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The BULLETIN

of the

VANCOUVER MEDICAL ASSOCIATION

Vol. XIII. NOVEMBER, 1941 No. 2

With Which Is Incorporated
Transactions of the

Victoria Medical Society

the

Vancouver General Hospital

and

St. Paul's Hospital

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Inhibition of Lactation—One mgm three or four times daily, until flow has ceased.

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**Watson M. C. Academy of Medicine Bulletin, Toronto, March, 1940, p. 127.*

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THE VANCOUVER MEDICAL ASSOCIATION

BULLETIN

Published Monthly under the Auspices of the Vancouver Medical Association in the interests of the Medical Profession.

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All communications to be addressed to the Editor at the above address.

VOL. XVIII NOVEMBER, 1941 No. 2

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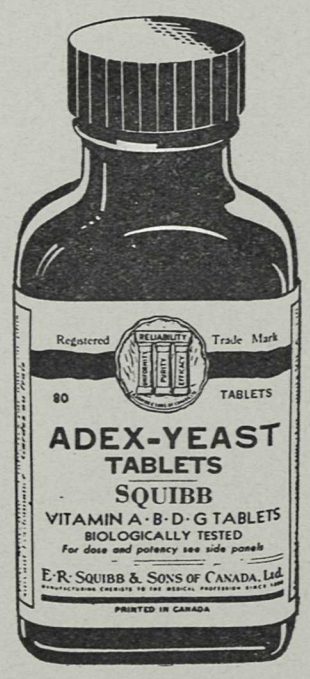

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*Strauss, M. B., *J. A. M. A.* 110:953, 1938.

For literature and samples write 36 Caledonia Road, Toronto

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VANCOUVER HEALTH DEPARTMENT

STATISTICS—SEPTEMBER, 1941

Total Population—estimated	272,352
Japanese Population—estimated	8,769
Chinese Population—estimated	8,558
Hindu Population—estimated	360

	Number	Rate per 1,000 Population
Total deaths	248	10.72
Japanese deaths	4	5.4
Chinese deaths	6	8.3
Deaths—residents only	222	9.3
BIRTH REGISTRATIONS:		
Male, 233; Female, 228	461	19.9

INFANTILE MORTALITY:	Sept., 1941	Sept., 1940
Deaths under one year of age	13	12
Death rate—per 1,000 births	28.2	26.8
Stillbirths (not included in above)	6	11

CASES OF COMMUNICABLE DISEASES REPORTED IN THE CITY

	August, 1941		September, 1941		Oct. 1-15, 1941	
	Cases	Deaths	Cases	Deaths	Cases	Deaths
Scarlet Fever	6	0	7	0	7	0
Diphtheria	1	0	0	0	0	0
Chicken Pox	0	0	18	0	35	0
Measles	6	0	4	0	1	0
Rubella	5	0	0	0	0	0
Mumps	1	0	9	0	14	0
Whooping Cough	4	0	0	0	2	0
Typhoid Fever	1	0	2	0	0	0
Undulant Fever	0	0	0	0	1	0
Poliomyelitis	1	0	0	0	0	0
Tuberculosis	22	12	18	10	10	–
Erysipelas	0	0	1	0	0	0
Meningococcus Meningitis	1	0	1	0	4	0
Paratyphoid Fever	0	0	0	0	0	0

V. D. CASES REPORTED TO PROVINCIAL BOARD OF HEALTH, DIVISION OF VENEREAL DISEASE CONTROL

	Burnaby	West Vancr.	Richmond	North Vancr.	Vanc. Clinic	Hospitals & Private Drs.	Totals
Syphilis	0	0	0	0	22	22	44
Gonorrhœa	0	0	1	1	53	19	74

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VANCOUVER MEDICAL ASSOCIATION

Founded 1898 . . . Incorporated 1906

Programme of the Forty-fourth Annual Session

1941.

October 7—GENERAL MEETING.

Dr. W. D. Keith: "Safety in the Operation for Toxic Thyroid.

October 21—CLINICAL MEETING.

November 4—GENERAL MEETING.

Dr. E. J. Curtis: "Meningococcus Meningitis."

November 18—CLINICAL MEETING.

December 2—GENERAL MEETING.

Dr. F. E. Saunders: "Sterility in the Female."

December 16—CLINICAL MEETING.

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Guinness often supplies just the necessary fillip to nudge the patient out of the rut of low health."

M. B.

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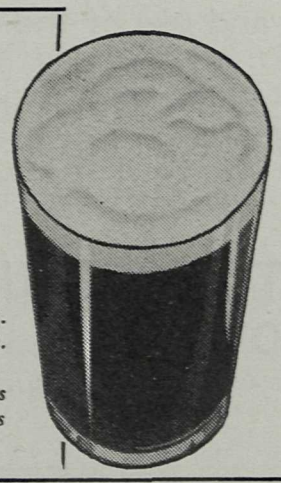
AN ANALYSIS OF GUINNESS STOUT 100 cc.

Total solids	5.87 *gm.*
Ethyl alcohol (7.9% by volume)	6.25 *gm.*
Total carbohydrates	3.86 *gm.*
Reducing sugars as glucose	0.66 *gm.*
Protein	*None*
Total nitrogen	0.10 *gm.*
Ash	0.28 *gm.*
Phosphorus	38.50 *mg.*
Calcium	7.00 *mg.*
Iron	0.072 *mg.*
Copper	0.049 *mg.*
Fuel value	*61 cal.*
Vitamin B_1	*6 Int. Units*
Vitamin G	*33 Sherman Bourquin Units*



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In Europe, apples have been used therapeutically for over two centuries. More recent research in Canada and the United States has confirmed many of the European findings and has, in addition, shown many new uses and values in the apple.

The physical and nervous strains of these war years make national health even more a matter of supreme importance, and medicinally and therapeutically, the Canadian apple has the elements necessary for playing a major role in the maintenance of Canada's war-time health.

From an economic viewpoint, the use of the Canadian apple takes on an added importance in that no foreign exchange need be spent for it that could be spent for essential, imported armaments.

The twenty-six hundred apple growers in the interior valleys of British Columbia, by whom this advertisement is published, are interested in the further nutritional and medical knowledge and use of the Canadian apple.

Your comments on this would be much appreciated. Address your letters to—

BRITISH COLUMBIA FRUIT BOARD
KELOWNA B. C.

THE EDITOR'S PAGE

Within the past few months, we have seen arising in Vancouver a number of quasi-insurance organisations, known by various names. They undertake the sale to the public of policies, purporting to insure the beneficiary against the costs of sickness—chiefly, it may be noted, the costs of operative conditions.

The sale of these policies is being very energetically pushed—and many people are buying them. When the patient has had an operation, the bill is given to the company involved, and a cheque is sent to the surgeon.

There is no doubt that the rapid increase in this sort of insurance has been brought about by the success of such mutual health insurance associations as the B. C. Telephone, the B. C. Electric, the Vancouver School Teachers and the Medical Services Association. All these organizations, as our readers know, have made contracts with the medical profession of British Columbia through its organised B. C. Medical Association. A 25% cut in scheduled fees is accepted on certain well-defined terms.

There is no contract or agreement between the B. C. Medical Association and any of these other organisations to which we refer. Therefore, when they send in a cheque in full settlement, subject to a 25% reduction, we *should not accept it*. Our contract is with the patient—not with *any* insurance company—and we should make it clear to our patient that he or she is liable for the full amount of the bill.

There are several reasons why this should be so; we take leave to mention a few:

(1) As stated, we have made no contract with any of these people and they have no right to dictate to us what our charges shall be.

(2) They make an agreement with the patient, based on our ordinary schedule. Then they cut the bill, and pocket the difference. This is why there is such a rapid increase in this sort of thing—it is becoming very profitable.

(3 They do not pay for all medical services, as do the Telephone, B. C. Electric, M-S-A, etc. They only pay for operative work.

(4) A very serious point for us to consider is that by accepting these people and their terms we are allowing a very dangerous principle to be introduced into the practice of medicine: this is, third-party gain. It is a dangerous principle, that a third party should make money out of the sick and squeeze out of both the sick and the doctors attending them, profit which they have not earned. Our Medical Services Association exists, and we should urge people to join this. It gives infinitely more value for their money, and is under close supervision and control.

The *modus operandi* of these gentry is to send a curtailed cheque, and if the doctor protests, to utter all sorts of threats of blacklisting, etc., as well as to assure the doctor that everyone else is accepting the cut. We think that the only answer to this sort of blackmail is to insist firmly upon payment of our bill, and ignore completely their threats. If we tell our patients the facts and shew them where they can get equitable, honest, and complete medical service on a health-insurance basis, we shall have done them a service, and helped to protect them, as well as ourselves, against what is fast becoming a racket.

We hope to publish a brief account of the result of a court case where a doctor here sued for his bill, and where the presiding judge handed down a decision which is of great importance to us all. It is by way of being a test case. If we all take the same stand as did this doctor, we shall soon force these companies either to act fairly and honestly, or to go out of business.

NEWS AND NOTES

In the passing, on Octover 7th, 1941, of Dr. D. J. Bell of Vancouver, the profession has lost a very loyal member.

* * * *

Dr. G. E. Kidd of Vancouver has the sympathy of his colleagues in the loss of his wife on October 26th.

* * * *

Sympathy is extended to Dr. R. B. Robertson of Victoria in the loss of his mother on October 28th.

* * * *

Capt. A. W. Bagnall, who is now serving with a Field Ambulance, was made a Fellow of the Royal College of Physicians of Canada by examination. Capt. Bagnall is the son of Dr. A. W. Bagnall of Vancouver.

* * * *

Dr. and Mrs. A. B. Schinbein of Vancouver were visitors in Toronto.

* * * *

Dr. and Mrs. A. M. Agnew of Vancouver are visiting in Toronto.

* * * *

Dr. .W Harold Brown of Vancouver travelled by air to the meeting of the American Academy of Ophthalmogy and Otolaryngology. Dr. Brown will receive life membership in the Academy.

* * * *

Surgeon-Lieut. H. G. Farish, son of Dr. J. C. Farish of Vancouver, and Dr. Hazel W. Krause of Montreal were married on October 18th. They have our best wishes.

* * * *

Dr. D. E. H. Cleveland will leave on November 11th to do post-graduate study in New York. While in the East he will attend the American Academy of Dermatology and Syphilology, returning to Vancouver on December 22nd.

* * * *

Flying Officer H. B. McGregor, Medical Officer with the R.C.A.F., returned to Penticton for a short visit before leaving for Toronto.

* * * *

Penticton's contribution to His Majesty's Forces includes: Capt. R. P. Borden, Capt. W. Roy Walker of the R.C.A.M.C., and Flying-Officer H. B. McGregor of the R.C.A.F.

* * * *

It is reported that Dr. W. M. Toone of Nelson is planning to enter War Service, and Dr. R. B. Brummitt of Smithers will carry on in a holding capacity during Dr. Toone's absence.

* * * *

Nelson has already lost Dr. B. Dunham, who is now serving with the R.C.A.M.C., and Dr. W. McC. McCallum, who was associated with Drs. Borden and Morrison.

* * * *

Dr. J. J. Gibson, formerly of Tulsequah, is now associated with Dr. R. Geddes Large of Prince Rupert.

* * * *

Dr. W. T. Kergin, formerly of Premir, is now at Ocean Falls.

* * * *

Dr. W. T. Kergin and Dr. C. A. Armstrong are carrying on the practice at Ocean Falls, both Dr. R. D. Coddington and Dr. G. D. Saxton having entered the Forces. By arrangement the latter are on extended leave from their positions at Ocean Falls.

Dr. T. J. Agnew, who has been at Courtenay associated with Drs. P. L. Straith and H. A. L. Mooney, is now located at Campbell River, holding the practice of Dr. N. B. Hall, who is now serving with the R.C.A.M.C.

* * * *

Dr. J. A. Murison of Powell River has been away on vacation. Dr. W. B. Clarke has been with Dr. O. O. Lyons during Dr. Murison's absence.

* * * *

Dr. G. E. Darby of Bella Bella is having a vacation.

* * * *

Dr. B. J. Hallowes, who has been at Alexis Creek, is now located at Port Renfrew.

* * * *

Dr. W. Sutherland Groves has left Port Renfrew and is now at Chemainus, holding the practice of Dr. R. N. Dick. * * * *

Dr. R. N. Dick of Chemainus is now serving as Medical Officer with the Royal Canadian Air Force. * * * *

Dr. T. C. Harold, formerly of Ladysmith, is now serving as a Medical Officer with His Majesty's Forces. * * * *

Dr. J. H. Rivers is assisting Dr. Gordon James at Britannia.

* * * *

Dr. R. B. Brummitt, formerly of Smithers, has taken over the practice of Dr. W. M. Toone of Nelson. * * * *

Dr. L. F. Brogden of Penticton called at the office when in Vancouver on vacation.

* * * *

Dr. J. P. Ellis of Lytton was in Vancouver over the week-end.

* * * *

Dr. H. Cantor of Atlin, who has been relieved by Dr. G. W. Meyer of Telegraph Creek, has returned to Vancouver to join the Medical Services with the Forces.

* * * *

We are glad to report that Dr. V. E. Latimer, formerly of Penticton, and latterly of Port Alberni, is making a good recovery following his recent illness, and will spend the winter months in Vancouver.

LIBRARY NOTES

RECENT ACCESSIONS TO LIBRARY

Medical Clinics of North America, Symposium on Specific Methods of Treatment, Boston Number, September, 1941.

Arthritis and Allied Conditions, 2nd ed., 1941, by Bernard I. Comroe.

