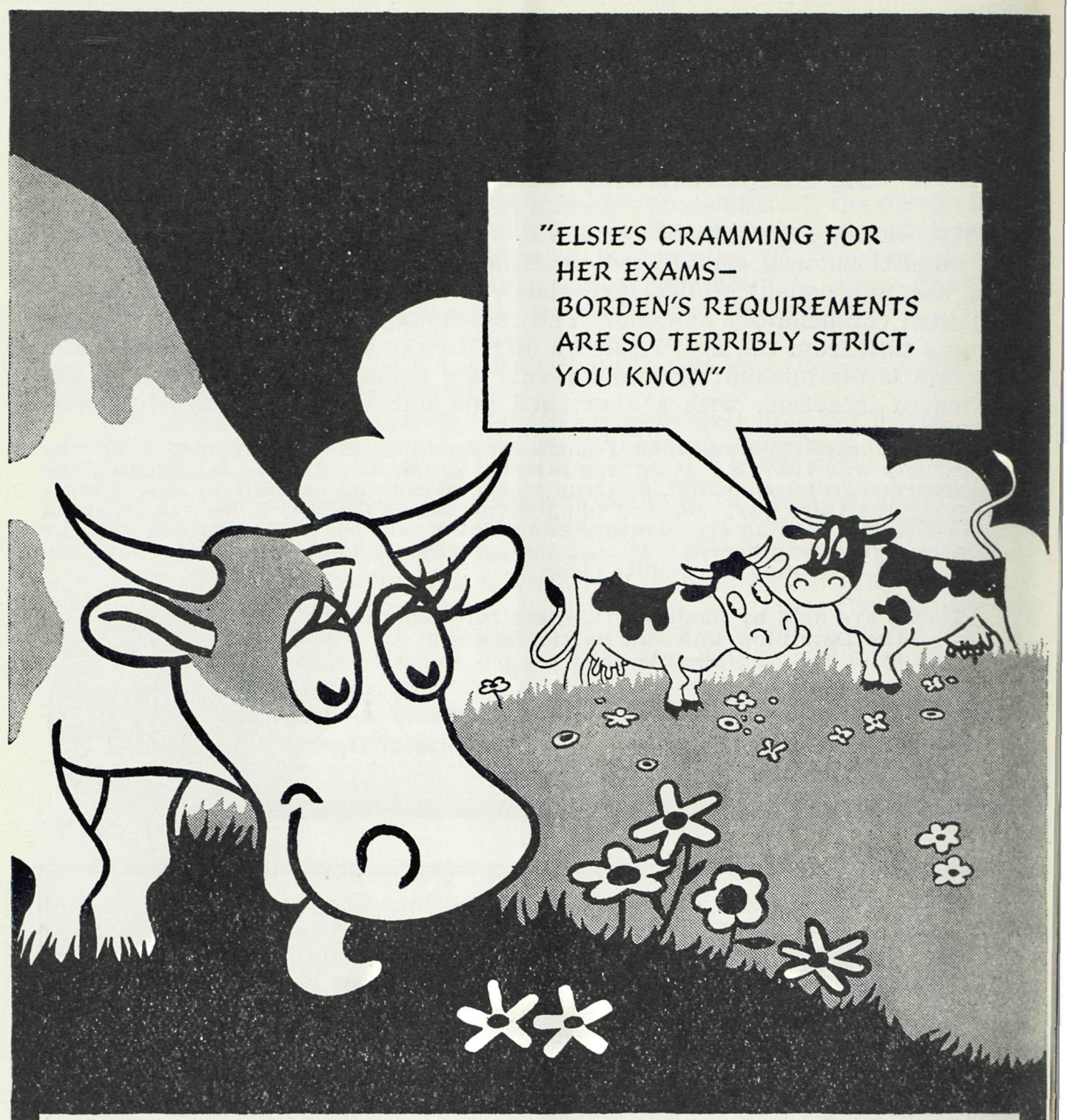

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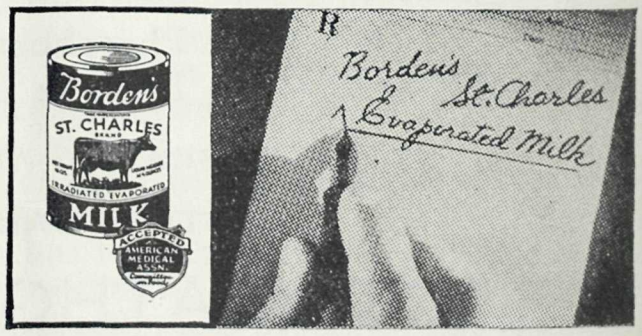

