



THE BULLETIN

of the

Vancouver Medical Association

Menorrhagia

Thyroid Disturbances in Children

Metastases in Cancer of Female Genital Tract

News and Notes

PACIFIC NORTH-WEST MEDICAL ASSOCIATION

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THE VANCOUVER MEDICAL ASSOCIATION BULLETIN

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VANCOUVER HEALTH DEPARTMENT

STATISTICS, APRIL, 1933.

Total Population (estimated)	247,251
Japanese Population (estimated)	8,429
Chinese Population (estimated)	7,759
	Rate per 1000 of Population
Total Deaths	203 10.0
Japanese Deaths	3 4.3
Chinese Deaths	8 12.5
Deaths—Residents only	179 8.8
Birth Registrations	264 13.0
Male 128	
Female 136	

INFANTILE MORTALITY—

Deaths under one year of age	12
Death Rate—per 1,000 births	45.4
Stillbirths (not included in above)	7

CASES OF CONTAGIOUS DISEASES REPORTED IN CITY

	March, 1933		April, 1933		May 1st to 15th, 1933	
	Cases	Deaths	Cases	Deaths	Cases	Deaths
Smallpox	0	0	0	0	0	0
Scarlet Fever	9	1	7	0	5	0
Diphtheria	0	0	0	0	0	0
Diphtheria Carrier	1	0	0	0	0	0
Chicken-pox	154	0	141	0	78	0
Measles	3	0	2	0	0	0
Mumps	80	0	90	0	77	0
Whooping-cough	31	0	23	0	3	0
Typhoid Fever	4	0	2	0	3	0
			Outside cases		1	Outside case
Paratyphoid	0	0	1	0	0	0
Tuberculosis	118	10	84	11	34	—
Poliomyelitis	1	0	0	0	0	0
Meningitis (Epidemic)	0	0	0	0	0	0
Erysipelas	3	0	3	0	1	0
Encephalitis Lethargica	0	0	0	0	0	0

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Investigation of an Outbreak of Typhoid Fever in Warsaw

Almost exactly ten years after a typhoid epidemic in Warsaw and Winona Lake a second epidemic began. The first case was reported August 28th, and was followed by approximately forty cases and two deaths.

The official report on this epidemic by the State Board of Health is as follows:

"An outbreak of typhoid fever consisting of fifteen cases resident in Warsaw and Winona Lake caused an investigation of the milk supply on September 8th and 9th, 1932. Representatives of the State Board of Health assisting Dr. O. H. Richer, City Health Officer of Warsaw, Indiana, investigated the patients' source of Milk. In every case, patients were either regular or irregular customers of the Dairy of Warsaw, operated by It was later shown that approximately 25 persons who were transient in Winona Lake and who used milk from the Dairy became ill after leaving Winona Lake.

"Warsaw has a city ordinance requiring all milk sold within the city to be pasteurized. A thorough inspection of the equipment and methods of the Dairy was made. Feces and urine specimens were taken of members of the immediate family and no typhoid carrier was identified. Samples were taken from the dairy water supply and the examinations showed no trace of contamination. Recording thermometer charts showed many discrepancies and irregularities in respect to both temperature to which the milk was heated and in the length of the holding period, indicating incomplete pasteurization. The verbal statement and the records of showed that he was buying and selling more than 100 gallons of milk daily. The pasteurizer capacity was only 100 gallons and the recording thermometer charts showed that not more than 100 gallons of milk were pasteurized daily.

"It was later learned that the operator's nephew had worked in the dairy during the summer. Examination of his body discharges indicated him to be a typhoid carrier.

CONCLUSIONS

"The typhoid fever epidemic of Warsaw, Indiana was caused by one, or a combination of all of the following items:

- "1. A typhoid carrier working in the Dairy.
- "2. Incomplete pasteurization of milk by the Dairy.
- "3. Sale of raw milk for pasteurized milk by the Dairy.

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EDITOR'S PAGE

It is with great pleasure that the Bulletin draws its readers' attention to certain articles that it has been publishing recently. These articles represent original thought and work of a high degree of excellence, done by some of our own members, and such work is of the greatest value, as shewing the keenness and interest that are so essential if our profession is to go ahead. It is not the importance of the particular piece of work that matters: what matters is that a man practising in a small country town should be so alive and keen on his work that he takes the trouble to think to a conclusion the problem of puerperal septicaemia as it affects his own practice. He does not only think, but follows Hunter's advice, and tries: the result is a short paper in the May issue by Dr. Coy of Invermere, which makes us all sit up and think in turn. How far is the nurse a potential danger in the handling of maternity cases? The suggestion may lead to the clearing of several doubtful points.

Again, Dr. Brodie's paper on Subarachnoid Insufflations represents an actual piece of work done by himself, from which he can and does draw definite conclusions: it is a highly finished product, and its roundness and completeness add greatly to its value.

So also with Dr. Curtis' paper on Thyroid Disturbances in Children. This is particularly gratifying, in our opinion, since he has done what should be done more often, namely, made use of the material which lies so abundantly to our hand in the hospitals of Vancouver. Dr. Curtis was not content with the *ex cathedra* statements of the great ones of thyroidology, if there is such a word: he again obeys the immortal Hunter, and tries for himself. The result may not be of world shaking significance. That does not matter a scrap; after all, one never knows just which log in the jam is the key-log, the loosening of which will break up the whole mass and set the drive free. It is the fact that we have men who will have a vision and then follow it where it leads them.

Dr. Burwell's short paper, too, on lymphatic paths of metastasis, is an excellent bit of work, it summarizes, in a form that makes for great convenience and usefulness, our knowledge of lymphatic paths, and will be very welcome to all of us who have to consider treatment and prognosis in the cases of cancer.

We are making rather a point of these papers, some may think too much so, but we think not. It augurs well for the future of medicine in Vancouver. For these men are not alone. We have from time to time had other work to publish which reflects the same keen interest in research, and without research, continuous and everlasting, medicine would never be the magnificent thing it is. No man may say that one piece of research is more important than another. Many of the greatest discoveries have come through some seemingly small and relatively unimportant observation—all of it is of inestimable value—so that we congratulate these men, and ourselves in that we are able to help them to make themselves vocal.

* * *

Have you read the advertisements in this number? We urge you to do so, and as far as you possibly can patronize our advertisers. They alone make this journal possible, and they are all carefully selected. Their advertisements will be of interest to you and may be profitable.

* * *

The forthcoming meeting of the Pacific North-West Medical Association is going to be a red-letter event in the medical history of Vancouver. It takes the place this year of the Summer School, which has generously suspended its operations for 1933, in order to give the P. N. W. M. A. every opportunity.