Abdominal Surgery of Infancy and Childhood, 1941, by William E. Ladd and Robert E. Gross.

Dietetics for the Clinician, 4th ed., 1941, by the late Milton Arlanden Bridges.

William Henry Welch, and The Heroic Age of American Medicine, 1941, by Simon Flexner and James Thomas Flexner.

CURRENT LITERATURE

Some interesting symposia appear in the current issues of several periodicals.

Annals of Surgery presents two subjects—

I. Peptic ulcer: Surgery of its complications and differentiation from cancer.

II. Cancer of the body and of the ducts of the pancreas.

The American Journal of Surgery devotes its entire number to Thoracic Surgery.

The Practitioner publishes Part I of a Special Number on Advances in Treatment, this issue including Medicine, Surgery, Gastro-Enterology, Dietetics, Diseases of Children, Endocrinology, Neurology and Rheumatic Diseases.

The September issue of Medical Clinics of North America (Boston Number) is devoted to Specific Methods of Treatment, and covers a wide range of material.

DOCTOR J. B. THOM

OBIIT OCT. 18, 1941.

The medical profession of British Columbia has lost one of its outstanding figures in the passing of Doctor Thom.

Doctor Thom arrived in Trail in 1908, shortly after graduating in medicine from the University of Manitoba: and in the ensuing years filled a large place as a professional man and a citizen of the community.

In his professional career he served in many capacities in local and provincial circles. His inspiration and leadership made a large contribution to the organization of the Trail-Rossland Clinic, later known as the C. S. Williams Clinic, in honour of one of is early members, and now one of the finest organizations of its kind in Western Canada.

Doctor Thom also served as Coroner and Provincial Medical Officer of Health for the district, and was regarded as the dean of the profession in the area.

He took a prominent part in organized medicine in the Province: serving for several years on the Council of the College of Physicians and Surgeons, of which he was Vice-President. He kept himself well-informed, and made a contribution to the study of economic and social changes as they related themselves to the medical profession. His professional attainments secured him a Fellowship in the American College of Surgeons.

As a citizen, Doctor Thom was the friend and supporter of every good cause. He served one term as Mayor of Trail. He served at one time as President of the Trail Curling Club, and was a member of the Trail Board of Trade. He served, too, as Past Master of Fidelity Lodge A.F. and A.M. The unusual distinction of being made an honorary member of the local branch of the Canadian Legion bore testimony to the esteem in which he was held.

Doctor Thom was versatile in his talents. An able organizer, executive and administrator; he was equally guide, counsellor and friend to untold numbers of people in every walk of life. In discussion, his thought went straight to essentials, and his subtle humour or kindly sarcasm often relieved a tense moment. Doctor Thom had steadfastness of purpose and was capable of carrying through a programme with inflexible determination when necessary.

Doctor Thom was a man of sterling character and deep religious convictions—not with ostentation, but as the dominating force in a personality that was widely respected and beloved. He was a member of the original Session of Knox United Church in Trail and also served on its Trustee Board. He was the friend and confidant of ministers; and, in thinking of his life, one calls to mind the requirements of the ancient Hebrew prophet—"What doth God require of thee but to do justly, love mercy, and walk humbly with thy God?" Doctor Thom measured up to that standard.

It was characteristic of the man that nearly a year ago he left directions for his own funeral service—there was to be no laudatory address: he desired that his life tell its own story. He chose the hymns he wanted—one being the universally beloved "Easter Hymn"—and they were to be sung by a full choir, in joyful tempo, and triumphant strains.

As one so beloved passes from our ken into the Unknown, we, his confreres, bid him adieu, "till the day break, and the shadows flee away."

F. M. A.

DR. D. J. BELL

OBIIT OCT. 7, 1941.

In the passing of Dr. J. Bell of Vancouver, at the age of 79, our profession has lost one of its oldest and most beloved members.

Some few years ago, almost the entire population of Vancouver Heights and vicinity turned out to honour him at a reception held by his patients and friends, to celebrate his long and faithful service to them as their family doctor and friend. Few men evoke such warm affection and esteem.

Dr. Bell graduated in 1888 in Maine, and later went to McGill where he obtained the degree of M.D.C.M. He practised in the Yukon for some time, then moved to Vancouver, where for many years he conducted a very large practice in Vancouver Heights and Grandview.

Kindly and gentle, he was a man of high professional attainment ,and his personal character was above reproach. He belonged to an old school of doctors, who did their best work perhaps through the confidence and sense of security that they were able to inspire, as well as through their ability and medical skill: and his reward was the love and trust of a large host of people.

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Dr. Ethlyn Trapp, Vancouver ..... Cancer
Dr. J. H. MacDermot, Vancouver ..... Editorial Board

CORRESPONDENCE

We publish herewith a letter that speaks for itself, from Capt. W. M. G. Wilson, the Adjutant of No. 13 Field Ambulance, R.C.A.M.C. The BULLETIN, while regretting its failure to note these facts publicly, assures No. 13 Field Ambulance that it was through no slightest lack of interest in the doings of our friends and colleagues. Military movements are conducted, as they should be, silently and without tuck of drum, and so are often missed by the onlooker. We are grateful to Capt. Wilson for his letter, and wish all the best of good luck to him and all in his unit. ED.

No. 13 Light Field Ambulance, R.C.A.M.C., C.A.(A.)
Camp Borden, Ontario,
8th September, 1941.

Dr. J. H. MacDermot,
Editor, Vancouver Medical Assn. Journal,
203 Medical Dental Building,
Vancouver, B. C.

Dear Sir:

I am directed by the Officer Commanding to write to you.

We have noted with some regret that there has been no mention in your journal of the fact that this unit left B. C. early in July. Since this is the first medical unit to leave B. C. in the present war, it is felt that this fact would be of definite interest to the medical profession in the province. All of the officers formerly practiced in B. C.

Below follows our slate of medical officers.

Lieut.-Col. Roy Mustard, M.C., Officer Commanding, Vancouver; Major C. A. Watson, Victoria; Capt. J. S. McCannel, Victoria; Capt. G. L. Stoker, Vancouver; Capt. W. M. G. Wilson, Kamloops; Lieut. G. C. Johnston, Vancouver; Lieut. T. K. MacLean, Vancouver.

This unit is one of three Light Field Ambulances attached to the 5th Canadian (Armoured) Division, at Camp Borden, Ontario. The other Ambulances are from Ontario.

Other B. C. medical officers with the Division are Capt. A. J. Stewart and Capt. H. E. Gislason, with the B. C. Dragoons and the Westminster Regiments, respectively.

Your admirable journal is welcomed each month by our officers, and we hope it will continue to reach us. We also hope you will afford space in a forthcoming issue for some of the above mentioned facts.

Yours very truly,
W. M. G. WILSON, *Capt. and A.-Adj.*,
No. 13 Light Field Ambulance, R.C.A.M.C., C.A.(A.)

Doctor J. H. MacDermot,
Vancouver, B. C.

184 College Street, Toronto 2,
October 28th, 1941.

Dear Doctor MacDermot,

Your esteemed favour of October 21st enclosing a cheque in the sum of $1147.50 for the War Relief Fund of Great Britain is hereby acknowledged. A copy of your

letter together with the cheque is going immediately to our Honorary Treasurer who, I am sure, will be glad to transfer the money to England.

You folks in British Columbia are doing a great job for this fund and I think you are to be highly congratulated on the result of your efforts.

Yours sincerely,

T. C. ROUTLEY, *General Secretary.*

INSTRUMENTS AND SUPPLIES
MEDICAL AND SURGICAL
for
GREAT BRITAIN
COLLECTION OF INSTRUMENTS
as requested by the
CANADIAN MEDICAL ASSOCIATION
is being made by the Office,
203 Medical Dental Building.

RECEPTACLES WILL BE PLACED IN HOSPITALS ALSO.

BULLETIN WAR RELIEF FUND

A cheque for $1147.50 was sent to Dr. T. C. Routley, General Secretary of the Canadian Medical Association, in October, for transfer to the British Medical Association's Relief Fund. A further list of contributors is attached. ED.

Bagnall, A. W., Vancouver	$ 15.00
Ball, Norbert J., Oliver	5.00
Barrett, G. R., Nelson	5.00
Beevor-Potts, C. H., Cowichan Lake	5.00
Bowles, A. W., New Westminster	15.00
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McK., M.D.	5.00
MacPherson, T., Victoria	50.00
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Watson, H. N., Duncan	5.00
C. S. Williams Clinic, Trail	200.00
Wride, G. E., Hedley	10.00

SPECIAL NOTICE

Subscribers to AMERICAN JOURNAL OF SURGERY —Please get in touch with Librarian, 203 Medical Dental Building, MA. 4622.

UPPER ISLAND MEDICAL ASSOCCIATION HOLDS ANNUAL MEETING

The Annual Meeting of the Upper Island Medical Association was held on Wednesday, October 29th.

In the afternoon, the members played golf at Qualicum. At 7:30 that evening, they foregathered at the Island Inn, Parksville, and made ready for their Annual Dinner. Following an excellent Dinner, the business meeting was held, which was presided over by Dr. R. W. Garner, President.

The elections placed the following in office: Dr. T. L. Briggs of Courtenay as President; Dr. E. N. East of Qualicum as Vice-President; Dr. G. K. MacNaughton of Cumberland as Honorary Secretary; Representative to the Board of Directors of the British Columbia Medical Association—Dr. R. W. Garner of Port Alberni; Reporter—Dr. A. H. Meneely of Nanaimo.

The retiring officers, Dr. R. W. Garner, President, and the Honorary Secretary, Dr. G. B. Helem, were complimented and thanked for their splendid programme which had been prepared for the two meetings held during the year.

During the business session, Dr. M. W. Thomas, Executive Secretary of the College of Physicians and Surgeons, addressed the members.

The clinical programme was provided by Drs. Lee Smith and J. R. Neilson of Vancouver. The subject of Dr. Neilson's paper was, "Biliary Tract Disease, Medical and Surgical," and Dr. Lee Smith dealt with "Genito-Urinary Conditions in General Practice." Both speakers used lantern slides and radiological films. The interest shown by the members strongly supported the vote of thanks passed by the meeting.

Those present at the dinner inluded: Surg.-Lieut. Ross of the R.C.N., Lieut.-Col. F. W. Lees, Major S. A. Wallace, Capt. J. A. Ganshorn, Capt. J. E. Walker, Lieut. K. J. Haig, Capt. H. N. C. Begg, Capt. Ira S. White, Doctors R. W. Garner, G. B. Helem, W. C. Pitts, A. P. Miller, of Port Alberni; C. C. Browne, A. H. Meneely, W. F. Drysdale, S. L. Williams, E. D. Emery of Nanaimo; W. R. S. Groves of Chemainus; E. N. East of Qualicum, T. L. Briggs of Courtenay, E. R. Hicks of Cumberland, T. J. Agnew of Campbell River, H. N. Watson and C. H. Beevor-Potts of Duncan, J. R. Neilson, Lee Smith and M. W. Thomas of Vancouver.

COMMITTEE ON THE STUDY OF CANCER TO BIOPSY OR NOT TO BIOPSY

The physician is often faced by the problem of a lesion that is seemingly benign, but possibly might be an early malignancy. Is the lesion to be observed carefully over a period of time, during which time metastases may occur, or is a biopsy to be taken early—thinking of the slogan, "Biopsy early and save a life"?

If he decides to biopsy, what is the best method of go about the procedure? Oftentimes the patient cannot afford any extensive procedure necessitating loss of time or even moderate financial outlay unless the procedure is necessary. Also the doctor cannot afford to gain the reputation of operating indiscriminately on suspicion. If the biopsy could be made a simple office procedure that could be carried out frequently without great physical or economic distress to the patient, then more biopsies would be taken and more lives saved.

The biopsy of a lesion on the surface of the body can readily be done in the office in many cases. Some novocaine, a sharp scalpel and perhaps a stitch, plus a drachm or so of 5% formalin from the nearest pharmacy is all the equipment needed. A wedge-shaped piece of firm tissue, the size of a grain of wheat or larger, taken at the edge of the lesion to include normal and abnormal tissue for comparative purposes is the ideal small specimen. Infected or degenerating areas should be avoided, or, if unavoidable, larger portions should be removed. The specimen should immediately be placed in the

formalin and accompanied by a notation of the patient's age, sex, site of biopsy and a brief history, sent to the nearest pathologist.

This type of biopsy usually does not discommode the patient greatly as the wound is small and painless and will heal readily with little care. The taking of the biopsy in this manner is recognized as not tending to spread the disease unduly in epidermoid malignancies.

There are many instruments devised for biopsy work. Of these the punch—a small inexpensive instrument for taking a biopsy of skin lesions—is about the best and should be standard equipment in all doctors' offices. This instrument is pencil shaped, one end having a circular hollow knife. The instrument is placed over the selected, anæsthetized site and twirled in the fingers with slight pressure. A core is cut out quickly and this is separated off at the base easily with a scalpel or scissors and little damage is done.

Biopsies of lesions situated in the deeper structures of the body need special consideration. These problems will be dealt with in discussing malignancies in various parts of the body.