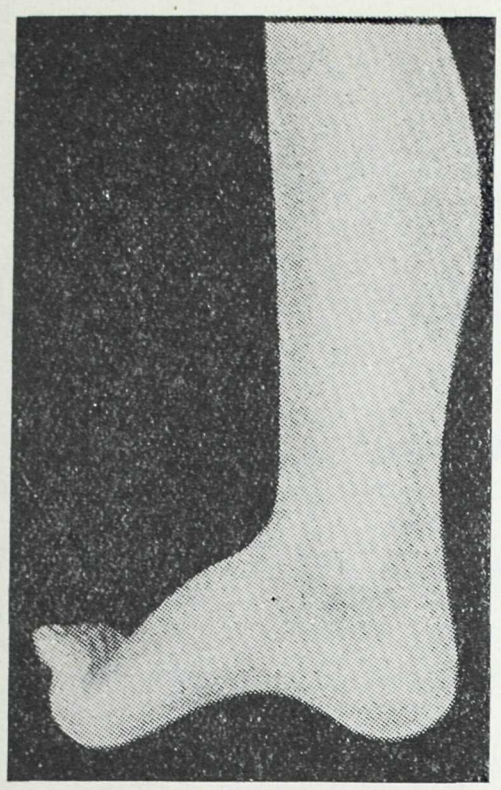

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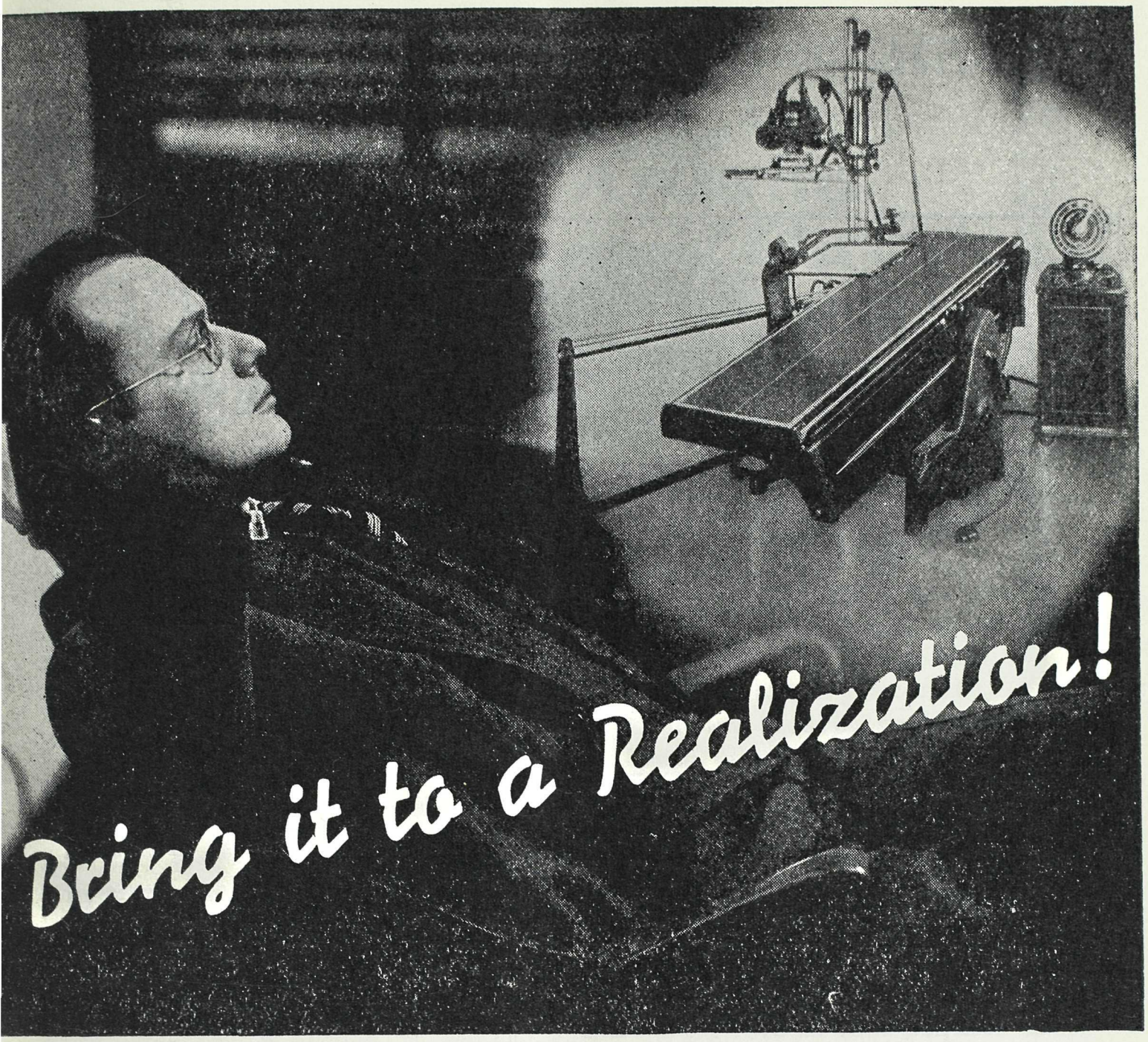