The programme this year is a most excellent one. It is entirely British, and except for one speaker, entirely Canadian. The one exception, Dr. Kinnier Wilson of London, is well known to Vancouver medical men, who will not forget the addresses he gave here a few years ago. Those of us who heard these know that we are sure of a most delightful and profitable time when he returns in July.

The rest of the programme is equally good. It is very well-balanced, and has something for everybody; nor is it, as sometimes happens, a specialist's programme. It is carefully designed to meet the needs of the general practitioner, i.e. the bulk of the profession, though there is plenty for the men in special practice as well.

We are glad to see that the Committee has, except for clinics, left the afternoons alone. It is very difficult, admittedly, to please everybody in this matter, but we believe that, on the whole, the plan followed here is the best one, and the least upsetting to the man who has to keep one eye on the stove, while he listens to the preacher over the radio. The only proper way to attend one of these meetings is to go to another town for it. Anyway, the month of July is the best that could have been chosen, it is not a busy time for most of us, and we can take a few days off.

We feel strongly that every man in the Province who can possibly come to this meeting will be well repaid. The Committee in charge, with Dr. B. D. Gillies, this year's President, at the head of it, has worked hard to make this a success. They have provided a programme that will be as good as a post-graduate course. They promise us some entertainment in the way of golf, and a Dinner which is to be especially memorable. Sister professions are to be invited to send representatives, and speeches will be short and good: one or two of the speakers are men of renown in this regard, and it is for us to get behind them and reward their efforts in the only way that they would want a reward, namely to take advantage of the service they have rendered us and enjoy the meal of good things they have provided. Let us make this the best meeting the Pacific North-West has ever known.

Oh yes, about fees. Well, \$12.50 (if you pay before June 30) or \$5 a day, is, we think, very reasonable, even in these hard times, which, we are assured on all sides, are rapidly coming to an end. We have to have a holiday of some kind, why not make this part of it?

IMPORTANT NOTICE

The B. C. Medical Association will hold a Dinner at the Hotel Vancouver at 6:30 p.m. on Monday, July 3rd, at which all members of the College of Physicians and Surgeons are urged to be present.

At this Dinner the speakers will be Members of the Council of the College of Physicians and Surgeons who are authorized to present to the meeting a report of the activities of the Council since the re-organization of the B. C. Medical Association on January 1st, 1933; also selected speakers from the B. C. Medical Association.

Immediately following the Dinner, the ANNUAL MEETING of the B. C. Medical Association will be held.

* * *

NEWS AND NOTES

Dr. Murray McCheyne Baird has at last taken the step, and will join the great majority about the beginning of June. We learn that he has chosen Thursday afternoon for the fateful event but this is probably due to the fact that he is used to encountering hazards on this particular day of the week and feels that it will be in keeping.

* * *

Dr. Lavell Leeson admits that he intends to follow Dr. Baird's example but is very much more reticent about the exact date. The only facts we can gather about this are that it will be somewhere between June and August.

* * *

A casual visitor to the maternity pavilion some three or four weeks ago would have seen Dr. Roy Huggard gazing adoringly through one of the nursery windows on the third floor, while Dr. W. G. Gunn was gazing equally adoringly through another at the far end of the corridor. These two gentlemen are to be congratulated on the arrival of two beautiful examples of the genus boy.

* * *

Dr. A. C. Frost has been spending a short and well earned holiday on the Island with Mrs. Frost. We understand that they have played an average of thirty-six holes of golf a day and they are looking very fit on their return. The Bulletin congratulates Mrs. Frost on her very fortunate escape from serious injury in the motor accident of a month or so ago.

* * *

Dr. H. B. Maxwell, who used to practise in Vancouver some years ago and has since been practising on Vancouver Island and the lower mainland is leaving for England shortly where he intends to take up

practice and hopes to remain, he says, for the rest of his natural life. We shall all miss him very keenly as everyone who knew Bertie was very fond of him for his genial and kindly spirit. Mrs. Maxwell accompanies him and his two boys will follow later on.

* * *

Dr. J. J. Mason recently spent a couple of weeks on the Island holidaying. He looks very well and fit since his return.

* * *

Dr. J. C. Haramia who has been away at Hazelton for the past three months has now returned to Vancouver.

* * *

We congratulate Dr. Harry Milburn on the miscellaneous collection of *objets d'art* that he accumulated at a recent golf tournament. One's only fear is that nobody will again believe that his handicap should be 22.

* * *

A team of golfers from Seattle and Victoria invaded the city recently and have gone home with the scalps of the Vancouver braves who are grimly waiting for next year to take their revenge. The game was played at Shaughnessy Golf Course and everyone had a delightful time.

* * *

We are very glad to see that Dr. F. N. Robertson has completely recovered from the very painful effects of an accident to his eye some weeks ago: which confined him to bed for several days.

* * *

Dr. J. L. Turnbull has returned from Savary Island, where he has been for some weeks. He looks ten years younger and in some mysterious fashion has accumulated a coat of tan. This will be no surprise to those who know Savary Island, but looks rather novel to those of us who are living in the land of perpetual rainfall that Vancouver has proved itself to be for the past year or so.

* * *

Dr. J. A. (Okey) Smith goes about these days with a happy smile on his genial face for has he not succeeded in adding half the medical population of Vancouver to the membership of Shaughnessy Golf Club? Thereby doing them a good turn, as well as fulfilling his duties as chairman of the Membership Committee.

MENORRHAGIA

By J. E. HARRISON, Vancouver.

A modern, thorough understanding of the principles involved in the production of menorrhagia (profuse or prolonged menstrual flow) presupposes a rather full acquaintance with the new physiology of menstruation and endocrinology, in both of which rapid advances have been made during the last few years by laboratory experiment and clinical study. Ideas on these subjects are, at the present time, in such a state of flux, that it is perhaps unwise for us to have dogmatic views of any kind in this relation. Many of our former convictions have, as in so many other branches of medicine, gone the way of all flesh, and have been replaced by newer, more or less proven theories and beliefs, which in turn are paving the way to still more amazing unplumbed truths.

Not so very long ago investigation of a case of menorrhagia was confined chiefly to the examination of the pelvic organs with a general search for constitutional diseases, and treatments were perhaps mainly operative efforts. To-day, however, although attention is still directed toward local pelvic abnormality and general disease, we are, or should be, endocrine-conscious.

May I first mention briefly the causes of menorrhagia which are most familiar to us. Menstrual haemorrhage, its amount and duration, may depend, in general, upon the functional state of the uterus and active or passive pelvic hyperaemia. The factors controlling the amount and duration of the flow then may be (1) the contractility and tonicity of the uterine muscle, (2) the degree of active or passive engorgement of the pelvic blood vessels, and (3) the coagulability of the blood.