COMMITTEE ON MATERNAL WELFARE
POST-NATAL CARE

(Part II)

Active movement in bed with muscles stretching and tensing is encouraged early. When breasts permit, face-down lying is advocated. From sixth to eighth day, patient begins abdominal muscle strengthening. Clasping the hands behind neck, the head, *and shoulders,* are raised to look down at the toes and this position is held for increasing periods of time. As strength improves, this is supplemented with leg-raising exercises such as "scissors" and "bicycle." The hands are placed palms down under the buttocks for support, the heels are held six inches off the floor during all exercises and counts up to 20 and 30 of each are done. These are probably the most important exercises a woman can do, for they not only restore the tone of abdominal musculature for future labours (not to mention cosmetic effect) but in the low back pain of forward lumbo-sacral strain (sway back) which occurs in a very high percentage of post-partum women, they shorten the anterior abdominal wall and take the strain off the anterior aspect of the lumbo-sacral joint.

Most patients nowadays insist on getting up tenth day and home by twelfth. This is all right if they stay in bed most of the day during the following week at home, while involution becomes more complete. During this period, they should increase their exercises and may supplement them with knee-chest position (separating vulva to allow air to enter the vagina), and the monkey walk.

Another exercise should now be started, which is hardly less important than the abdominal ones. Its purpose is to restore pelvic floor muscle tone. It consists of a tightening of the sphincter muscles of rectum, vagina and bladder, and a "drawing up" or contraction of the levator ani muscles. This is done in one effort, is maintained as long as possible and is followed by relaxation, then repetition. Patients should be encouraged to do this several times a day. Anyone who has watched the marked strengthening effect of this exercise on the whole pelvic muscle structure will advocate it.

The day of the patient's discharge from hospital, pelvic examination should be done. The condition of the episiotomy and vaginal walls, the state of parametria and position of uterus may be noted, and it also gives one a chance to stress the treatments or exercises most needed.

At about six weeks, patient should return to the doctor's office, for a complete physical examination, and the points which should be particularly noted are: General

condition, weight, blood count, hæmoglobin, condition of teeth, breasts and abdominal muscles. The perineum, vagina and cervix are inspected and bi-manual palpation of uterus determines its position, size, shape and mobility, as well as the state of the parametria and adnexa. If retroversion is not congenital, with short anterior vaginal wall, a pessary may be introduced for two or three months to hold fundus forward,—lying on face, knee-chest postures, and pelvic floor exercises to be stressed the while.

Cervix erosions may be treated with strong silver nitrate solutions but preferably with cautery. All exercises should again be encouraged and patient should be brought back again in one month, if any treatment has been given, for final check-up.

The breasts should not be neglected during the post-natal period. Heavy breasts must be supported, and all patients should be given exercises to strengthen the fascial attachments of the breasts to the underlying pectoral muscles. This is particularly important during weaning, and will do much to restore the breasts to former tone and contour.

College of Physicians and Surgeons

President.....Dr. Wallace Wilson, Vancouver
Vice-President.....Dr. W. A. Clarke, New Westminster
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Registrar.....Dr. A. J. McLachlan, Vancouver
Executive Secretary.....Dr. M. W. Thomas, Vancouver

WHAT THE SURGEON OUGHT TO BE ACCORDING TO GUY DE CHAULIAC

The conditions necessary for the surgeon are four: first, he should be learned; second, he should be expert; third, he must be ingenious, and fourth, he should be able to adapt himself. It is required for the first that the surgeon should know not only the principles of surgery, but also those of medicine in theory and practice; for the second, that he should have seen others operate; for the third, that he should be ingenious, of good judgment and memory to recognize conditions; and for the fourth, that he be adaptable and able to accommodate himself to circumstances. Let the surgeon be bold in all sure things, and fearful in dangerous things; let him avoid all faulty treatments and practices. He ought to be gracious to the sick, considerate to his associates, cautious in his prognostications. Let him be modest, dignified, gentle, pitiful ,and merciful; not covetous nor an extortionist of money; but rather let his reward be according to his work, to the means of the patient, to the quality of the issue, and to his own dignity.

(From the Introduction to the General Chapter, *Ars Chirurgica.*)

The above is copied from a translation of the *Ars Chirurgica* published in Venice in 1546 and translated by William A. Brennan of Chicago in 1923. It was originally written by Chauliac and completed in 1363. An English edition was published in 1541.

(The last sentence as regards fees is just as appropriate at the present time.)

IMPORTANT

The Registrar has received a communication from the Commissioner, British Columbia Provincial Police, informing him that when making investigations of thefts from doctors' cars it is found in a large percentage of cases narcotics are included.

It is suggested, since this is the main reason for such theft and rummaging in doctors' cars, that narcotics and hypodermic syringes be carried on the person of the doctor rather than in his professional bag. If this practice were followed, it would eventually become known that narcotics cannot be found in doctors' cars and such plunderings would be discouraged.

NARCOTICS ACT
WARNING TO ALL PHYSICIANS!

It is necessary to lay special emphasis on certain points in connection with the prescribing of narcotics. These are constantly being overlooked by doctors, and are absolutely vital.

1. **All narcotic prescriptions *must* be written in *ink*.**
2. **They *must* be dated.**
3. **They *must* be signed *in full* by the doctor. *Initials alone must not be used*.**

Medical men must recognize the fact that these rules are mandatory, and there is no exception. Druggists who fill a prescription improperly written are breaking the law, and render themselves liable to fine or other penalty: and we ourselves are similarly liable to penalties for breach of this Act.

***Do not forget*. A properly written, dated and signed prescription must be in the hands of the druggist before he can fill it. *There is no exception to this rule*.**

(Signed) A. J. MACLACHLAN, *Registrar*,
B. C. College of Physicians and Surgeons.

D. E. H. Cleveland, M.D.,
THE BULLETIN OF THE VANCOUVER MEDICAL ASSOCIATION,
Vancouver, B. C.

Dear Doctor:

The principal object of the American Urological Association is "to encourage the study, improve the practice, elevate the standards and advance the cause of Urology." The simplest way to impress upon neophytes the value of true scientific work is by means of a material award. Hence, we would like to have each year an outstanding medical paper that would warrant a $500.00 check, but if such is not forthcoming we can make several smaller prizes. We are not interested in stereotyped theses for an advanced degree unless they represent original work of potential value. The competition is open to all properly trained urologists, and for that reason we would like to have this chance of a young man obtaining some money at a period when it is badly needed, widely publicized, so that all may have an equal opportunity.

Please publish in your magazine the following notice:

"*Urology Award:*—The American Urological Association offers an annual award 'not to exceed $500.00' for an essay (or essays) on the result of some specific clinical or laboratory research in Urology. The amount of the prize is based on the merits of the work presented, and if the Committee on Scientific Research deem none of the offerings worthy, no award will be made. Competitors shall be limited to residents in urology in recognized hospitals and to urologists who have been in such specific practice for not more than five years.

"Essays shall be in the hands of the Secretary, Dr. Clyde L. Deming, 789 Howard Avenue, New Haven, Conn., on or before April 1, 1941."

Yours very truly,

MILEY B. WESSON,
Chairman, Committee on Scientific Research.

MEDICAL ADVISORY COMMITTEE

Report presented to Annual Meeting by Dr. Murray Blair, Chairman.

It is probably known to most medical men that at the outbreak of war the Canadian Medical Association offered its services to the Department of National Defence. Its object was two-fold:

First—To aid and advise in supplying competent medical care for the armed forces.

Second—To see that the civilian population did not seriously suffer because of medical enlistments.

Provincial Advisory Committees were set up in the various Divisions of the Canadian Medical Association, and the Advisory Committee for this Division has been, I believe, of some use to the District Medical Officer of this Medical Division No. 11. Certainly we have had a harmonious relationship with that office at all times.

Your Committee has met regularly during the past year, has been in constant touch with the Central Advisory Committee, and has a contact member in Victoria who has kept us in touch with the D.M.O.

Your Committee has entertained the D.M.O. as its guest some three times. It has also entertained the Chief Surgeon Commander of the Navy, and the Principal Medical Officer of the Air Force in this area. At each of these meetings we have placed the facilities of our Committee before these men and have made plain our desire to be fo assistance to all branches of the Armed Forces.

We have made it clear that we are an advisory body, not an enlistment committee. It is not our function or aim to urge medical men to join the army. It is our duty, however, I take it, to advise medical men of the need—and there is a need, a very grave need.

At a meeting of the Canadian Medical Association central committee in Winnipeg in June of this year a statement was received, signed by the medical heads of the three Armed Services. I quote in part:

"1. The requirements in medical officers for the balance of the current year will be approximately 350. These officers are divided into two classes:

(a) For service in Canada—Approximately 140.
(b) For service overseas—Approximately 210.

The officers for service in Canada may be in categories "A", "B" or "C" and up to 55 years of age, or, in special circumstances, over. The officers required for service overseas must be in category "A" and should be preferably under 40 years of age.

"2. It is becoming increasingly difficult to obtain medical officers and it is anticipated that during the next year it will be still more difficult. There is approximately 12% of all the doctors registered in Canada now in the services."

In view of the latter figure it might be of interest to review the enlistment figures for our own province. Much has been said and written about general enlistments—what about voluntary medical enlistments in this province? There are in Canada, in round figures, 12,000 doctors. About 12%, or about 1400, have enlisted and are engaged, full time, in one of the armed services. In this province there are some 750 on the active colls of the College—of these there are 130 enlistments among medical men in this province, to date, or some 17% of our total enrollment. It is on the whole, perhaps, a fair record, neither good nor bad.

Your committee will continue to function during the coming year. It will, I hope, continue to serve a purpose. Again we emphasize the need—350 medical enlistments are needed in the armed forces in the next few months. Medical men may contact either the office of the D.M.O. at Victoria or our Executive Secretary, Dr. Thomas, at Vancouver, for information.

SAFETY IN THE OPERATION FOR TOXIC THYROID

By Dr. W. D. Keith.

(Delivered before the Vancouver Medical Association October 7th, 1941)

Sub-total thyroidectomy properly performed is, in the opinion of the majority of the medical profession, the best therapeutic measure yet known to overcome hyperthyroidism.

However, in considering this operation it is important as physicians and surgeons that we have as thorough a knowledge as possible of the histo-pathological changes which take place in other organs than the thyroid gland in this disease.

A generation ago Sir James Barry, the leading thyroid surgeon of his day in London, considered that the thymus gland was really a lymph gland draining the thyroid gland. Berry stressed the fact that all cases coming to post-mortem after an operation for exophthalmic goitre had a much enlarged thymus gland.

Whartin of Ann Harbour believed from his study that there existed a thymico-lymphatic type or condition which forms the soil from which, under certain conditions, toxic goitre springs, and that this constitution is congenital and can be recognized clinically.

Quite a number of studies of the changes in the thymus gland in hyperthyroidism have appeared from time to time. Margolis in the Mayo Clinic 1930 volume reports a study of the thymus gland in toxic goitre in 85 cases which came to post-mortem after operation in that clinic. Fifty-five of the cases were exophthalmic goitre, forty-seven of which showed varying degrees of hyperplasia of the thymus gland. Thirty cases were associated with toxic adenoma and fourteen of these showed thymic hyperplasia.

In a general sort of way the more acute and recent the disease the more active and widespread the hyperplasia of the thymus.

Of the eight cases of exophthalmic goitre which failed to show any hyperplasia of the thymus, four had a thymus gland much larger than normal; one of these weighed 62 grammes, the greatest weight of any of the glands in this series. This greatly enlarged gland contained practically no glandular tissue, merely areolar, fatty and fibrous tissues. Thus it is important to bear in mind that because a thymus gland is enlarged is no indication that it is hyperplastic.

The hyperplasia of the thymus in cases of toxic adenoma of the thyroid was not so extensive or complete as that found to be associated with exophthalmic goitre. This finding seemed to be consistent with the longer, slower toxic history of hyperthyroidism in toxic adenomatous goitre.

Thus from the above study and from similar findings in other reports one must conclude that there is a very close relationship between the thyroid and thymus glands.

The other organ besides the thymus gland which shows histo-pathological changes in this disease is the liver.

In an article in the *Annals of Internal Medicine*, vol. 7, 1933-4, D. C. Beaver and J. deJ. Pemberton report a study of 107 cases of exophthalmic goitre which came to post-mortem during a period of ten years. The changes found in the liver were divided into: *Acute*—fatty; necrotic—central or focal; *Chronic*—simple atrophy; toxic cirrhosis; subacute toxic atrophy.

The authors state the lesions in the liver are due to thyroid intoxication, as they are intimately related in their severity to the intensity and duration of the disease.

In all cases in which there was a crisis or near crisis, acute hepatic lesions were found. Very often the liver exhibited both acute degenerative and chronic atrophic changes side by side or at least in the same liver.

In November, 1933, *Annals of Internal Medicine*, p. 543, C. V. Weller reports a study of hepatic pathology in exophthalmic goitre. Changes in the liver from a slight

degree of chronic hepatitis to a widespread necrotizing and degenerative process—glissons islands enlarged; lymphocytic infiltration; patchy interlobar fibrosis—were found, the main lesion being patchy chronic parenchymatous interlobular fibrosis.

In this study of forty-four cases, the liver was normal in only six, hepatic changes were moderate in sixteen and marked in twenty-two.

In view of these observations the condition of liver function should be a most important consideration in the success of the operation for hyperthyroidism.

Lahey even suggests that liver failure is the main cause of thyroid crisis which is one of the most serious complications following thyroidectomy for hyperthyroidism.

A liver function test which is considered fairly satisfactory was described by Bartels in 1938. It is known as the hippuric acid test. Six gm. of benzoic acid are given and in four hours three gm. of hippuric acid should be excreted by the kidneys. Bartels reported results in 148 cases of hyperthyroidism. Only eight cases were normal by this test on admission.

The absence of weight loss or the administration of iodine for some time prior to admission was associated with normal liver function.