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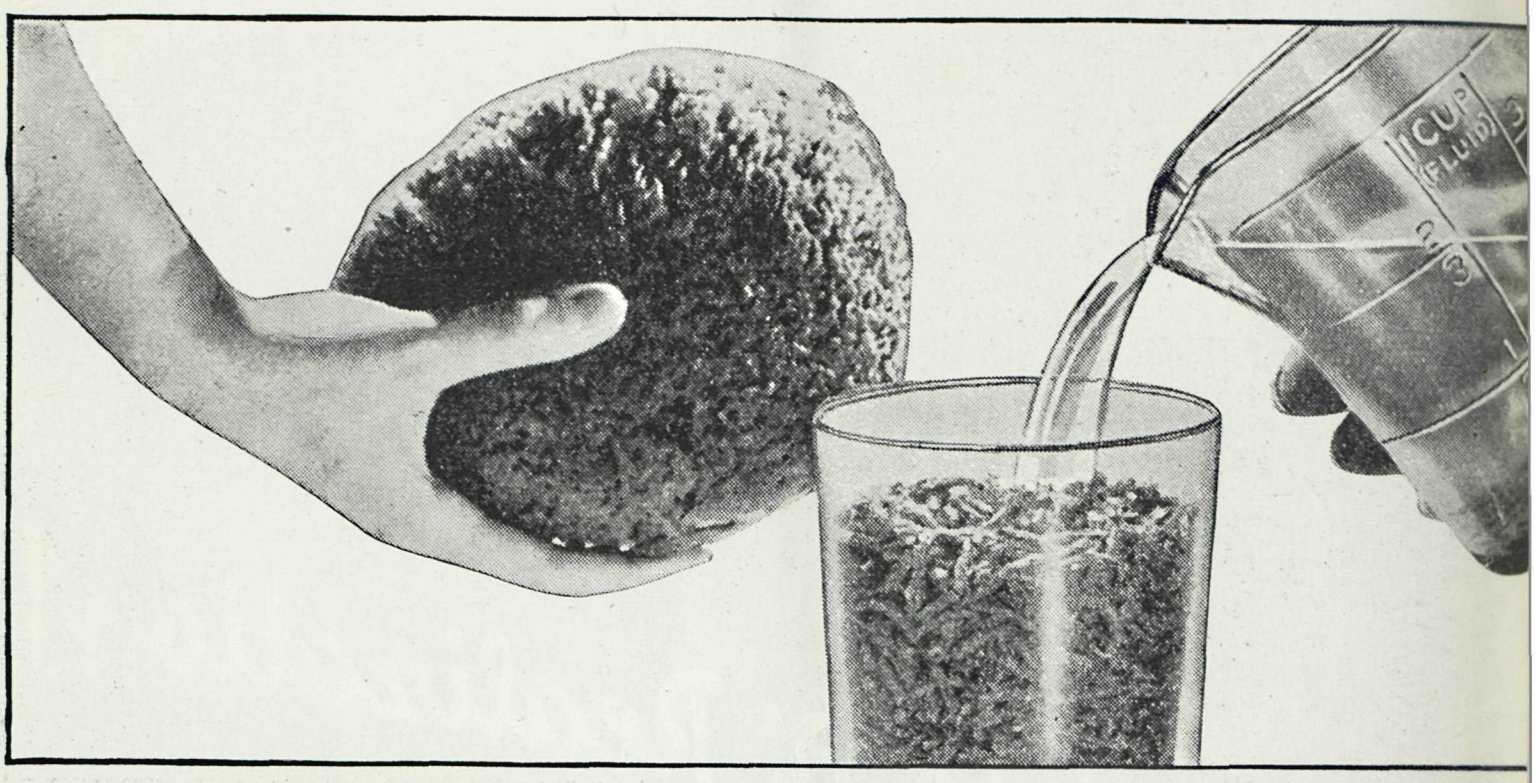

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