Loss or decrease of contractility and tonicity is associated with a hypoplastic state, congenital or acquired, general and uterine asthenia, subinvolution and fibrosis as related to chronic metritis following puerperal and other infections and myomata or polypi. Hyperaemia may be active or passive. *Active hyperaemia* results from infections and displacements of the genital organs. This, of course, includes all types of metritis, parametritis and endometritis, salpingitis, oophoritis, acute or chronic; also the congenital and acquired displacements. *Passive hyperaemia* is caused by cardiac, pulmonary, hepatic and nephritic disease. Coagulability of the blood may be altered by blood dyscrasias, such as purpura. Uterine or ovarian cancer and lues are also found frequently to be causes of menstrual haemorrhage.

The principles of treatment of these pathological states are familiar to us all. General toning up of the asthenic and non-contractile types, through regulation of diet, proper exercise, sleep, rest and suitable medication. Hot vaginal douches and possibly diathermy may be used. Curettage may occasionally be performed as a stimulating measure to promote contractility of the uterus, or to secure material for histologic study: for often only by such means may insidious malignant growths be discovered. Curettage will be found to arrest haemorrhage in 50% of cases but at

best is usually only a temporary measure. Many of these types of menorrhagia which have in the past fallen into this classification are found now to be benefited by suitable endocrine therapy, of which more will be said anon. Certainly the more radical forms of treatment should be postponed until these measures have been tried. In some cases, especially those associated with great irregularity of haemorrhage, x-ray radiation or radium implantation may be indicated, and should be used in many instances in preference to surgery. Radical surgical procedures, particularly in these types of bleeding, are becoming less popular.

Treatment of active hyperaemia resulting from infection and displacements of the genital organs, shows also a modern tendency to conservatism and expectant management, displacing many surgical methods of a decade or so ago. The handling of those cases of menorrhagia caused by general constitutional diseases is obvious, and may be specific or palliative.

Let us direct our attention, for a moment, to some of the newer conceptions of the physiology of menstruation, and how they affect the treatment of menorrhagia. The periodicity of the menses probably depends upon the time-duration of ovulation and the life-duration of the expelled ovum. When the ovum is not fertilized, but succumbs, we may look upon the result as an afertile or menstrual abortion. The menstrual decidua becomes detached, menstruation begins, resolution of the corpus luteum ensues and another Graafian follicle develops. During the last few decades, research workers have been endeavouring to find out how far the regulation of the female sexual cycle is dependent upon the influence of hormones.

In the normal menstrual cycle the Graafian follicle develops and matures during the first half of the intermenstrual period—from 14-18 days. It can now be taken as definitely proved that the ripening follicle elaborates an oestrus-inducing hormone or rather a group of closely related chemical compounds to which is given the name of follicular hormone. The chief function of this hormone is to stimulate the development of the secondary sex organs of the female, such as the uterus, vagina and mammae. The concentration of this oestrus-inducing hormone in the blood increases during the first half of the intermenstrual period and attains a maximum about two weeks prior to the onset of the next menstruation. This rise in concentration in the blood is paralleled by a rise in the excretion of the hormone in the urine. After rupture of the follicle on approximately the 15th day the concentration of the hormone drops rapidly to a low value, followed about nine days later by a short rise just before menstruation. Accompanying this appearance of the follicular hormone in the early part of the intermenstrual period, there is growth and development of the endometrium characterized by an increase in blood vessels and stroma. This is sometimes called the interval type of endometrium. If growth and rupture of the follicle are followed by normal development of a corpus luteum, the latter generates another hormone whose main purpose is to stimulate the uterus to prepare a decidua suitable for the reception of a fertilized ovum. These further changes, under the influence of the corpus luteum hormone are often

called pseudo-pregnant or true pre-menstrual changes, and comprise the corpus luteum phase of the cycle. If pregnancy takes place the corpus luteum phase continues, and facilitates the retention of the fertilized ovum and protects the developing embryo. When the corpus luteum does not develop properly, on account of failure of ovulation or follicle rupture, these final changes do not occur in the endometrium, but if there has been follicle growth and production of adequate amounts of follicular hormone, there develops the so-called interval type of endometrium, and bleeding occurs which may simulate menstruation.

It is obvious, then, that the maintenance of a normal menstrual cycle depends upon adequate development of corpora lutea, and demands a reasonable supply of both hormones.

These processes occurring in the mature ovary have been shown by Evans and others to be dependent upon the secretory activity of the anterior lobe of the pituitary body. Aschheim and Zondek showed that a substance is found in large quantities in the urine of pregnant women which is either identical, or closely related chemically with the gonad stimulating hormone of the anterior pituitary lobe. They believe that two separate components or hormones, which they call Prolan A and Prolan B, are essential for the control of the ovarian cycle. "A," for the production of mature follicles and follicular hormones and "B," for luteinization and production of the premenstrual phase.

Neither the preparation of these two components in pure form, nor their separation, has yet been accomplished, but it has been found that administration of small quantities stimulates the follicular hormone, while in larger quantities the dominant effort is that of Prolan B. According to Weisner, this is because the "A" principle becomes inert rapidly, even on standing, and its maximum effect is reached long before that of the "B" element. For this reason the administration of Prolan, or similarly, anterior pituitary lobe extract, in large dosage gives a definite luteinizing effect. This has been also noted by other workers.

When we consider that experimental removal of the Graafian follicle or corpus luteum is followed in from 48-72 hours by sometimes profuse uterine bleeding, we can readily see the application of hormone therapy of this kind. Any influence which will tend to promote a normal follicular development, with its accompanying secondary changes, normal ovulation, and a normal corpus luteum phase with its associated premenstrual uterine changes, will in all probability produce a normal menstrual period.

The particular gynaecological problem which invites the application of such observation is that of functional uterine bleeding. Novak made some interesting observations on this condition. He believes the immediate disturbance to be in the ovaries, the historical picture showing an absence of corpora lutea or other lutein elements, with the persistence of unruptured Graafian follicles. On the basis of this he assumes that the characteristic "hyperplasia of the endometrium" and the associated uterine bleeding are due to absence of progesterin or corpus luteum principle,

and a relative excess and persistence of the folliculin effect. The endometrium in these cases confirms this impression for it presents a picture of over-grown interval endometrium. The administration of extract of corpus luteum or the luteinizing hormone contained in anterior pituitary lobe, then, should convert the hyperplastic non-secreting endometrium into a pregravid or normal premenstrual one, thus completing the cycle and causing cessation of bleeding. Novak used a preparation of anterior pituitary substance in a series of fifty-one cases of this type, many of them recurrent, often with a history of several previous curettements, and in 44 of these bleeding was checked satisfactorily.