Another organ of the body which is directly affected by hyperthyroidism is the heart. Tachycardia, usually with an increased pulse pressure, is one of the most constant symptoms of hyperthyroidism. The cause of the increased heart rate is probably the result of the direct stimulation of the heart muscle by a very much increased output of normal or altered thyroid secretion.

If the hyperthyroidism is not diagnosed and continues for months and years, besides tachycardia, a slight enlargement of the heart not infrequently occurs, cardiac arrhythmias may develop, particularly auricular fibrillation, and finally congestive heart failure may result.

Pathologists have found no specific pathological changes in the heart tissues due to this disease. Many pathologists have described segmentation and fragmentation of muscle fibres, increase of fibrous tissues, fatty degeneration and lymphocytic infiltration as being found in the heart in hyperthyroidism, but these changes have also been described as occurring in other diseases.

It seems to be generally agreed that great enlargement of the heart rarely or never occurs as the result of uncomplicated hyperthyroidism. Parkinson and Cookson found by orthodiagrams and teleroentgenograms that cardiac enlargement—usually slight or moderate—occurred in 45% of uncomplicated hyperthyroidism.

Kepler and Barnes state: "In 89 cases of fatal hyperthyroidism without evidence of hypertension or complicating heart disease, the weight of the heart in 49% exceeded maximum standard values calculated on the basis of the patients prior to illness."

Physiological research has shown that the heart muscle in hyperthyroidism contains very little glycogen, nad this may have a weakening effect on the heart muscle itself. Ingenious experiments by various investigators have shown that the tachycardia of hyperthyroid animals persisted after the heart had been isolated from the peripheral vascular tree and from all neural pathways.

Cecile, Markowitz and Yates further showed that thyroxine causes tachycardia to occur in fragments of the heart muscle removed from two-day-old chick embryos, before any nerve cells within the heart or neural pathways have been formed.

Now, with this mental picture of the pathological changes in the thymus gland and the liver, and the physiological and metabolic changes which occur in the heart, we are in a better position to evaluate clinical conditions properly as they present themselves in hyperthyroidism.

Iodine:

In 1922 Plummer found that iodine given in large doses daily lowered the B.M.R. and the pulse rate within a period of from 7 to 10 days after beginning its administration, in cases suffering from hyperthyroidism. It was then widely accepted that in

this way sub-total thyroidectomy could in almost all cases be done as a one-stage operation, on or about the tenth day after the start of the administration of iodine. It was felt also that a great deal of the danger of the operation had been overcome.

Let us now consider the mortality rates reported from various surgical clinics where diseases of the thyroid receive special consideration.

During the last forty years the mortality rate for thyroidectomy in toxic goitre has gradually declined, as the following reports will show:

1894-1907—Over 10% in 20 hospital reports.
1908-1917—Over 5% in 7 out of 28 hospital reports.
1907-1920—2-5% Mayo Clinic.
1921—3.39% Mayo Clinic.

After the introduction of iodine by Plummer in 1922:

1922—Mayo Clinic, 1.74%.
1924—Mayo Clinic, .84%.
1925—Mayo Clinic, 1.1%.
1926—Mayo Clinic, .83%.
1929—Crile Clinic, .6%.
1925-9—Lahey Clinic, .72%.
1902—Kocher Clinic, 6.5%.
1915—Kocher Clinic, 1%.
1939—Richter, H. M.—900 cases with 3 deaths—0.33%.
1939—Young reports from two general hospitals in Duluth—St. Mary's and St. Luke's—2569 thyroidectomies for Hyperthyroidism with 54 deaths—a mortality rate of 2.1%.

In spite of iodine Von Eiselberg reported 6% mortality in 1930. And Dunhill of London 2.7% in 1930. Joll states that the mortality for sub-total thyroidectomy for toxic goitre should not be more than 1%. Bevan states that he believes that the average mortality in the U.S.A. is between 3 and 5%, but he recognizes that to a large extent two or more stage operations have been done away with and cases which were formerly considered inoperable are now in the operable class.

From the above statistics one realizes that there were measures of great value in the safe conduct of thyroidectomies practised before the introduction of iodine in the preparation for this operation.

Let us now pursue the problems which here and there occur in the preparation of patients with toxic goitre for thyroidectomy by the administration of iodine. Certain cases of hyperthyroidism are refractory to iodine—by that is meant that even with the administration of iodine in adequate dosage the symptoms become more pronounced and the metabolism rises—a general increase in the tempo of the disease results. It is uncertain whether the refractoriness of the disease is due to iodine or to the general progress of the disease.

Thompson states that the administration of even 100 min. of Lugols solution is of no more value in the refractory period than the use of smaller doses.

Many hold to this belief now, though I understand that at the Mayo Clinic large doses of iodine are still found of help in some of these cases.

However, it has been shown by a number of observers that if the iodine be discontinued for 4-6 weeks and then given, the metabolism and pulse rate respond satisfactorily.

Thyroidectomy is not an emergency operation and therefore should be made to fit in with a satisfactory condition of the patient.

The 10 days or so of pre-operative administration of iodine has practically no effect on the thymus gland or the liver.

Lahey has remarked that "it is distinctly possible to have such an apparent improvement following the use of Lugol's solution that one is tempted to do a complete operation only to have the patient die in extreme hyperthyroidism."

Lahey and Clute reported cases which died in crisis before operation could be taken, in spite of active measures, including iodine in large doses.

Therefore we must realize that there is more to the treatment of toxic goitre than the administration of iodine and the performance of sub-total thyrodiectomy.

In regard to the dosage of iodine given preoperatively, it has been shown by Thompson *et al* that large doses must be given from the beginning, that doses smaller than 6 mg. a day are ineffective.

Probably no article in recent years, on account of its clarifying candour, has done more to reduce the mortality in thyroidectomy in the average general hospital than that by W. O. Thompson *et al*—(*Arch. Intl. Medicine*, Dec. 1938, p. 217), and I cannot do better than quote freely from this article.

Cook County Hospital in Chicago has 3200 beds and its patients are the poorest in the city. Disease is seen in its most advanced stage as a rule and in the case of toxic goitre a large number of severe cases of long standing in markedly undernourished individuals had to be treated.

During 1931 there were 16 deaths in 159 thyroidectomies for toxic goitre—*i.e.* 1% mortality.

The factors responsible were inadequate pre- and post-operative care and operators without special training in this procedure.

The usual ward diet for seven to ten days, with iodine, regardless of other conditions, was given. The B.M.R. tests were inadequately carried out.

In the latter part of 1932 the authors took charge of half of the toxic thyroid cases in the hospital. Each case was treated as an individual problem. Surgery was withheld till the condition of the patient justified operation, no matter how long this took. The surgeon who operated was specially trained in this field.

It is our contention that the battle is practically won or lost before the operation is begun, and that in most cases a post-operative crisis means inadequate pre-operative preparation.

During 1932-7 there were 54 deaths following 572 thyroidectomies—a mortality of 9.4%, and during the same time 9 deaths followed 317 thyroidectomies for toxic goitre in patients under their care—a mortality of 2.8%.

In 1935-7 there were 19 deaths in 249 operations on patients not under their care—a mortality of 7.6%. During the same time in cases under their care there were 188 thyroidectomies with 3 deaths—mortality 1.6%.

Of the nine deaths which occurred in this series eight had exophthalmic goitre and one toxic adenoma.

The causes of death were: Thyroid crisis, 2; pneumonia, 3; heart disease, 1; sudden respiratory failure, 3.

In two of the cases of sudden respiratory failure there was bi-lateral vocal cord paralysis. The other death from this cause was due to a hæmatoma pressing on a collapsible trachea.

These three deaths were purely surgical complications and could have been prevented by early tracheotomy in two of the cases and the third by early recognition of the seriousness and nature of the condition by a nurse experienced in the possible serious complications that may follow thyroidectomy.

A more careful search for upper respiratory infection prior to the operation might have prevented the two deaths from pneumonia.

I might add that Thompson considers it most inadvisable to do a thyroidectomy till at least two weeks have elapsed since the occurrence of an upper respiratory infection, otherwise one is courting a possible pneumonia.

The two cases dying from thyroid crisis would probably have been saved by more careful preparation.

The rather sudden death of a man of sixty years of age ten days after operation was probably unavoidable.

In St. Paul's Hospital, from 1935-9 inclusive, 263 operations were performed on the thyroid gland by 35 different surgeons; 216 of these were for hyperthyroidism, all

having microscopical evidence of an over-active thyroid. Some, of course, were of a very severe grade; others presented moderate or even slight degrees of hyperplasia.

Of the 216 cases with hyperthyroidism, 207 had the usually performed sub-total thyroidectomy and 9 had a lobectomy or partial resection of the gland.

I might add that of the remaining 47 of the 263 cases operated on for thyroid disease during the above mentioned period, 17 had a partial removal of the gland. Three cases proved to be carcinoma of the gland, one tuberculosis of the thyroid, and one the so-called woody thyroid. The microscopic study of the 42 remaining cases showed them to be either colloid goitres or simple adenomatous thyroids or goitres of an adenomatous type undergoing degenerative changes—cystic, calcareous, or fibrous.

Of the 216 thyroid operations for toxic goitre there were seven deaths—a mortality rate of 3.2%.

It is well for us to consider the deaths in this series, seven in all:

(1) Female, aet 44, was admitted one day and operated on the following day and died a few hours after the operation.

This patient had a severe grade of hyperthyroidism and, as post-mortem revealed, a myocarditis, chronic pleuritis, and an enlarged thymus gland.

(2) Female, aet 59, was in the hospital 13 days and then operated on. The patient died the day following a sub-total thyroidectomy.

The post-mortem showed general arterio-sclerosis and myocardial degeneration. According to the records of this case cardiac enlargement was noted in the history and an electrocardiogram was done four days before operation: this report read myocardial changes probably coronary sclerosis, auricular extrasystoles—urinary report, albumin plus 2.

(3) Male, aet 37. Immediately after the operation there seemed to be a great deal of thick mucus in the larynx. The pulse was very rapid though Lugol's solution was given in large doses per rectum, death occurred about twenty-four hours after the operation. A trachetoomy was performed a few hours before death without any apparent improvement.

Post-mortem—Lungs airless, thymus gland 72 gms., spleen three times normal size. Considerable thick mucus in the larynx and trachea—one small branch of the left recurrent laryngeal nerve was included in a suture. Mediastinal emphysema and collapse of the lungs.

(4) Female, aet 46. Died two days after the operation. This was a death which followed a complication in the actual technique of the procedure. In the removal of a substernal projection of the gland, the thyroidea ima artery was seized close to the aorta and as the artery was pulled on in some way by a movement of the forceps before being tied, it was torn off at its point of origin from the aorta and could not be secured again. The wound had to be packed, mediastinitis ensued and death occurred in a day or two.

(5) Female, aet 48. Died within a few hours of the operation.

The patient was admitted to the hospital with a fractured right femur. The pulse was 136 on admission and continued around 120. A diagnosis of hyperthyroidism was made and eight days after admission a thyroidectomy was performed. No post-mortem was obtained.

(6) Female, aet 43. Died six days after the operation. There was a certain amount of oozing on her return to the ward. Six days before the operation the N.P.N. was 47.

Laboratory report—occasional areas of hyperplasia; extensive cystic degeneration.

(7) Female, aet 56. Died a few days after the operation. Death was considered due to sudden cardiac failure. This patient had quite a severe grade of hyperthyroidism over a period of years.

The operation was a difficult one as there was a large substernal portion of the gland.

Considering the seven deaths in retrospect as if they had occurred in one's own practice, one would feel that some of the deaths might have been avoided.

Thee cases where myocardial degeneration is known to be present should not be operated on simply because the patient elects to take the chance.

In my opinion careful meticulous physical examination should be made by a physician as well as the surgeon so that a combined opinion should decide for or against the advisability of such a severe undertaking.

The method not infrequently followed in Vancouver is for a patient suffering from thyroid disease to be referred by an out-of-town or local physician to a surgeon who has an excellent reputation for his skill in thyroid surgery. Or the patient may go to a surgeon whose reputation is known to him. Or thefamily physician who makes the diagnosis in the first place may feel himself competent to undertake the operation himself. The operator then takes full charge and when he things the patient is ready, having been prepared usually in the hospital, the operation is performed. The reports from the metabolic and where thought necessary from the electrocardiographic departments, are considered as sufficient guides. Very seldom is the opinion of a physician as to the advisability of the operation been sought.

In recent years, owing to a wider knowledge amongst the medical profession of the signs and symptoms of hyperthyroidism and the freer use of the basal metabolism apparatus, many more patients of over 60 years are recognized as suffering from this disease.

Angina pectoris, hypertensive heart disease, arterio-sclerosis, chronic nephritic, prostatic hypertrophy and diabetes may be complicating factors. Kepler and Barnes, in a study of a series of cases of fatal heart failure associated with hyperthyroidism, found that one-third of the cases had no other disease than hyperthyroidism, one-third had mild hypertension or minimal independent cardiac disease, and another third had marked hypertension or severe valvular lesion or coronary disease.

Therefore in two-thirds of the cases of congestive heart failure associated with hyperthyroidism the patients will be greatly improved by the removal of the burden of the diseased gland.

In the preparation of the thyrocardiac for possible operation Pemberton states that digitalis is very seldom indicated and should be given with caution to elderly patients. Rest, partial or complete, high caloric diet and Lugol's solution for two or three weeks are usually sufficient to prepare these patients for operation. Where congestive failure is present a moderately restricted intake of fluids, with salt restriction and the use of mercurial diuretics where necessary, will often result satisfactorily enough to permit operation. Where auricular flutter is present quinidine, given cautiously at first in order to avoid an idiosyncrasy, should be tried.