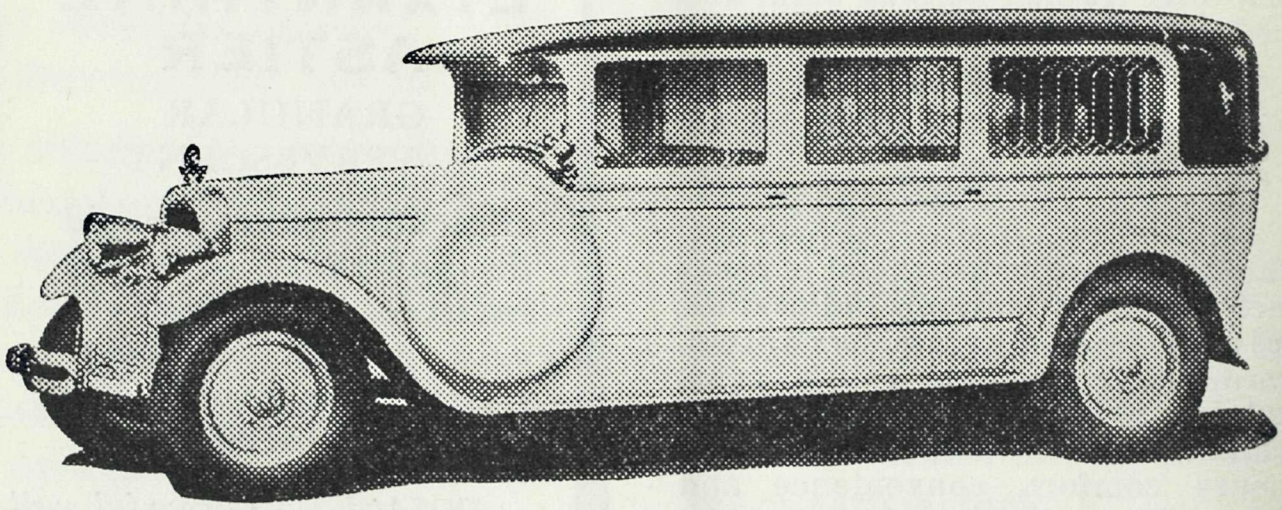

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