Adequate stimulation of the ovary, of course, by either follicular hormone or corpus luteum hormone or Prolan may not produce a typical response in the presence of local or ovarian disease.

That the substance called Prolan which is found in large quantities in pregnancy urine, is not identical with the anterior pituitary sex hormone, is shown by the fact that it has no effect in an animal from which the pituitary gland has been removed. It is looked upon, therefore, as an activator, stimulating the gland itself to produce more of its sex hormone. Prolan is supposed, according to most recent investigation, to be elaborated in the chorionic portion of the placenta during pregnancy. Collip found that what he calls a second placental principle was similar to anterior pituitary extract. He names it H.P.L. or anterior pituitary-like hormone of the human placenta and he has proved it to be of exceptional value in menorrhagia. The dosage employed is from 1-2 cc. injected subcutaneously daily or every 2 days. In the simpler types of menorrhagia, treatment for one week before the menses are expected, reduces the flow. The more severe types may require treatment for three months or longer before normal periods are established.

From these remarks it may be seen that gradually there is being established, by means of laboratory experiment, a number of facts concerning the physiological effects of active principles purified to a greater or lesser degree and derived from ovarian tissue, pituitary glands, placenta, and pregnancy blood and urine. Knowledge of the physiology of any one of these hormones, does not, however, help us greatly to understand the exact manner in which some or all of these principles harmoniously interact, or to what extent hypo- or hyper-activity of any one gland may affect the activity of the others. The exact manner in which, therefore, an active principle of placental or pituitary or ovarian origin may restore a case of excessive menstrual bleeding to somewhat normal functioning, must remain for the time being an unknown quantity.

This little treatise on menorrhagia would not be complete without mention of the role played occasionally by hypothyroidism, and even some cases of toxic goitre. Excessive bleeding is the menstrual disturbance most frequently associated with hypothyroidism, amenorrhoea rarely, if ever, occurring when the thyroid gland alone is deficient in function. In patients of any age whose menorrhagia cannot be attributed to pelvic pathology, a basal metabolism test should be made and even though this

Meeting of Pacific North-West Medical Association

July 4th, 5th, 6th, 7th, Hotel Vancouver, Vancouver, B. C.
President—Dr. B. D. Gillies

GUEST SPEAKERS

- Dr. A. T. Bazin, Professor of Surgery, McGill University, Montreal.
Dr. C. H. Best, Professor of Physiology, University of Toronto.
Dr. Wm. Boyd, Professor of Pathology, University of Manitoba.
Dr. J. G. Fitzgerald, Dean of the Faculty of Medicine, and Director of the School of Hygiene and Connaught Laboratories, University of Toronto.
Dr. A. H. Gordon, Professor of Medicine, McGill University, Montreal.
Dr. A. T. Mathers, Associate Professor of Medicine, University of Manitoba, Winnipeg.
Dr. S. A. Kinnier Wilson, 14 Harley St., London, England.
Dr. D. E. S. Wishart, Junior Demonstrator of Oto-laryngology, University of Toronto.

Tuesday, July 4th—

- 8:00- 9:00 a.m.—Registration.
9:00- 9:40 a.m.—Dr. A. T. Mathers, "Medico Legal Problems."
9:45-10:25 a.m.—Dr. Wm. Boyd, "Tumours of the Neck."
10:30-11:10 a.m.—Dr. A. H. Gordon, "Migraine."
2:00 p.m.—Surgical Clinic, Dr. A. T. Bazin.
8:00- 8:40 p.m.—Dr. D. E. S. Wishart, "Vertigo."
8:45- 9:25 p.m.—Dr. Kinnier Wilson "Visceral & Affective Epilepsy".
9:30-10:10 p.m.—Dr. J. G. Fitzgerald, "Some aspects of the Problem of Meningococcic Meningitis."
10:15-10:55 p.m.—Dr. C. H. Best, "Recent Work on Carbohydrate Metabolism."

Wednesday, July 5th—

- 8:30- 9:10 a.m.—Dr. A. T. Bazin, "Acute Osteomyelitis."
9:15- 9:55 a.m.—Dr. A. T. Mathers, "Psychoneuroses."
10:00-10:40 a.m.—Dr. C. H. Best, "Recent Work on Fat Metabolism."
10:00-11:00 a.m.—Dr. D. E. S. Wishart, "Mastoiditis in Children."
10:45-11:25 a.m.—Dr. Wm. Boyd, "Why Does a Patient Recover from Infection?"
2:00 p.m.—Medical Clinic, Dr. A. H. Gordon.
8:00- 8:40 p.m.—Dr. A. T. Bazin, "Tumours of the Colon and Rectum."
8:00- 9:25 p.m.—Dr. J. G. Fitzgerald, "Recent work in Staphylococcic Infections."
9:30-10:10 p.m.—Dr. Kinnier Wilson, "Cerebral Tumours."
10:15-10:55—Dr. A. H. Gordon, "The Diagnosis of Disease with Coincident Enlargement of the Liver and Spleen."

Thursday, July 6th—

- 8:30 -9:10 a.m.—Dr. C. H. Best, "Liver Function Tests from the Physiological Point of View."
9:15- 9:55 a.m.—Dr. A. H. Gordon,
9:00-10:00 a.m.—Dr. D. E. S. Wishart, "Sinusitis in Children."
10:00-10:40 a.m.—Dr. Kinnier Wilson, "Hysteria from the physiological side."
10:45-11:25 a.m.—Dr. A. T. Mathers, "Sleep and its Disorders."
2:00 p.m.—Golf Tournament, Shaughnessy Golf Course.
7:30 p.m.—DINNER.

Friday, July 7th—

- 9:00- 9:40 a.m.—Dr. J. G. Fitzgerald, "The Nature of Antigens."
9:45-10:25 a.m.—Dr. Wm. Boyd, "The Pathology of the Breast regarded as Disordered Physiology."
10:30-11:10 a.m.—Dr. A. T. Bazin, "Lesions of the Breast."
2:00 p.m.—Neurological Clinic, Dr. Kinnier Wilson.

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may be normal, a therapeutic test with thyroid gland administration should be given before more radical measures are contemplated. Definite hypothyroidism may occur in the presence of an apparently normal BMR.

I sincerely hope that my few remarks tonight do not leave you more hopelessly entangled than ever in the maze of endocrinology.

METASTASES FROM MALIGNANCY INVOLVING THE FEMALE GENITAL TRACT

K. M. BURWELL, Vancouver.

The question of metastases from malignancy involving the female genital tract is far too comprehensive for me to even scratch the surface in the time allotted for it. In addition, one cannot even think of any primary malignant growth in this or any other organ without wondering how great a swath it will cut. All of us are well acquainted with the organs and tissues involved in cancer spread by continuity and contiguity; most of us recall the blood supply without any great difficulty; but fewer are well acquainted with the lymph circulation; and is not this the greater menace? However, to cover this tonight is not possible, sufficient will it be for us to pass through the genital tract step by step, and point out certain salient characteristics in metastasis from a growth of a particular part; to mention some interesting findings, which, although not so common, are none the less worthy of note.