Barnes sums up his ideas on the operability for thyroidectomy as follows: "It seems to me that the operability of such patients can be determined on a rather simple basis, namely, that any patient with cardiac failure and hyperthyroidism may become an acceptable risk for thyroid surgery, provided compensation can be restored by rest and therapeutic measures, and provided further that this compensation can be maintained for at least a few days with the patient on a moderate ambulatory programme."

St. Paul's Hospital, around which this paper particularly is built, possesses an operating department equipped with every essential necessity for the successful conduct of thyroid operations. The anæsthetic department is under skilled and specially trained physicians, the hospital laboratory department has supervision of all solutions for intravenous therapy and is equipped with an up-to-date metabolism apparatus and also an electracardiographic apparatus.

The only other task which the hospital might include in its responsibilities is to see that a nurse conversant with the complications and emergencies liable to follow a thyroidectomy is in charge of the patient for the first 24 hours subsequent to operation.

This is important, since there are certain immediate complications, *e.g.*, hæmorrhage, difficulty in breathing from damaged recurrent laryngeal nerves or pressure from a

blood clot on a soft trachea or tracheitis with thick mucus in addition to partial cord paralysis—these conditions as well as the early symptoms of thyroid crisis should command instant recognition and treatment if lives are to be saved.

In conclusion, there are certain general guiding points which should be carefully considered in undertaking the operation of sub-total thyroidectomy for toxic goitre:

(1) Thyroidectomy is never an emergency operation. Do not be in a hurry to operate. The preparation for this operation should have no set time. It may take a week or several weeks. Iodine has not altogether done away with two or more stage operations—a procedure which may be life-saving here and there.

(2) The signs and symptoms necessary to permit operation are: A definitely lowered metabolism; a pulse rate not too rapid; a gain in weight; a lessening of the nervous symptoms; an absence of upper respiratory infection. Follow Thompson's advice to wait two weeks after the subsidence of an upper-respiratory infection before operating.

(3) Each case should be meticulously examined by an internist conversant with the prolbems of thyroid disease before operation is decided upon. Close co-operation should exist between the surgeon and internist during the pre- and post-operative care of the patient.

(4) Nurses specially trained in the post-operative complications which may arise after a thyroid operation should be in charge for the first 24 hours after the operation.

Vancouver General Hospital

CHOLECYSTOGRAPHY
PRACTICAL AND THEORETICAL CONSIDERATIONS

By G. E. Trueman, M.D.,

In this paper the approach of the radiologist to the problem of biliary disease will be outlined, and an attempt will be made to indicate what interpretation may be put on the radiological findings, both as regards diagnosis and choice of treatment.

The principle of visualization of the gall-bladder is simple. The dye is given orally, is absorbed in the small bowel, and excreted exclusively by the liver. The dye passes into the gall-bladder where it is concentrated in the same manner as bile until it is of sufficient density to cast a shadow on the X-ray film. Following a fatty meal, the gall-bladder empties, and bile and dye pass through the duct system into the duodenum. This process can be studied radiologically.

The commonly recognized contra-indications to the use of dye are advanced cardiac disease, asthma, cachexia, acute infections of the liver and gall-bladder, and hepatic insufficiency.

The question is often asked, "Is jaundice a contra-indication to cholecystography?" The answer would seem to be that jaundice itself is not a contra-indication unless it be accompanied by hepatic insufficiency of a degree which can be detected by the more reliable liver-function tests. In the presence of jaundice, cholecystography may be of value in differentiating between obstructive and hepatogenous jaundice. In three series of cases[1], tested in the presence of jaundice, the total number of cases of catarrhal jaundice or hepatitis was thirty-two; of obstructive jaundice, fifteen. Of the thirty-two "medical" cases, the gall-bladder was visualized in twenty-five. In the fifteen obstructive cases, the gall-bladder was visualized only once, and in this case revealed a gall-bladder containing a great number of non-opaque stones. Later work[2] has shown that in "medical" jaundice where the gall-bladder is visualized, it emptied normally

under the stimulus of the fatty meal, but in small number of cases of obstructive jaundice, the gall-bladder failed to empty after the fatty meal and the shadow disappeared gradually, presumably by absorption of the dye through the gall-bladder wall. Successful visualization, then, followed by normal emptying, points to hepatitis or catarrhal jaundice as the cause of the jaundice. Successful filling with failure to empty suggests obstructive jaundice. However, failure of the gall-bladder to visualize in the presence of jaundice cannot be used for diagnosis at all because one does not know whether the dye reached the gall-bladder.

In addition to the above considerations, the problem involves the differentiation of stone, cholecystitis, dyskinesia, and, less commonly, other diseases from each other and from a normal gall-bladder. Radiological opinion is built on four types of evidence, namely, stone, concentration of the dye, rate of emptying, and changes in the size and shape of the gall-bladder and changes in the size of the ducts.

A stone may be diagnosed directly or indirectly. The demonstration of a stone by direct means is dependent upon the presence in the stone of radiopaque substances, usually calcium, and the dye is of value in these cases only insofar as it enables one to distinguish between intra-cholecystic and extra-cholecystic opacities. The common extra-cholecystic opacities are calcified glands and renal calculi.

Gall-stones may be demonstrated indirectly only by the use of the dye method and only in cases in which the dye is concentrated to a degree sufficient to throw a shadow on the X-ray film. In such cases, the evidence of the stone is to be found in a negative shadow produced by a radiotranslucent stone occupying a space which would otherwise be occupied by the radiopaque dye. TABLE I[3] exhibits two series of cases in which the presence of stone was verified at operation, and in which a previous gall-bladder visualization had been attempted. The table shows with accuracy which may be expected in a particular type of case, namely, that type of case which the surgeon deems it advisable to treat surgically. These percentages will be influenced by the care and skill of the radiologist and by the surgeon's selection of cases.

The absence of a shadow outlining the gall-bladder is presumed to indicate loss of the gall-bladder's physiological function of concentration and may be considered presumptive evidence of cholecystitis. There are several alternative explanations which must be ruled out before the diagnosis of chronic cholecystitis can be made with certainty. The patient may have failed to take the dye, or having taken it may vomit, or be purged of it, or it may not be absorbed. If his liver function is depressed he may excrete it not through the liver but through the kidneys. The duct system may be blocked so that the dye does not reach the gall-bladder or the gall-bladder may be obliterated by non-inflammatory disease. The dye may pass into the bowel through an inconstant sphincter of Oddi or cholecysto-colic fistula. TABLE II presents a comparison of the X-ray diagnosis and the clinical diagnosis in twenty-seven cases. Bearing in mind the pitfalls numerated above, the cases in which a presumptive diagnosis of chronic cholecystitis was made incorrectly were investigated to determine the source of error.

Normal concentration is presumptive evidence of a normal gall-bladder. TABLE III is an analysis of thirty-six cases in which cholecystitis was eliminated radiologically. The subsequent clinical course indicated that the cholecystographic conclusion was correst in twenty-five cases and clinically incorrect in eleven cases. The basis of the inaccuracy of the test was the persistence of biliary dyspepsia which, as we shall see, in many cases is not relieved by cholecystectomy, so that in these eleven cases there is included a number in which the negative diagnosis may have been correct.

The diagnosis of stone is one matter; the expression of an opinion regarding the probability of existing disease apart from stone is another. The radiological diagnosis of chronic cholecystitis is frequently reported as being inaccurate in upwards of 95% of cases. This accuracy is of value in distinguishing between those cases which must be considered normal and those which have chronic cholecystitis. Beyond this, it is of

little value. It does not indicate the severity of the disease, whether treatment should be medical or surgical, or what results may be expected from either form of treatment. Hodges and Lampe[3] report a series of cases as outlined in TABLE IV, where the radiological and the pathological finding was not the all-inclusive term "chronic cholecystitis" but "major inflammatory disease readily recognized in the gross or microscopic findings beyond question of dispute." By these standards the test is less accurate (than 95%) but it lends itself to more direct clinical interpretation.

Kunath[3] reports an analysis in which a series of one hundred cases of stone-less gall-bladder was compared with a similar series of cases in which stones were present at operation. The stone-less cases showed a greater morbidity, a higher post-operative mortality, and only about half as many cures. The stone-less cases were analyzed carefully from the standpoint of cholecystographic evidence and also pathological changes present in the gall-bladder wall, but little help was offered from either of these sources in regard to the prognosis following cholecystectomy. In general, the end result seemed to be better as the pathological changes became more marked. From this the radiologist must conclude that the demonstration of stone is all important and that the syndrome of "biliary dyspepsia" is related not so much to pathological change in the gall-bladder as to disturbed function of that organ together with the rest of the extra-hepatic biliary tract and every endeavour should be made to increase the radiological and clinical accuracy of this diagnosis. Radvin[3] writes in a similar vein: "The end results of cholecystectomy in the absence of stone are so bad that surgeons now realize that regardless of the roentgenological evidence and the pathological findings that in over one-half the cases operatod upon the cause of the patient's symptoms was not to be found in the gall-bladder.

Let us refer again to the eleven cases in the Vancouver General Hospital series which showed normal concentration and in which biliary dyspepsia persisted. The clinical and radiological diagnosis which should be made in this type of case is not well understood. Until recently infection has been considered to have played a major, if not indispensible role in the production of biliary disease. In the last decade a considerable amount of new work has been done in an attempt to show that the major role is played by stasis rather than by infection. These workers contend that stasis is the end result of a disturbance of motor function or dyskinesia of the gall-bladder of which three types have been described: (1) hypotonic, (2) hypertonic, and (3) reflex hypertonic. These dyskinesias have definite clinical signs and symptoms when they occur in their pure form. Radiologically, they present the features shown in TABLE V. The diagnosis of these conditions is being studied at the Outpatient Department Gall-Bladder Clinic. Our department has been co-operating in this study. An attempt to correlate the clinical findings and radiological findings has so far met with only a moderate degree of success. In summing up, it may be said that the hypothesis of dyskinesia seems to be a rational one, there is considerable clinical, radiological, and therapeutic evidence to support it, and it provides, so far as one can determine, the only explanation for a large number of cases which radiologically and pathologically do not have cholecystitis but who do have persistent biliary dyspepsia. Workers[4] supporting this hypothesis report an evidence of 1 to 15% of all biliary disease. The treatment of this type of case is medical.

The hypothesis of biliary dyskinesia can be carried one step further. If the biliary dyspepsia can be explained on the basis of malfunction of the extra-hepatic biliary tract which is organically normal, may not the biliary dyspepsia which accompanies a case of known chronic cholecystitis be due to the biliary dyskinesia which preceded and may still accompany the chronic cholecystitis. The removal of the gall-bladder would not, then, remove the cause of the patient's symptoms. In other words, a clinical and radiological diagnosis of chronic cholecystitis may be correct and yet the cause of the patient's symptoms is a derangement of the motor function of the whole of the extra-hepatic biliary tract.

The diagnosis of cholesterosis[5] of the gall-bladder is not commonly made. Clinically and radiologically, it may be confused with the diagnosis of biliary dyskinesia and must

be differentiated. Most cases complain of indigestion, gas and distress after meals. Jaundice and colicky pains are absent. The condition is almost entirely confined to women and is frequently seen in relation to a recent pregnancy. The cholecystogram shows a good gall-bladder shadow. The gall-bladder is seen to be much more active than normal, particularly if cholesterol stones are present. The emptying may be extremely rapid.

The interpretation of a "faint gall-bladder shadow" is very difficult. In fact, it is difficult sometimes to determine what is a faint shadow and what is a normal shadow, even for an experienced radiologist. According to Hodges and Lampe's[3] figures, 60% of gall-bladders having a faint shadow show major inflammatory change. On the other hand, some authorities[6] feel that if the oral administration is used and a faint gall-bladder shadow is obtained, the gall-bladder should be checked by the intravenous method and that a faint shadow obtained in this way warrants the radiological diagnosis of a pathological gall-bladder. The contra-indications to the intravenous method are more rigid. The dye solution must be freshly prepared, diluted in at least 200 c.c. of fluid, given over a period of twenty minutes, and followed by another 100 c.c. of fluid.

Kirkland suggests the following plan for reporting the cholecystographic findings:

(1) Normal visualization without stone.
(2) Normal visualization with stone.
(3) Faint visualization without stone.
(4) Faint visualization with stone.
(5) Non-visualization without stone.
(6) Non-visualization with stone.

It is further suggested that the gall-bladder be described as large, medium or small, hypertonic or hypotonic, and that an estimation of the amount of emptying at one and a half hours and, if necessary, at three hours after the administration of the fatty meal be made.

In concluding, I would like to express my appreciation to Dr. B. J. Harrison for his personal interest and for the use of his library. I wish to thank Dr. Perry, with whom I reviewed the Outpatient charts. I am indebted also to Mr. Fish of the Records Department, to Miss Roberge for the preparation of the slides and to Miss Ross for her valuable assistance in the preparation of the manuscript.

TABLE I.

X-RAY FINDINGS IN CASES OF PROVEN STONE.

	Hodges & Lampe			V. G. H.		
	Cases	Diagnosed	%	Cases	Diagnosed	%
No Dye Shadow	88	28	32	34	19	56
Dye Shadow	33	31	94	5	5	100
Total	121	59	49	39	24	61
Stone Falsely Reported	2			0		

TABLE II.

COMPARISON OF X-RAY DIAGNOSIS AND CLINICAL DIAGNOSIS—27 CASES.