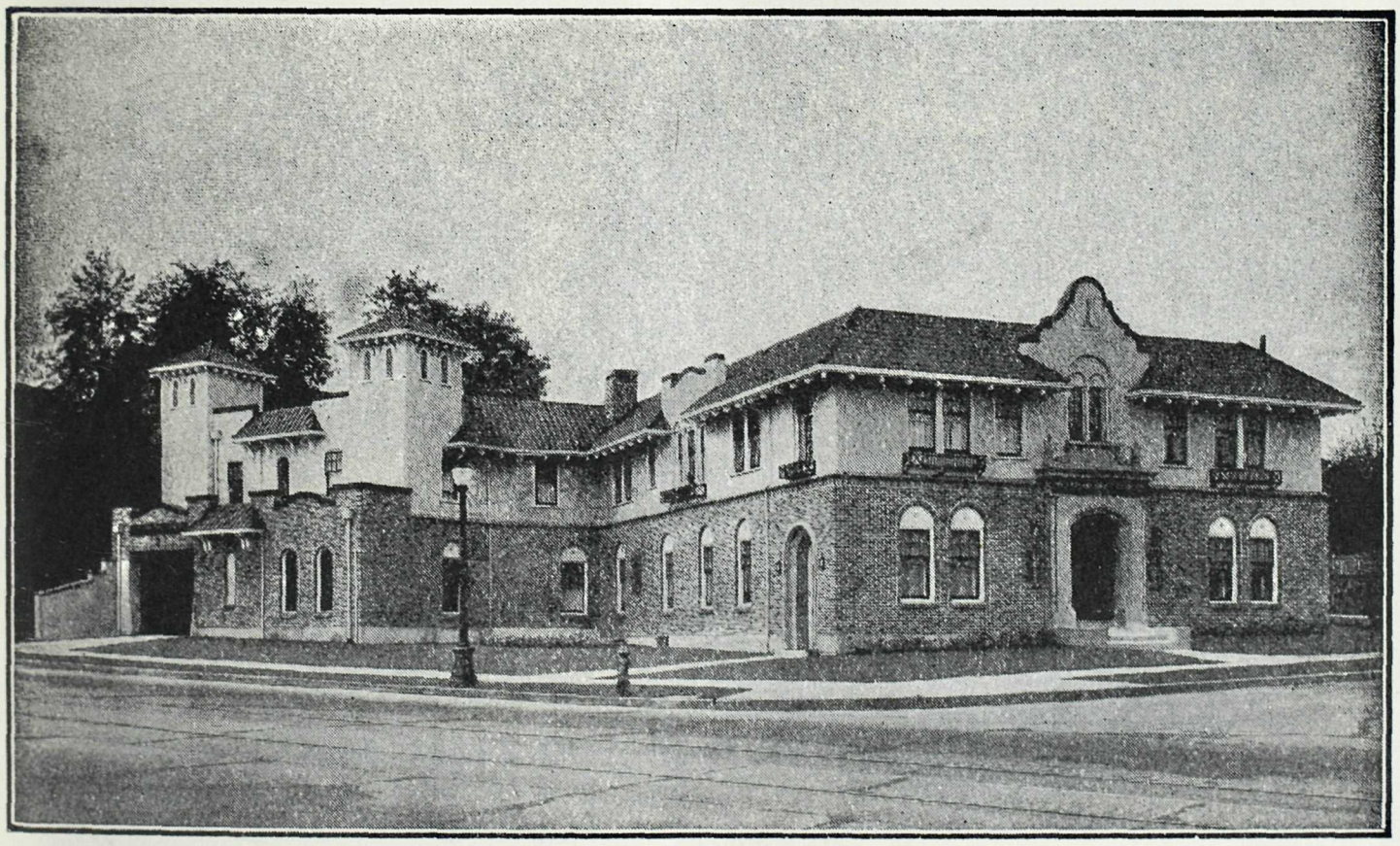

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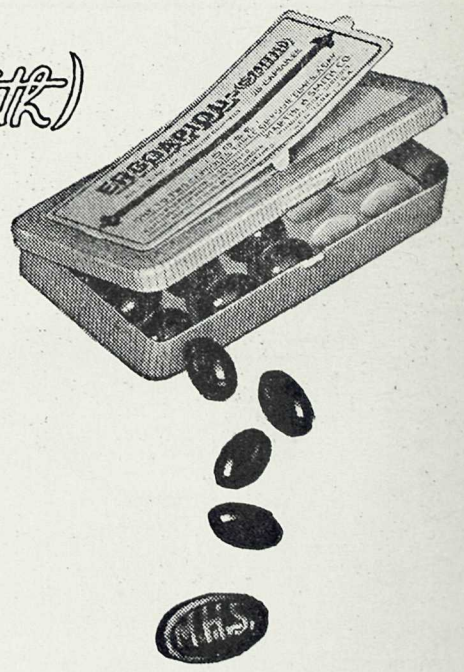