THE VULVA

Metastasis from squamous-celled cancer of the vulva is early and exists long before palpability. The inguinal and femoral glands are most frequently involved. Stoeckel believes that when surgery is indicated the iliac glands should be removed as well.

Dissemination in melanoma of the vulva is so rapid that Erichsen does not believe in local treatment if the primary growth is larger than a filbert. Florini's case, reported in 1932, involved the clitoris and at the time of excision was not marked by any inguinal adenopathy. Eight months later the patient died, and at autopsy metastases were found in the abdominal nodes.

Adenocarcinoma of the gland or duct of Bartholin metastasizes early to the inguinal glands.

Whether rodent ulcer is malignant or not is still under discussion. Crossen does not consider it so. At any rate the lymph glands and viscera are never involved.

Primary cancer of the urethra is very rare. Metastasis to the inguinal glands occurs in about 20% of cases. Dr. Arbuckle had such a case last year and should be able to give first-hand information on this subject.

Read before the Cancer Section of the Vancouver Medical Association on February 27th, 1933.

THE VAGINA

Cancer of the vagina secondary to cancer of the uterus, rectum, bladder or external genitalia, is far more common than the primary form. Gellhorn and Fleischmann report metastatic hypernephroma of the vagina arising respectively from the kidney and left suprarenal gland.

The paravaginal tissues are early involved with resulting fistular development and extension to the broad ligaments, ureters, and ovaries. Glandular metastases depend on the situation of the growth; if near the vulva to the inguinal glands, and from the remainder of the vagina to the hypogastric, external iliac and sacral promontory nodes.

FALLOPIAN TUBE

Many cases considered to be primary are really secondary, reaching the tube by direct extension from an ovarian or uterine growth, or by way of the lymphatics, abdominal ostium or viscera.

Metastases from carcinoma of the Fallopian tube are in the direction of the uterus, ovary, or regional glands. Stein, of New York, recently reported a case of primary chorionic cancer of the Fallopian tube with metastasis to the liver and abdominal nodes but none to the lung. The patient died from haemoperitoneum.

THE OVARIES

Adenocarcinoma of the ovaries is the most malignant of all ovarian tumours. The omentum is the favorite site of metastasis; nodules are frequently found in the intestine.

The papillary variety of adenocarcinoma is almost always cystic and tends to proliferate. These metastasize by way of the perivascular lymphatics and to the regional glands (late); especially the retroperitoneal and inguinal ones. Peritoneal implants from rupture of the capsule may fill the pouch of Douglas. In Hoffmann's case tumour metastases were found in the liver and thyroid gland and gave symptoms of Basedow's disease.

As I have mentioned in dealing with the tube, the growth found may be secondary to a primary growth elsewhere; and in this case always resembles the parent growth, whether or not it arises in the colon, liver or breast. In Hempel's case the origin was in the pylorus; in Reichel's the uterus. Marken's case followed linitis plastica, Goinard's was from the rectum, and Bennett's from the jejunum.

Last spring you will recall Dr. Mason bringing before the Clinical Section of this Association at the Vancouver General Hospital a case of Krukenberg tumour of the ovary. The presentation of the case and the discussion which followed was sufficient to warrant no further mention of this clinical entity.

Chorionic cancer may occur at the site of an ectopic pregnancy or result from malignant evolutionary changes in an embryoma.

Sarcoma of the ovary is very malignant and metastasizes early by continuity, contiguity, and by way of the blood stream to the viscera, peritoneum and pleura.

THE CERVIX

A thorough study of this subject is not within the scope of this or any other single paper. The space given over to it in the larger textbooks and the necessity of knowing the anatomy and histology of the tissues involved, make it almost necessary to enumerate the issues one by one.

The study of autopsy specimens has been very illuminating, at times discouraging, and again hopeful. Sampson's twenty-seven cases showed that twenty had extended beyond the uterus, of which twelve had metastasized to the parametrium and iliac glands. In this same series the pelvic lymph nodes were studied in nineteen cases, of which nine showed metastases. Schauta made a very thorough study of sixty cases and noted that in 43.3% the glands were entirely free. Kundrat's analysis of eighty cases showed only four in which the glands were involved with the parametrium free.

Certain general points are worthy of mention. There is no demonstrable relation between the size of the primary growth and the occurrence of metastases. A large lymph node is not necessarily metastatic, while a small one is not necessarily free. There is about the same proportion of free glands found in inoperable cancer as there is involved glands in operable cases, which is about one-third. Cancerous glands are frequently not much enlarged, firmer than normal, sometimes hard as opposed to septic soft glands.

The seriousness of malignancy of the cervix is due to the complex lymphatic system in the parametrium about it; for it is directly to the parametrium, utero-sacral ligaments and sides of the rectum that all lymphatic channels lead. As regards the blood stream, cancer spreads less frequently in this way than does sarcoma.

Let us now note the extension to the various organs of the body. Growth beyond the internal os to the body of the uterus occurs only late. The tubes and ovaries are rarely involved, and even then only in advanced cases. As may be readily understood, direct extension to the vagina is frequent, and involvement may also take place by implantation, by retrograde lymphatic spread, or by direct extension along the lymph node. At times one finds the deep tissues involved, forming submucous lumps and areas of induration which later ulcerate.

The proximity of the bladder and rectum necessitates not infrequent involvement. The presence of the cul-de-sac of Douglas protects the rectum for some time against invasion. Direct extension occurs along the vaginal walls and may eventually lead to obliteration of the cul-de-sac.

The parametrium is the blood-vascular-lymphatic-hilum of the cervix. About one hundred and twenty ganglia are present in the paramet-

rium. There are three groups of parametrial nodes; one where the artery crosses the ureter and which is often first involved; the small lymph nodes; and nodes along the wall of the main vessel. Kundrat found in seventy-six cases operated upon by Wertheim in which the parametrium was involved on one or both sides, that there was 71% in which the glands were entirely free from metastases. This a little higher percentage than in G. Winter's series. As a result of necrosis and sloughing a zone of cellular infiltration may develop which cannot be distinguished clinically from malignant infiltration; thus not all parametrial infiltration is malignant.

The pelvic lymphatics are not involved as often as previously considered. The parametrial glands may escape entirely; the cancer cells lodging in the iliac or sacral nodes. Other glands as the sacral, superficial and deep lumbar, inguinal and colic glands may be invaded from time to time. Schauta considered the glands to be in four stations; parametrial, promontory, intermesenteric, and coeliac. The acceptance of his operation shows how relatively infrequent is involvement of the latter stations.