Cholecystitis diagnosed correctly ..... 16 cases
Cholecystitis diagnosed incorrectly ..... 11 cases

Source of Error:

Gall-bladder removed	1 case	Senility	1 case
Portal cirrhosis	1 "	Duodenal ulcer	2 "
Catarrhal jaundice	1 "	Renal calculus	1 "
Carcinoma of glall-bladder	1 "	Steatorrhœa	1 "
Widespread tuberculosis	1 "	Dyskinesia	1 "

TABLE III.

CASES DIAGNOSED AS NOT CHOLECYSTITIS.

1. Cholecystitis eliminated correctly 25
2. Cholecystitis eliminated incorrectly 11

The basis of Group 2 is the persistence of biliary dyspepsia, which may be due to cholecystitis or dyskinesia.

TABLE IV.

RADIOLOGICAL FINDINGS COMPARED WITH PATHOLOGICAL FINDINGS.

	Cases	Major Disease	%
No Dye Shadow	131	104	80
Poor Dye Shadow	23	14	61
Normal Dye Shadow	44	7	16

TABLE V.

GALL-BLADDER DYSKINESIAS.

Roentgenological Characteristics	*Hypertonic Type*	*Atonic Type*
1. Concentration	Normal.	Poor.
2. Size	Normal.	Long and thin.
3. Emptying after fatty meal	Delayed.	May be delayed.
4. Ducts dilated	Reported in some cases.	Probable, though none reported.
5. Stomach	Hyperesthenic and empties rapidly unless there is associated pyloro-spasm.	Hypoesthenic and empties slowly.

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THE GAME OF GOLF

Golf is a form of work made expensive enough for business men and doctors to enjoy. It is what letter-carrying, ditch-digging and carpet-beating would be if they all had to be performed on the same hot afternoon.

The game is played on carefully manicured grass with little white balls and as many clubs as the players can afford. A golf-course is 18 holes, 17 of which are unnecessary and are put in to make the game harder. A hole is a tin cup in the centre of the green. A green is a small parcel of grass costing about $1.65 a blade and usually located between a brook and a couple of apple trees or a lot of unfinished excavation.

The game is to get the ball from a given point into each of the tin cups with the fewest number of strokes and the greatest number of words. The ball must not be thrown, pushed or carried. It must be propelled by about $200 worth of curious looking implements, especially designed to provoke the owner. After the final or 18th hole the golfer adds up the score and stops when he reaches 87. He then has a shower, a pint of rye, sings Sweet Adeline with six or eight other liars and calls it a perfect day.

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THE ROLE OF VITAMINS IN CELLULAR METABOLISM

R. Y. Stanier
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Delivered before Victoria Medical Society at their regular monthly meeting on Monday, Sept. 8, 1941.

I should like to start this evening by posing a seemingly very simple question which I am sure every member of this audience would feel ready and able to answer—namely, what are vitamins? Actually, during the forty-odd years which have elapsed since the first recognition of the role of vitamins in health and disease, the answers given by experts in the field would have shown remarkable differences from time to time.

During the earliest and longest stage the answer would have been that they were mysterious and probably rather complex substances chemically, the omission of which from the diet of animals produced pathological symptoms of various descriptions. In other words, vitamins were recognized solely by the symptoms resulting from their deficiency in the diets of higher vertebrates.

The second stage, beginning about ten years ago, was ushered in by intensive work on the chemical constitution and synthesis of the various vitamins. In an extremely short space of time it has been shown that the vitamins are comparatively simple chemical substances, many of which can be synthesized without difficulty by the organic chemist. An interesting and significant point which has emerged from these studies is that the vitamins do not fall into any one chemical class; in fact, from the chemical standpoint they comprise an extremely heterogeneous group of compounds.

The vitamin chemist of this second period could have given a chemical formula representing, say, Vitamin B_1, thus providing a valuable supplement to the previous picture. However, he would have been completely unable to explain *why* the absence of this simple organic chemical from the diet should have provoked the well-marked and profound symptoms characterizing B_1 deficiency in the rat or in man.

Another great extension of our knowledge of the vitamins which took place about the same time as the chemical work was the outgrowth of a new field—comparative biochemistry. Comparative biochemistry is what its name implies: the analogue of comparative anatomy. Just as the comparative anatomical concept strengthened and unified our knowledge of zoology by directing attention to the underlying similarities of *structure* in the various forms of animal life, so has comparative biochemistry illuminated and clasified the basic identity of *function* in living organisms. The statement that the fundamental biochemical activities of man, of a flowering plant and of a bacterium are essentially similar will probably come as a shock to most of you, yet this is a statement which few biochemists today would care to contest. The study of vitamins provided at first a challenge, and later an important support for the concepts of comparative biochemistry. When the great Dutch biochemist Kluyver put forward his ideas on comparative biochemistry in 1926, vitamins were only known to be of importance in a few of the vertebrates; yet it is obvious that if these ideas were correct, the vitamins might be expected to play an equally important part in other forms of life. The work of the last six years has shown that this is a fact.

Let us first consider the case of the higher plants. It has long been known that one can grow plants in a solution containing various inorganic substances alone. The nitrogen requirements are met by nitrates or ammonia and in addition simple compounds of P, Ca, Fe, S, K, and Mg, as well as traces of other elements, are needed. The carbon requirements are met by CO_2 of the atmosphere and energy is obtained by the utilization of light through photosynthesis. From these, all the complex organic substances composing the structure of the living plant are produced. Can we then conclude that the plant *does not need* vitamins? The evidence might be thought to point to this, but there is another possibility: namely, that the plant requires and uses vitamins just as do animals, but is able to synthesize them itself. As a support for this view, there is the fact that green plants are the major sources of many vitamins. Actually, it has been definitely proven that some vitamins are necessary for the growth of plants. A few years ago, biologists began studying the growth of plant roots in the absence of stem and leaves. It was soon found (1) that under sterile conditions excised roots were unable to grow in a simple salt solution such as supported the whole plant, even when this was supplemented with glucose to compensate for the carbon and energy no longer supplied by photosynthesis. However, the further addition of traces of vitamin B_1 provoked a prompt and rapid growth. This can only be explained by assuming that the root did indeed require B_1, but that under ordinary conditions the total needs of this vitamin were synthesized by the stem and leaves.

The study of micro-organisms, particularly bacteria, has provided ample additional evidence of the universal importance of vitamins. The work of the past twenty years has demonstrated that the bacteria are a sort of vast biochemical melting-pot in which can be found parallels to all the individual biochemical processes of higher forms of life, as well as many reactions which are peculiar to bacteria alone. This is nowhere better brought out than in the field of vitamins. Bacteria range from organisms with as simple nutrient requirements as the higher plants to forms whose requirements are almost as complex as those of man. Furthermore, it is often the case that one can find within a single closely-interrelated group of bacteria a graduated series of increasingly complex vitamin requirements. Interestingly enough, it is nearly always the parasitic or pathogenic forms in such a series which have the most complex requirements; rare indeed is the parasite which will grow well on a simple medium. This has led to a new and fruitful concept of the nature of parasitism and other forms of organic interdependence, as being conditioned by the loss of ability to synthesize vitamins and other needed nutrients. For example, a bacterium which has lost the ability to synthesize vitamin B_1 will be forced into a closer relationship with other organisms which are able to produce this substance themselves (*e.g.*, higher plants) or else have access to external supplies (*e.g.*, higher animals) and may thus become parasitic on them. Once an association of this type has developed the abundant presence of other vitamins produced by the host organism makes their synthesis by the parasite superfluous, so that a gradual functional degeneration or simplification sets in, the bacterium sloughing off one part of its biochemical apparatus after the other, much as parasitic invertebrates throw off those organs which are only of use in a free-living existence. This thesis was first put forward by the French protozoologist Lwoff, and has been brilliantly developed in his "Etude sur les fonctions perdues"[4].

A striking experimental demonstration of the biochemical causation of symbiosis has been provided by the Swiss plant physiologist Schopfer[6]. He made an intensive study of vitamin B_1 requirements among the yeasts and fungi, for many of which this is the only vitamin which must be supplied preformed. Chemically, B_1 consists of two different ring compounds, pyrimidine and thiazole, which are linked together. Schopfer found that certain fungi did not require the whole molecule, but could synthesize it provided that they were given a fraction. Thus the organisms he studied could be graded into a series as follows:

1. Can synthesize the entire B_1 molecule.
2. Can synthesize B_1 if given the pyrimidine half.

3. Can synthesize B_1 if given the thiazole half.
4. Can synthesize B_1 if given both halves separately.
5. Must be provided with the whole molecule.

It occurred to Schopfer that organisms of groups 2 and 3 might be able to grow in a medium completely devoid of B_1 or its fractions by supplying each other with the complementary, unsynthesizable half of the molecule. Consequently, he inoculated a simple medium containing only glucose and the necessary inorganic salts with a representative of each group. The two organisms not only grew luxuriantly, but even lost to a considerable extent their morphological identity, becoming so closely intermingled as to resemble a single organism. It is an interesting fact that there exists in nature a large group of plants, the lichens, which consists of a symbiotic association between an alga and a fungus, both of which have lost to some extent their individual morphology. It seems quite likely that the lichen association is a biochemically conditioned one similar to that produced artificially by Schopfer.

One aspect of the studies on the vitamin requirements of bacteria has already assumed great practical importance: namely, the development of vitamin assay methods which use bacteria as the test organisms instead of the higher animals. Already recognized assay methods for several of the B group are based on this. The advantages are great; one can obtain in a few days with the use of inexpensive equipment data which would require weeks of laborious work with animals (see, *e.g.*, Woolley[9]).

From the foregoing it is clear that we can regard the need for vitamins as an index of the *loss of synthetic function* in any given organism. How does the necessity for vitamins differ from other needs based on the loss of synthetic function? As an example of other needs we might consider the nitrogen requirements. Many micro-organisms and all the higher plants are able to build up the complete array of necessary amino-acids—and hence proteins—from nitrates or ammonia alone. However, the higher animals and a number of micro-organisms cannot synthesize certain amino-acids and have to be supplied with these in a preformed state, although the remaining non-essential amino-acids can be synthesized from ammonia and the intermediary products of carbohydrate metabolism. In a certain respect these unsynthesizable amino-acids might be regarded as "vitamins" if we base the definition of vitamins solely on the loss of synthetic ability. However, there is one significant difference between the amino-acid requirements and the vitamin requirements proper of an organism. Relatively enormous amounts of the amino-acids are needed, but only a minute quantity of the vitamins. This has long been regarded, and rightly so, as an indication that the vitamins must have a *specific function* in metabolism, since if they were used, like the necessary amino-acids, for a non-specific purpose such as the building up of body proteins are requirements would be very much greater.

The unravelling of this great scientific problem—the specific function of vitamins—has only just begun, but the facts already obtained (almost entirely in the past four years) form one of the most revolutionary advances in all biochemistry. So far the specific roles of three vitamins—B_1, B_2 and nicotinic acid—have been elucidated. As it happens, they are all involved in the metabolism of carbohydrates, or, to put it more generally, carbon compounds. This must not be taken to mean that all vitamins function in carbohydrate metabolism; probable the fat-soluble ones at least have entirely different activities. Carbohydrate metabolism has received a disproportionate amount of attention from biochemists, and it is not surprising that the vitamins involved in it should first have been tracked down.

In order to make what follows intelligible I must turn for a moment to a seemingly entirely irrelevant topic, the mechanism of biological oxidation.

According to the classical theories of oxidation, this phenomenon is due to the addition of oxygen to the substance being attacked. Thus, the complete oxidation of one molecule of glucose is expressed as:

$$C_6H_{12}O_6 + 6\ O_2 \rightarrow 6\ CO_2 + 6\ H_2O$$

Another example is the oxidation of ethyl alcohol to acetic acid, a process carried out by certain bacteria:

$$CH_3CH_2OH + O_2 \rightarrow CH_3COOH + H_2O$$

After Lavoisier's discovery of oxygen at the end of the 18th century, these equations were the accepted way of describing oxidations for well over a hundred years. At the beginning of this century the German chemist Wieland put forward an entirely different picture of oxidation: namely, as the removal of hydrogen atoms from the molecule to be oxidized rather than as the addition of oxygen. According to the Wielandian concept [8], the above-mentioned oxidation of ethyl alcohol was pictured as:

$$CH_3CH_2OH + H_20 \rightarrow CH_3COOH + 4\ H.$$

or, broken down into three steps, as:

$$CH_3CH_2OH - 2\ H \rightarrow CH_3CHO$$
$$CH_3CHO + H_2O \rightarrow CH_3CH_3O_2$$
$$CH_3CH_3O_2 - H \rightarrow CH_3COOH$$

Wieland postulated that in order for this process to occur, there had to be present a *hydrogen acceptor* to take up the hydrogen atoms removed. He showed that a large number of substances, both organic and inorganic, were capable of acting in this manner. His theory was backed by much convincing experimental evidence which it would take too long to describe here. However, one of the great difficulties was that it did not appear to accord with the known facts of biological oxidation. For this reason, considerable opposition to Wieland's theory arose, headed by Warburg, another German chemist who had done much work on biological oxidations and had considerable evidence to show that oxygen itself, when activated by catalysts, could carry out oxidations[7]. It was not until 1925 that the solution of this controversy was reached, and as it turned out both Wieland and Warburg had been partially correct. Biological oxidation is a process which involves both hydrogen transfer and the activation of oxygen; these men men had all the time been studying the opposite ends of the same chain of events. As Wieland postulated, the *first step* in oxidation is the removal of hydrogen atoms from the sugar or whatever other substrate is being oxidized. These atoms are taken up by a substance A acting as a hydrogen acceptor:

$$A + 2\ H \rightarrow AH_2$$

and then passed on to a second hydrogen acceptor B:

$$AH_2 + B \rightarrow BH_2 + A,$$

A then being ready to accept two more hydrogen atoms from the substrate. Substances capable of undergoing this periodic oxidation and reduction are known as hydrogen carriers. In this way the hydrogen atoms torn off the substrate are passed along a chemical chain of intermediary substances acting as hydrogen carriers until, at the far end of the chain, they come in contact with actviated oxygen and unite with it to form H_2O_2, which is immediately broken down into water and oxygen. In this way, the classical picture of biological oxidation can be fulfilled. The sugar molecule, after the removal of sufficient hydrogen atoms, will fall apart forming CO_2, while the oxygen is used up uniting with the removed hydrogen atoms to form water.*

Once this interpretation became generally accepted, biochemists turned their attention to discovering the nature of the links in this chain which act as hydrogen carriers. As a result, we have today a fairly good picture of the entire chemical sequence between the substrate and the oxygen; what is more, this chemical sequence appears to be almost the same in all living organisms which carry on an aerobic type of metabolism. The links in this chain have received the name of *oxidative enzymes,* a name designed to stress the differences between them and the enzymes of digestion. It is particularly the first two enzymes in the chain which deserve attention. Ironically enough, the study of these two substances, which show so clearly the essential correctness of the

* This is, of course, a highly simplified account; for a detailed chemical presentation see Oppenheimer and Stern[5].