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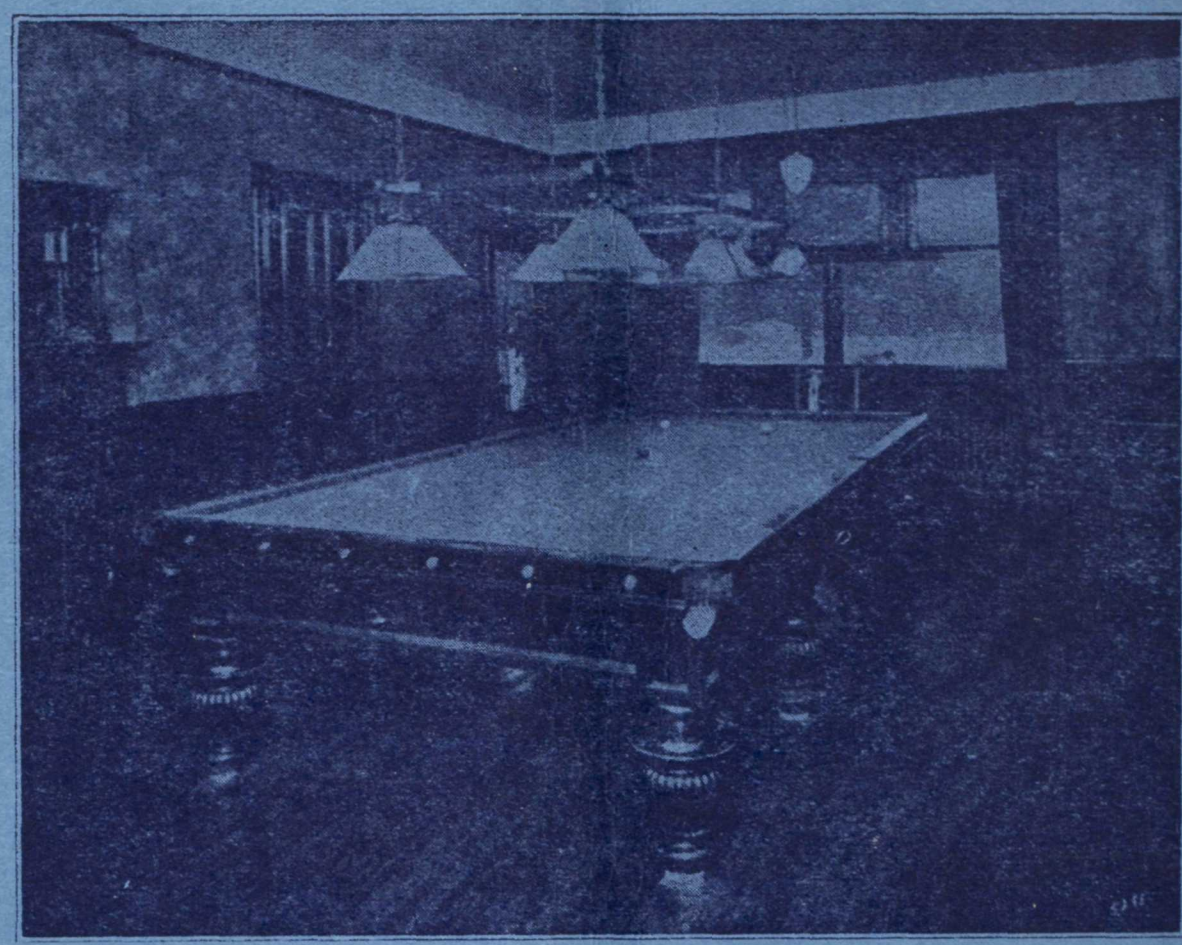

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