The ureters in their terminal portions are frequently obstructed by compression from infiltration or by direct extension from the growth.

Metastases to distant organs are only found in advanced cases. Prone are the liver and spleen. MacCormac autopsied one hundred and nine cases noting visceral metastases in only 20%. In the some series, kidney lesions occurred in 43.5% (hydro-and pyonephrosis).

Extension by the blood stream reproduces the parent growth wherever the cells may lodge. The lungs are frequent sites. Fournier reported two very interesting cases of left supraclavicular cancerous adenopathy in cancer of the cervix treated surgically; the route probably was by way of the hypogastric nodes through the prevertebral, lumbar and mediastinal nodes to the neck.

This aspect of the subject would not be complete without reference to the question of radium. There is no real evidence to prove that radium causes metastasis; rather does it serve to prolong life to such an extent that at times quiescent cells in a lymph node, lying dormant for years, suddenly proliferate.

CORPUS CANCER

Cancer of the body of the uterus as opposed to cervical cancer is more circumscribed, less infiltrative, and shows a diminished tendency to lymphatic extension. The lymphatics draining the body run along the upper border of the broad ligaments in close relation with the ovary and tube, and then accompany the ovarian vessels over the brim of the pelvis to reach the chain of lumbar lymph glands lying on either side of the spinal column. Other lymphatic vessels run with the round ligaments to the inguinal glands. At times cells are carried in the uterine discharges, lodging and growing in the vagina to produce secondary growths from

which metastases may be found in the liver and omentum. Strachan found vaginal metastases in five of thirty cases.

Chorionic cancer of the uterus spreads to various organs through the blood stream by erosion of the vessel; especially prone being the brain and lungs. Occasionally the growth perforates the uterus leading to intraperitoneal haemorrhage.

Sarcomata of the uterus metastasize relatively later than carcinomata. The endometrial type is much more malignant than the fibromuscular form on account of the earlier infiltration to the perimetrial tissues and the more frequent metastases to other organs; especially the lungs, more rarely to the iliac glands.

THYROID DISTURBANCES IN CHILDREN

By E. JOHNSTON CURTIS

In September 1932, Dr. Helmholtz of the Mayo Clinic spoke on "Thyroid Disturbances in The Child," before the Summer School. The title of this paper is the same. Far be it from me to re-hash what so able a paediatrician has told you. This paper will deal with our findings in children who have an enlargement of the thyroid as we see it in Vancouver.

This paper is the result of mere curiosity, which was aroused some time ago by the insistence that Jimmy Jones or Mary Jones had goitre, and he or she should be treated for the condition. I carried on for a long while in the time-accustomed manner: with each visit came another "repeat" of the old prescription for sodium iodide. There was no consideration of the patient's age, hereditary influence, living conditions, presence of parenteral infections, or of the actual state of the thyroid gland itself.

After a time I began asking myself questions—is this thyroid really enlarged? If it is, then by what means or standards am I gauging its size? Soon I found myself saying that if he or she had more fat or was not so under-nourished the gland would never have been noticed or given me any concern. Seldom was the so-called thyroid enlargement noted first by the parents (12% were first noted by the parent and all these were in younger children.)

Some cases returned at very long intervals, dissatisfied because the medicine had not made the gland disappear. Some were disgusted and did not return. Many more kept returning because the child was "still nervous." Others returned because of repeated parenteral infections. I was always remarking on the cold blue fingers.

This went on so long that it was felt that it would be worth while to begin a systematic study of the questions presenting themselves. Broadly speaking, were we doing the right thing by treating every individual in the same manner?

Read at a meeting of the Vancouver Osler Society, March 22, 1933.

I have found nowhere anything which satisfactorily tells me what constitutes an enlargement of the thyroid in children. Marine, however, states that the thickness of the isthmus is a good indication of enlargement. There it ends. One is taxed in this problem when it is realized that 83% of our cases were more than 5% underweight. I now know from experience that slight degrees of enlargement are difficult to determine. It seems to me that the gland need not only be visible but must also be enlarged to palpation and that its consistency must be different to the indefinite, soft, jelly-like mass that a normal gland presents. In the adipose individual inspection means little.

Then the personal equation of the examiner plays an important role.

The Out-patient Department of the Vancouver General Hospital, at the suggestion of Dr. Carder, set aside a period each week for the observation of these cases. This history and findings of the 156 cases I consider fairly accurate as there have been two of us handling them. There is thus more uniformity of opinion than if the material been taken from, say, six doctors. I am indebted to Dr. Grant for his patience in sticking to a definite scheme and an often uninteresting repetition of things for the past three years. I shall not try to bore you with percentages. (These cases had about three hundred distinct courses of treatment.)

As ever, girls predominate in number, but it is interesting to note that boys are increasingly affected. The youngest seen was three years of age. 50% of the cases were less than twelve years old. The frequency of foreign parentage—"the dregs of Europe"—is very noticeable. Is it generally because of their less hygienic mode of living or their diet? Allen of Winnipeg and others have found the incidence in cabbage-eating families much higher.

Is Greater Vancouver a goitrous district? Dr. Lamont gives me the information that he held special thyroid investigation clinics involving 7000 children. In these he found 24% had a palpable thyroid. The district was from Cambie St. east. It is interesting to note that that side of the city is not supplied with Capilano water. He also states that the prophylactic use of iodine tablets furnished by the schools is a negligible quantity for the whole city. In this 24%, the number of boys and girls was equal—ranging between the ages of 6 and 11 years. The incidence of thyroid enlargement, "goitre," given in the school annual reports for the city (1931) is approximately 5%.

However I would question whether we can consider our childhood community as goitrous in the same sense as the Ohio workers—in that iodine deficiency is the cause of goitre. True, we know that the iodine content of the water supply is negligible. It is to be noted that these cases were born on the prairies of already goitrous mothers, and the growing child lived east of this coast line for at least six years. Half can be considered goitrous families. The mothers all nourished their babies at the breast. No mother or infant had cod liver oil among these prairie folk.

McCarrison's animals on an iodine-free diet in clean cages did not develop goitre; those in dirty cages did. When those in the dirty cages

were given iodine or cod-liver oil goitre did not develop. Is there anything in the fact that today so many babies are receiving cod liver oil that it will be a preventative of goitre as well as of rickets? Is the iodine present in the cod liver oil in an amount sufficient to prevent goitre, or is it the vitamin content? Is this an argument for the use of cod liver oil rather than Viosterol in infant feeding?

McCarrison again has proved that diets deficient in vitamin content, particularly vitamin B, are capable of causing goitre in a type hitherto unproduced experimentally, and in no way related to iodine intake.