Wielandian concept of oxidation as a hydrogen transfer, has been carried out chiefly by Warburg and his colleagues[8].

What are enzymes? Ten years ago this question could not have been answered, but since then a considerable number have been isolated and purified, so that today we can say with fair confidence that all enzymes are proteins. In itself, this statement tells us nothing about the mechanism of enzyme action; however, the further study of the oxidative enzymes in particular has shed much light on the way in which enzymic catalysis is brought about.

The oxidative enzymes belong to a special class of proteins known as conjugated proteins; that is, ones which have linked to them some other different chemical substance. In the first two members of the oxidative chain the linked substances are vitamins or vitamin derivatives. In one the linked substance is a somewhat complex derivative of nicotinic acid amide known as codehydrogenase, while in the other it is simply vitamin B_2 or riboflavin. In both these cases the vitamin fractions are the active portions of the enzyme since they are the hydrogen carriers and by their successive oxidation and reduction the hydrogen torn off the substrate is transferred. The role of the protein is, however, in neither case negligible. The riboflavin and codehydrogenase can only act when linked to them; in their free states these two substances are biochemically inert. Furthermore, the protein linked to the codehydrogenase has another important function; it determines the specificity of the oxidation to be carried out. Thus there are a large number of *different* protein molecules which can link to codehydrogenase and each one will activate it for the oxidation of a different substance.

Protein 1 + codehydrogenase will oxidize glucose
Protein 2 + codehydrogenase will oxidize ethyl alcohol
Protein 3 + codehydrogenase will oxidize lactic acid

and so on.

The third vitamin whose specific function has been elucidated—B_1—is not a link in the chain between foodstuff and oxygen, but it has an equally vital part in oxidation; the release of CO_2 from the carbon skeleton of the foodstuff after the removal of hydrogen. In order to understand this, it is necessary to examine first a little more closely the fate of a sugar molecule undergoing oxidation. Generally such a molecule does not, as I have previously indicated for the sake of simplicity, undergo an oxidation as such, but is first split into two equal halves with 3 carbon atoms each:

$$C_6H_{12}O_6 \rightarrow 2\ C_3H_6O_3$$

Each of these C_3 molecules is then oxidized by the removal of two hydrogen atoms:

$$C_3H_6O_3 - 2\ H \rightarrow C_3H_4O_3$$

resulting in the production of a keto acid, pyruvic acid ($CH_3COCOOH$). Pyruvic acid is the keystone of intermediary metabolism, since it can easily be built up into fatty acids and thence fats or amino-acids and thence proteins. However, it may simply be destroyed to furnish energy, in which case it next undergoes a decarboxylation (*i.e.*, a removal of CO_2 from the molecule). It is in this way, by the decarboxylation of keto acids, that all the CO_2 resulting from oxidation is released. Phosphorylated vitamin B_1, linked to a specific protein, is the enzyme which carries out this decarboxylation.

In summing up, I should like to give you a general definition of vitamins. An organic substances is a vitamin for any given organism if it performs the function of an active group in some enzyme system and cannot be synthesized by that organism. Its deficiency will then result in a definite metabolic deficiency which may or may not (depending largely on the structural complexity of the organism in question) result in the development of pathological symptoms. Thus the important thing about a B_1 deficiency is not that it produces nerve degeneration in man, but that in *all* living organisms it results in incomplete carbohydrate metabolism due to weak decarboxylation. The neurological symptoms of B_1 deficiency in the higher vertebrates are essentially secondary and superficial. This is one reason why, since the general acceptance of the

tenets of comparative biochemistry, scientists have devoted so much greater attention to micro-organisms in their studies of general biochemical problems. In bacteria, all biochemical processes are reduced as it were to their lowest common denominator, and an avitaminosis can usually be recognized by its primary symptoms. A very striking example of this is provided by some recent studies on the importance of nicotinic acid for the dysentery bacterium[2]. It has been shown that nicotinic acid is not a vitamin if the bacterium in question is grown on a proteinaceous medium. However, as soon as the medium is supplemented by a fermentable carbohydrate, nicotinic acid becomes necessary for proper growth and development; in its absence the carbohydrate is only superficially attacked. As it happens, this particular discovery merely confirms what we already know about the function of nicotinic acid, but had it been made ten years ago it would certainly have led to a more rapid appreciation of the function of this substance. I venture to predict that it will be through similar studies on the lowlier forms of life rather than through investigations made on animals that most future discoveries concerning the biochemical function of vitamins will be made.

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The simplest yet one of the best sources of information on this subject is "On oxidation, fermentation, vitamins, health and disease" by A. von Szent-Gyorgi (Abram Flexner lectures, series No. 6, Williams and Wilkins Co., Baltimore, 1939). An excellent, but more technical, recent monograph covering much of the work on the biochemical functions of vitamins is "Mechanisms of biological oxidations" by D. E. Green (Cambridge University Press, 1940).

ERRATUM

In the October, 1941, issue, on page 12, the dosage of Argyrol to be instilled into the bladder following catheterization was mistakenly given as an ounce. It has been called to our attention that such an amount used routinely after catheterization or frequent irrigation, is much too large—a drachm should be quite enough. Therefore for "one ounce" read "one drachm."

PATHOGENESIS OF JAUNDICE

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Synopsis of Lecture given at the Summer School of the Vancouver Medical Association, Vancouver, June, 1940.

Formation and Excretion of Bilirubin:

Bilirubin, the chief pigment of human bile, is identical with the iron-free pigment, hæmatoidin, which is found in old blood extravasations. It is formed by the reticulo-endothelial cells of the body from hæmatoglobin liberated from disintegrating erythrocytes. It is then transferred to the liver in the blood stream and excreted through the liver cells into the bile passages.

In man the bone marrow and the spleen are the chief depots of the reticulo-endothelial cells, and it is in these organs that the greater part of the bilirubin is manufactured. A small amount of bilirubin is produced in the human liver by the reticulo-endothelial cells (Kupffer cells) which form an interrupted lining for the sinusoids. The parenchymatous cells of the liver excrete bilirubin but play no part in its formation.

In its passage through the livel cells the bilirubin is altered from a form which yields only an indirect van den Bergh reaction (Bilirubin I of Aschoff; "Direct negative" bilirubin of Elton) to a form which yields a direct van den Bergh reaction (Bilirubin II of Aschoff; "Direct positive" bilirubin of Elton). The nature of this change is uncertain but there is evidence that it is one from a colloid to a crystalloid state.

Formation and Excretion of Urobilinogen:

In the intestines bilirubin is transformed into urobilinogen by bacterial action. Some of the urobilinogen is passed in the fæces (as stercobilin), the remainder is absorbed, carried to the liver in the portal blood and again excreted into the intestines. Normally only very little urobilinogen escapes through the liver into the general circulation and is excreted by the kidneys. The presence of an excess of urobilinogen in the urine (positive reaction with paradimetheylaminobenzaldehyde in urine dilutions of 1 in 20 or greater) indicates either damage to the liver cells (impaired excretion of urobilinogen) or excessive destruction of red cells (excessive production of bilirubin and urobilinogen).

Normal Bilirubin Content of the Blood:

Normally the blood contains a small amount of bilirubin. This is the bilirubin which has been formed by the cells of the reticulo-endothelial system and is on its way to the liver to be excreted. It is the bilirubin I of Aschoff or the "direct negative" bilirubin of Elton. Opinions vary as to the bilirubin content of the blood in health. Greene, Snell and Walters found it to lie between 0.5 and 2 mg. per 100 cc. Vaughan reports that 93 per cent of 100 normal people showed values between 0.2 and 0.8 mg. per 100 c.c., and that in the other 7 per cent values up to 1.7 mg. per 100 c.c. were obtained. She concludes that figures up to 1.3 mg. per 100 c.c. should be considered as probably normal, and figures between 1.3 mg. and 1.7 mg. as probably but not necessarily pathological.

Hyperbilirubinæmia (Jaundice):

Theoretically, an excess of bilirubin in the blood, leading to jaundice or pigmentation of the tissues, may be due to the following causes:

(a) Overproduction of bilirubin I by the cells of the reticulo-endothelial system. (This is the "hyperfunctional jaundice" of Aschoff. It is caused by hæmolysis or increased destruction of red cells.)

(b) Impaired excretion of bilirubin I by the liver. (This is the "retentional jaundice" of Aschoff. It is caused by damage to the liver cells.)

(c) Escape of bilirubin II from the liver cells or bile capillaries into the blood. (This is the "resorptional jaundice" of Aschoff. It may be caused by disintegration of liver cells or by obstruction in the bile ducts.)

(d) A combination of two or more of these factors.

Hyperfunctional (Hæmolytic) Jaundice:

The belief that jaundice may be purely hyperfunctional or hæmolytic in origin (that is, that it may be due to excessive destruction of red cells and consequent excessive formation of bilirubin) is not universally accepted. In hæmolytic diseases, such as familial hæmolytic icterus, pernicious anæmia, sickle-cell anæmia and paroxysmal hæmoglobinuria, the blood bilirubin is increased in amount, the van den Bergh reaction is indirect, the stools are rich in pigment and the urine contains an excess of urbilinogen but no bile. It is difficult to explain these findings except upon the basis of overproduction of bilirubin I by the reticulo-endothelial cells and excretion of large amounts of bilirubin II by the liver. Those who deny the occurrence of purely hæmolytic jaundice (Rich and others) argue that the reserve excretory power of the liver is so great that hyperbilirubinæmia cannot be due solely to overproduction of bilirubin. They believe, therefore, that there must be a hepatic factor in so-called hæmolytic jaundice. To my mind this argument is fallacious. The jaundice of hæmolytic diseases is usually of slight degree and it may be latent (that is, there may be hyperbilirubinæmia without obvious pigmentation of the tissues). I find no difficulty in believing that the mild jaundice of these conditions is due entirely to overproduction of pigment. It seems obvious that the discharge of an increased amount of bilirubin from the reticulo-endothelial cells into the blood stream must cause an increase in the amount of bilirubin in the blood even in the presence of a perfectly normal liver.

Retentional Jaundice:

Following removal of the liver in dogs, deep jaundice develops and the icteric serum yields an indirect van den Bergh reaction (Mann). This is retentional jaundice. Bilirubin I is produced in normal amount by the cells of the reticulo-endothelial system, but owing to the absence of the liver it cannot be excreted. As no bile reaches the intestines, no urobilinogen is formed. It is probable that deficient excretion of bilirubin I is a factor in many cases of clinical jaundice, and it is possible that the mild jaundice of such conditions as lobar pneumonia and cardiac failure, in which the serum may yield an indirect van den Bergh reaction, is purely retentional. It seems justifiable to believe that slight damage to the liver may lead to depression of its excretory function, with retention of bilirubin I in the blood and the appearance of mild jaundice with an indirect van den Bergh reaction, whereas more severe injury to the liver causes jaundice with a direct van den Bergh reaction because not only is the excretion of bilirubin I impaired but, owing to disintegration of liver cells, disruption of bile capillaries and, possibly, blocking of bile capillaries, "direct-reacting" bilirubin II is resorbed into the blood.

Resorptional Jaundice:

Jaundice following obstruction of the common bile duct is primarily resorptional in type. That is, it is due to resorption (Aschoff) or regurgitation (Rich) of bilirubin II from the liver cells and bile capillaries into the blood. The serum yields a direct van den Bergh reaction. If obstruction is complete, bile pigment is absent from the stools and the urine contains large quantities of bilirubin but no urobilin. With incomplete obstruction, varying amounts of bile pigment reach the intestines and the urine contains both bilirubin and urobilin. Obstruction of the common bile duct is soon followed by degenerative and inflammatory changes in the bile-engorged liver, so that in jaundice which is primarily resorptional (due to mechanical obstruction of the outflow of bile and resorption of bilirubin II) the factor of retention or failure in excretion of bilirubin I comes to play a part.

Macrocytic, hyperchromic Anæmias.

It will be remembered that the "liver principle" or "anti-pernicious-anæmia factor" is formed in the stomach by the interaction of an intrinsic factor secreted by the gastric mucosa and an extrinsic factor present in the food, and that it is stored in the liver and, to a less extent, in the kidneys and pancreas. Deficiency of this substance causes a

profound disturbance in the maturation of the red cells and the appearance of a macrocystic, hyperchromic anæmia. Such deficiency may be due to: (1) failure in the secretion of the intrinsic factor, (2) failure in the supply of the extrinsic factor, (3) failure in the absorption from the intestinal tract of the substance formed in the stomach by the interaction of the intrinsic and extrinsic factors or, possibly, to (4) failure in the utilization of this substance by the bone marrow.

(1) Castle's work leaves no doubt that failure in secretion of the intrinsic factor is the cause of true (Addisonian) pernicious anæmia. In this disease the red cell count is usually below three million when the patient seeks advice, and it may be as low as one million. As the red cells are larger than normal the volume index is above unity (1.2 to 1.8), and as these large cells are fully charged with hæmoglobin the colour index is also high (1.2 to 1.8). The leucocyte count is usually below 5,000, and a differential leucocyte count shows neutropænia with relative lymphocytosis. The Arneth count or polynuclear count shows a shift to the right. The platelet count is reduced. In stained films the majority of the red cells are seen to measure 12 or 13 microns in diameter and many of these large cells (magrocytes or megalocytes) are oval in shape. Red cells of normal and reduced size are also to be seen and poikilocytosis is well marked. Nucleated red cells (normoblasts and megaloblasts) are usually to be found and there may be a considerable number of stippled red cells. In severe cases the serum or plasma shows an excessive bilirubin content (3 to 6 mg. per 100 c.c.) with an indirect van den Bergh reaction, and the urine and fæces contain an excess of urobilinogen. The gastric contents show absence of hydrochloric acid and, as has been mentioned, absence of the intrinsic factor of Castle. Postmortem examination shows generalized megaloblastic hyperplasia of the bone marrow, an accumulation of iron-containing pigment (hæmosiderin) in the liver, fatty degeneration of the myocardium and slight enlargement of the spleen. There may also be glossitis, atrophy of the gastric mucosa and degenerative changes in the postero-lateral columns of the spinal chord.

Anæmia which is indistinguishable from Addisonian pernicious anæmia, and which, presumably, is also due to a deficiency of the intrinsic factor, appears in a small percentage of patients with carcinoma of the stomach and in a small percentage of patients who have undergone partial or complete gastrectomy. The rare pernicious or macrocytic anæmia of pregnancy is probably due to a temporary, unexplained, suppression of the secretion of the intrinsic factor, but there is some evidence that it may be caused by deficiency of the vitamin B complex (? extrinsic factor) in the diet.

(2) Case reports, describing the successful treatment of pernicious anæmia by the oral administration of yeast or of liver residue devoid of the active "liver principle," sugest that, very rarely, this disease may be due, not to absence of the intrinsic factor from the gastric juice but to absence of the extrinsic factor from the food.

Tropical macrocytic anæmia, which differs from pernicious anæmia in that severe untreated cases do not show evidence of active hæmolysis (hyperbilirubinæmia and excess of urobilinogen in urine and fæces) seems to be due to a dietary deficiency, but it appears unlikely that this deficiency is of the nature of a lack of the extrinsic factor of Castle. This disease can be cured by the administration of an autolyzed yeast or by the injection of crude liver extracts, but not by the injection of the purified and concentrated extracts which are so efficacious in the treatment of pernicious anæmia.

(3) Failure in the absorption of the liver principle or anti-pernicious-anæmia factor (which is produced in the stomach by the interaction of the intrinsic and extrinsic factors) may be the cause of the macrocytic anæmia of tropical and non-tropical sprue (idiopathic steatorrhœa) and of the macrocytic anæmia found in patients who have had partial resection of the small bowel or intestinal anastomoses. Some years ago I saw a girl, 16, who had had several abdominal operations and who was left with an ileocolostomy and a cæcal fistula. This patient had achlorhydria and a severe anæmia which was indistinguishable from pernicious anæmia and which responded promptly and satisfactorily to liver extract therapy.

(4) There is a group of macrocytic hyperchromic anæmias which respond unsatisfactorily or not at all to liver therapy. Some of these are clinically similar to pernicious anæmia and run a more or less chronic course; perhaps improving temporarily on treatment with liver extract. In others the clinical course is that of an aplastic anæmia, as the red cell count falls progressively in spite of all treatment and death occurs in a few weeks or a few months. It has been suggested that such anæmias are due to non-utilization of the liver principle by the bone marrow (achrestic anæmias) but there is no evidence to support this theory. It would seem more likely that macrocytic anæmia may be due to some other cause or causes than deficiency of the liver principle. In leukæmia the anæmia is often of macrocytic type, and there is a form of hæmolytic anæmias which resembles falilial hæmolytic icterus in showing increased fragility of the red cells but which differs from it in showing macrocytosis instead of microspherocytosis. This disease is not benefited by liver therapy, but it is often cured by splenectomy.

Macrocytic Hypochromic Anæmia.

Macrocytic hypochromic anæmia occurs when there is a deficiency of both the liver principle and iron. Such deficiencies are often present in idiopathic steatorrhœa (sprue) and the patient shows a macrocytic anæmia with a colour index about 1. In stained films many of the large cells are seen to be deficient in hæmoglobin (large unstained centres) but, strangely enough, others show a normal hæmoglobin content. This variation in the hæmoglobin content of the red cells is stressed by Vaughan as being highly suggestive of a diagnosis of steatorrhœa.

Not rarely in pernicious anæmia there may be an associated deficiency of iron and films show hypochromasia as well as macrocytosis. This picture is seen most often in the second or third week of liver therapy, when the iron reserves of the body may become temporarily depleted as a result of the rapid outpouring of young red cells from the marrow.

In cirrhosis of the liver the blood often shows macrocytosis with hypochromasia. It is uncertain whether the macrocytosis is due to failure on the part of a diseased liver to store the active "liver principle" or whether it is explained by swelling of the red cells owing to physico-chemical changes in the blood plasma.

Microcytic Hypochromic Anæmia.

In pernicious anæmia, which is due to a deficiency of the "liver principle," the maturation of the red cells is retarded at the megaloblastic level, the marrow's store of normoblasts is rapidly depleted and the production of normal erythrocytes is almost completely suppressed. The normal deposits of red marrow become crowded with proliferating megaloblasts and the yellow marrow of the long bones is particully or completely replaced by similar megaloblastic red marrow. There is no interference with the formation of hæmoglobin and many of the megaloblasts undergo a pathological type of ripening and enter the blood as large hæmoglobin-rich corpuscles which are known as megalocytes. These changes in the marrow lead to the appearance of a severe macrocytic (megalocytic) hyperchromic anæmia.

Just as the liver principle is essential for the transformation of megaloblasts into normoblasts, so iron is essential for the transformation of normoblasts into erythrocytes. If the supply of iron to the marrow is deficient, the maturation of the red cells is retarded at the normoblastic level, the marrow becomes crowded with normoblasts which fail to mature, the output of red cells is reduced and those erythrocytes which do reach the blood stream are poor in hæmoglobin and smaller than normal. This type of marrow disturbance leads to the development of a microcytic, hypochromic anæmia.

A deficient supply of iron to the marrow may be due to: (1) a diet poor in iron-containing foods, (2) a need for iron which is greater than can be supplied from a normal diet, (3) failure in the absorption of the iron in the food, (4) loss of iron from the body or (5) a combination of two or more of these factors.

(1) A deficient intake of iron is the cause of the ordinary hypochromic anæmia of infancy. A normal infant possesses at birth three times as much iron in proportion to its weight as a child over one year of age (Sherman). This iron is stored, chiefly in the liver, and is utilized by the bone marrow in the production of hæmoglobin. Theoretically it should be sufficient to supply the need of the baby until the birth weight is tripled and, therefore, hypochromic anæmia should not appear during this period, even though the child is on a milk diet which is poor in iron. If the iron-poor (milk) diet is continued after the prenatal store of iron is exhausted, anæmia is likely to develop. In full-term infants, hypochromic or dietary anæmia rarely appears until at least one year after birth. Children who are born with an insufficient supply of iron, owing to the presence of iron deficiency and hypochromic anæmia in the mother, may show anæmia as early as the sixth month of extrauterine existence.

A deficient intake of iron-containing foods may also cause microcytic, hypochromic anæmia in adults. This is seen most often in women of the poorer classes. There is usually an associated lack of animal protein in the diet, and unless both these deficiencies are supplied, anæmia persists.

(2) The hypochromic anæmia of pregnancy may develop in women whose diet is in all respects adequate for the ordinary needs of the body. It is probably caused by a relative deficiency of iron due to a drain of iron from the material of the fœtal tissues.

(3) Microcytic hypochromic anæmia due to failure in absorption or utilization of the iron in the food is exemplified by the condition known as the idiopathic hypochromic anæmia, chronic microcytic anæmia or simple achlorhydric anæmia. This is common in middle-aged women. It resembles pernicious anæmia in the frequent presence of gastro-intestinal symptoms, achlorhydria, glossitis and splenomegaly. It differs from pernicious anæmia in the frequent presence of trophic changes in the nails (koilonychia) and dysphagia (anæmia + glossitis + dysphagia = Plummer-Vinson syndrome), in the changes which occur in the marrow and in the blood and, of course, in its failure to respond to liver therapy. In this disease the red cell count is usually between three and four million when the patient seeks advice, but it may be much lower. As the disease is essentially a hæmoglobin deficiency, the colour index is always reduced and it may be 0.5 or even lower. The height of the volume index depends upon the degree of microcytosis; it may be within normal limits but usually it is reduced. As a rule the leucocyte and platelet counts are normal. In stained films the majority of the red cells are smaller than normal with large unstained centres. The bilirubin content of the blood is low. In at least 80 per cent of cases there is achlorhydria. The marrow shows normoblastic hyperplasia.

It is important to remember that the changes in the blood in idiopathic hypochromic anæmia are similar to those in other types of anæmia due to deficiency of iron A diagnosis of idiopathic hypochromic anæmia should not be made until known causes of iron deficiency anæmia, such as chronic hæmorrhage and organic lesions of the gastro-intestinal tract, have been excluded.

(4) Microcytic hypochromic anæmia due to loss of iron is exemplified by the anæmia of chronic hæmorrhage. The differences in the blood pictures of chronic post-hæmorrhagic and chronic hæmolytic anæmias are due to the fact that profuse or repeated hæmorrhages leads to exhaustion of the body's store of iron and other red-cell building materials, and resulting inactivity of the marrow, whereas when red cells are destroyed within the body the products of their disintegration are available for the formation of new erythrocytes, and the regenerative response of the marrow is active and continuous. Hyperbilirubinæmia, urobilinuria, reticulocytosis, hæmosiderosis and normoblastic hyperplasia of the marrow are features which are common to all types of hæmolytic anæmia. In chronic post-hæmorrhagic anæmia, on the other hand, the blood picture is identical with that of other forms of iron deficiency anæmia. It is to be noted, however, that when profuse hæmorrhage occurs into the tissues or body cavities the disintegration products of the extravasated erythrocytes are available for the formation of new red

cells and the picture may resemble that of hæmolytic anæmia in showing re iculocytosis, hyperbilirubinæmia with an indirect van den Bergh reaction and an excess of urobilinogen in the urine and fæces.

Normocytic Hypochromic Anæmia.

In the early stages of an iron-deficiency anæmia, while the red cells show a reduction in their hæmoglobin content there may be little or no reduction in their size. The picture is then that of a normocytic hypochromic anæmia. The anæmias of vitamin C deficiency (scurvy) and of chronic infections are usually of similar type but they may be microcytic.

Normocytic Normochromic Anæmia.

Anæmias due to deficiency of hæmopoietic substances (liver principle, iron, vitamin B, vitamin C, animal protein) are characterized by changes in the size and hæmoglobin content of the red cells. In anæmias due to injury to the marrow such changes are commonly absent and the red cell picture is normocytic and normochromic. Thus in true aplastic anæmia, that is, anæmia characterized by marked hypocellularity of the marrow, whether it is of so-calle idiopathic type or due to the action of known toxic agents (benzol, arsenic), there is a rapid reduction in the numbers of erythrocytes, leucocytes and platelets in the blood but the red cells in stained films show no abnormality other than slight anisocytosis and poikilocytosis. In many cases which simulate true aplastic anæmia in showing a progressive fall in the numbers of all the cellular elements of the blood, the marrow is hyperplastic and blood films may show macrocytosis with variable numbers of immature red and white cells. Cases of this type should be classified under the heading of progressive hypocythæmia, rather than of aplastic anæmia (Krumbharr); many of them are examples of aleukæmic leukæmia.

The anæmia of renal insufficiency is, as a rule, monocytic and normochronic, but colour indices above 1.1 have been reported in this condition.

Other Types of Anæmia.

Two hæmolytic anæmias which are classified according to the shape of the red cells are the microspherocytic anæmia of familial hæmolytic icterus and the sickle-cell anæmia which is common in negroes.

The anæmia which is due to progressive mechanical destruction of the bone marrow by tumour growths (secondary carcinoma, multiple myeloma) or by osteosclerotic processes is known as myelophthisic anæmia. In it, while owing to reduction in the total amount of red marrow the output of red cells is greatly reduced, overactivity of the remaining red marrow leads to the appearance of many reticulocytes, nucleated red cells and immature leucocytes in the blood.

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