The living conditions of these children were found to be good in few instances, the vast majority were poor. Do the children in our better homes get goitre? My impression is that they do not with anything like the same frequency.

A sufficiency of iodine (that is, if we consider lack of iodine the cause of goitre) becomes an insufficiency in the presence of such unhygienic conditions as noted above. Does the same necessarily apply whenever an extra load of energy is required; as, for instance, during or as a result of repeated parenteral infections or persistent nutritional or developmental difficulties? A large number of these badly nourished youngsters gave a history of such difficulties in their infancy and pre-school periods.

It is known that metabolism is increased where malnutrition exists. I take it then, that an extra demand is made on the thyroid and the result is a compensatory enlargement. Surely the elimination of causes which produce the malnutrition is quite sufficient to influence for the better this thyroid enlargement and its symptoms.

Half the cases gave a history of repeated infections, many came with active infection, and half had decayed teeth of no mild degree. Does the dental decay mean an upset mineral metabolism and thus an added load for the thyroid?

We are dealing, it must be remembered, with a growing organism, the metabolism demands of the child are large and, with added stress, the thyroid must work overtime.

We have seen numbers of cases with bad tonsillar infection greatly improved by their removal. The elimination of a pyelitis produced a normal child within a short time. The drainage of an infected maxillary antrum slowed all the increased metabolic processes, and in a reasonable course of time all signs of thyroid disturbance disappeared following the clearing up of chronic chest conditions. Heart disease, acute and chronic, nephritis, diabetes, we have seen these influence the consistency and size of the thyroid..

In the latter, the linking of the endocrines is readily realized. It is important to remember that there is a very striking interdependence between the various glands of internal secretion, and that disturbances in metabolism, in diseases associated with pathological conditions of the

hypophysis may not necessarily be ascribable to that gland, but may be due to an alteration in function of another gland (thyroid, adrenals) resulting from a diseased pituitary.* I have seen two cases of Frohlich's syndrome in which the thyroid was very much enlarged and in both cases the thyroid gland practically disappeared with the use of pituitary substance.

The relationship of the sex glands and the pituitary you heard last month. These things I point out to emphasize that interrelationship.

This following discussion is based on 8.7% considered as non-goitrous, 16% not treated (puberty), 75.3% treatment in some form at all times.

The 91.3% of glands which we have considered as enlarged we divided into—small 32%, moderate 43.7%, and much enlarged 15.6%. The symptoms most marked were nervousness and tremors; the pulse rate was increased in 50% of the cases; headaches, warm, moist skin occurred with about the same frequency (55%); eye signs were present to some extent in 20% of the cases; dyspnoea and vertigo in 30.8%. The glands which were enlarged were described as 21.4% hard (all were taking iodized salt on admission) firm 39.4%; soft 49.2%. The lobes were unequal in 36%, and nodules were definitely made out in 7.5%.

From a general review of the symptoms and results of treatment I feel that 18% of the cases were hypothyroid although on admission only 6% were considered so. Of the remaining (those that were not hypothyroid), 22% were considered as severe types of thyroid enlargement (2 of these were considered to be cases of Graves' disease.)

Symptoms of hyperthyroidism in children are much the same as in the adult, but the severity of the signs is not as marked. Rapid pulse, nervousness, tremor, exophthalmos, polyphagia, dyspnoea, hyperhidrosis, loss of weight, enlargement of thyroid, are present in varying degrees but on the whole are less marked.

For a period we were using an organic compound of iodine instead of the old-time sodium iodide. It was noted we were getting nowhere, many became worse, many were helped by stopping its use. Then we turned to the use of thyroid extract with so much effect that it is now in almost universal use.

Dr. Helmholtz considers that these cases must all have been hyperthyroid, drawing his conclusion from the therapeutic test. Why, then, have only 6% shewn a low BMR on admission? He explains this for us by saying that the standards used for children have never been satisfactory—that from the rates obtained at the Mayo clinic (Dr. Boothby) we now have something authentic, and this, he claims, proves that our determinations were too high. However, as I said, many of the children became hypothyroid clinically and by the BMR test.

It is to be noted that 30% were taking iodine on admission. Half of these had taken it before the enlargement was noted. We found in

* Gerling—Chemistry in Medicine—p. 252.

many of these who were getting iodized salt on admission, or were given sodium iodide or organic iodine as treatment, that when the use of iodine was discontinued they became hypothyroid, and not infrequently the BMR would become 10 or less (10 or 12% became minus BMR). In all, however, when the iodized salt was stopped, there was improvement.

It is interesting to note what happened when these enlarged thyroid cases were given iodine or iodized salt. The gland became hard or firmer, and almost invariably enlarged. Tremors, nervousness and pulse rate increased in the majority. 77% became generally worse. In 65% of the cases the pulse rate increased. When later the iodine was discontinued 73% improved generally. In 70% the pulse rate decreased.

Turton, in the 'Lancet', 1927, states that it is not difficult to cause considerable distress by the use of iodine in the goitre of childhood.

For the past year those cases which we decided to treat have been treated with thyroid substance. This was because of (1) the lack of results from iodine, (2) the harm done by iodine (3) the fact that the gland, when iodine was being taken, became nodular, (4) the fact that the BMR findings were very inconsistent.

With thyroid extract 92.1% showed general improvement. In 82.9% pulse rate decreased or remained the same (the remainder increased because of definite hypothyroid state.)

It is to be noted only small doses of thyroid substance have been used, and I feel that the efficacy of thyroid substance is yet to be proven.

Only in one case did the BMR increase to any degree on thyroid substance; this was not a hypothyroid condition. A girl of 8 years (now 10 years) had been given iodine in various forms—always the gland enlarged, and she became highly nervous. Her condition was definitely toxic. Then with gradually increasing doses of thyroid substance it was discovered that not only did the thyroid decrease in size and become soft, but she became markedly improved. When the BMR was taken the gland could not be seen and could hardly be felt. The BMR was +40. This will show the discrepancy in the metabolic rates.

It is known that thyroid extract in relatively small doses does not have any effect on the BMR of a normal child other than a stimulative effect on growth.* This leads to the question whether the BMR should be the criterion of the effect of thyroid substance.

To me the BMR has some significance: I feel that the plus values mean little, if anything, but the negative values will certainly indicate a hypothyroid condition. For example: a plus 10 has no significance to me, but a minus 10 is indicative of less thyroid secretion than in the normal. From this experience the enlarged gland, then, would be expected to reduce in size on thyroid therapy—become softer, and there would be general improvement.

* American Journal Diseases of Children, February, 1928.

PUBERTY

If we segregate those girls of 12 years or over who secured no treatment (169), we find that they gained weight as did the whole group; that the pulse rate which was increased in the majority, decreased in 35%; the thyroid gland remained the same size in practically all; headaches were more frequent; the BMR increased in all and on the whole the symptoms were the same or worse in 36%.

I think one finds that as puberty appeared in the mother so it appears in the daughter. If the mother's menstrual history first began at 15 years rather than at 13 years, the daughter may be expected to act in the same way. That the thyroid enlarges at this time there is no doubt. However, I question whether in the normal girl—that is, where no previous diseases etc., have existed and where the previous endocrine balance has been good, the thyroid will be physiologically enlarged for a period of more than 3 or 4 months. The persistent enlargement means that some mechanism has gone wrong elsewhere.

Among the children of the Children's Aid Society there is an appreciable number of adolescent girls (approximately 100) which I like to consider as a control group. The physical health and incidence of illness is extremely low. Here only 4% have developed goitre and it is interesting to note that they had used iodized salt extensively.

SUMMARY

1. Measurement of the neck is unsatisfactory.
2. In estimating the size of the thyroid, consider the child as a whole, do not just look at the thyroid.
3. There is not one cause for goitre,—there are many.
4. Having a child with thyroid enlargement, clear up pathological processes elsewhere and you will be surprised at the results.
5. Thyroid enlargement is not always due to an iodine deficiency. A deficiency is relative only.
6. The BMR test by the usual standards is of very questionable value. As regards Reid's formula, I cannot give an opinion.
7. Enlargements of the thyroid are associated, more frequently than is generally suspected, with a hyposecretion.
8. Iodine is of doubtful value in prevention, or in the treatment of the enlarged thyroid which is secreting normal thyroxin.
9. Iodine given to such a child may do more harm than good. Iodized salt in the home should be thrown on the garbage heap.

10. Hyperthyroidism does occur in children, but the signs are much less marked than in the adult. The pulse rate is more reliable in these cases than the BMR.

1. Many children at puberty get well without treatment.

12. Remember that the youngster who is a live wire may wear out his thyroid.

13. If treatment seems indicated, is it not better to use thyroid substance?

CONCLUSION

It appears that a lack of iodine leads to a lack of thyroxin, because of a lack of the wherewithal to make it.

A lack of thyroxin causes an enlargement of the thyroid gland in response to an undersupply of this substance. When the gland has already enlarged, the giving of iodine may result in the formation of more thyroxin than is necessary, at least for a time. At any rate the gland is stimulated by iodine to produce thyroxin and so is kept active.

It would seem logical under such conditions to provide thyroxin rather than iodine, for this would give the gland rest and stimulate functional activity. When there is hyperfunction of the thyroid, the provision of liberal amounts of iodine may do distinct harm because of overproduction of the hormone thyroxin which stimulates metabolism to a marked degree.

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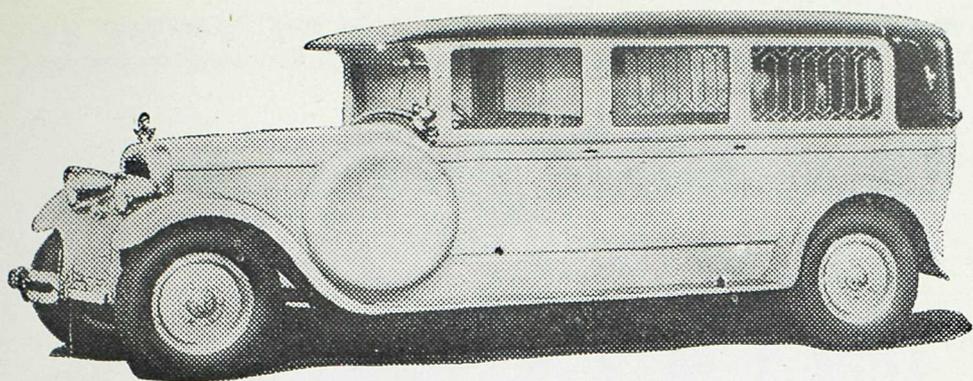
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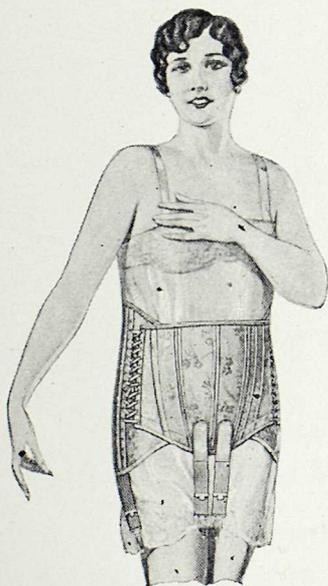
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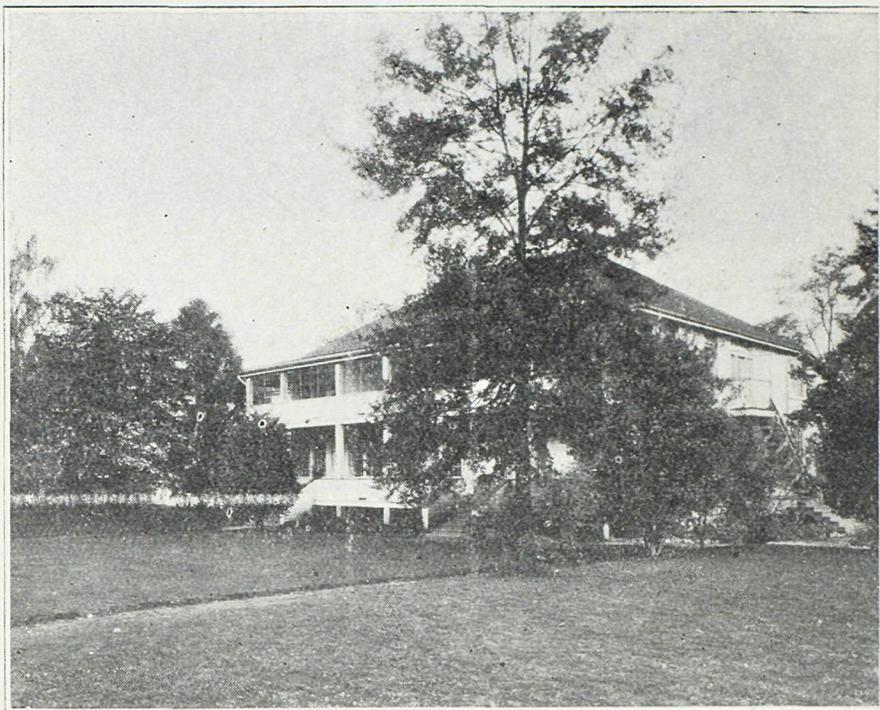
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