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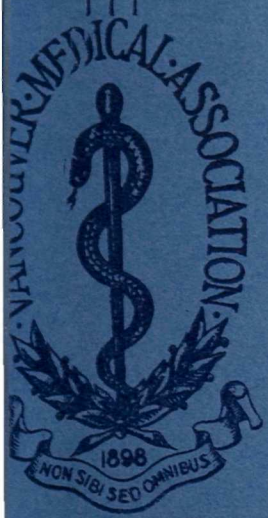

The BULLETIN

of the

VANCOUVER MEDICAL ASSOCIATION

Vol. XVI. MARCH, 1940 No. 6

With Which Is Incorporated
Transactions of the

Victoria Medical Society

the

Vancouver General Hospital

and

St. Paul's Hospital

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VANCOUVER MEDICAL ASSOCIATION
SUMMER SCHOOL, JUNE 25th TO 28th INCL., 1940

Old Way . . .

CURING RICKETS in the CLEFT of an ASH TREE

FOR many centuries,—and apparently down to the present time, even in this country—ricketic children have been passed through a cleft ash tree to cure them of their rickets, and thenceforth a sympathetic relationship was supposed to exist between them and the tree.

Frazer* states that the ordinary mode of effecting the cure is to split a young ash sapling longitudinally for a few feet and pass the child, naked, either three times or three times three through the fissure at sunrise. In the West of England, it is said the passage must be "against the sun." As soon as the ceremony is performed, the tree is bound tightly up and the fissure plastered over with mud or clay. The belief is that just as the cleft in the tree will be healed, so the child's body will be healed, but that if the rift in the tree remains open, the deformity in the child will remain, too, and if the tree were to die, the death of the child would surely follow.

*Frazer, J. G.: The Golden Bough, vol. 1, New York, Macmillan & Co., 1928

It is ironical that the practice of attempting to cure rickets by holding the child in the cleft of an ash tree was associated with the rising of the sun, the light of which we now know is in itself one of Nature's specifics.

New Way . . .

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THE VANCOUVER MEDICAL ASSOCIATION

BULLETIN

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VOL. XVI. MARCH, 1940 No. 6

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VANCOUVER HEALTH DEPARTMENT

STATISTICS, JANUARY, 1940

Total population—estimated	269,454
Japanese population—estimated	9,094
Chinese population—estimated	8,467
Hindu population—estimated	339

	Number	Rate per 1,000 Population
Total deaths	265	11.6
Japanese deaths	5	6.5
Chinese deaths	11	15.3
Deaths—residents only	226	9.9
BIRTH REGISTRATIONS:		
Male, 205; Female, 184	389	17.0

INFANTILE MORTALITY:	January, 1940	January, 1939
Deaths under one year of age	8	9
Death Rate—per 1,000 births	20.6	25.3
Stillbirths (not included in above)	10	8

CASES OF COMMUNICABLE DISEASES REPORTED IN THE CITY

	December, 1939		January, 1940		February 1st to 15th, 1940	
	Cases	Deaths	Cases	Deaths	Cases	Deaths
Scarlet Fever	18	0	10	0	4	0
Diphtheria	0	0	0	0	0	0
Chicken Pox	123	0	125	0	10	0
Measles	9	1	67	0	68	0
Rubella	3	0	1	0	0	0
Mumps	5	0	16	0	3	0
Whooping Cough	11	0	23	0	10	0
Typhoid Fever	0	0	0	0	0	0
Undulant Fever	0	0	0	0	1	0
Poliomyelitis	0	0	0	0	0	0
Tuberculosis	24	10	36	14	12	–
Erysipelas	5	0	7	0	0	0
Ep. Cerebrospinal Meningitis	0	0	0	0	0	0
Paratyphoid Fever	1	0	0	0	0	0
Trachoma	0	0	0	0	2	0

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

	Burnaby	West Vancr.	Richmond	North Vancr.	Vancr. Clinic	Hospitals, Private Drs.	Totals
Syphilis	1	0	0	1	24	26	52
Gonorrhœa	0	0	0	0	63	27	90

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VANCOUVER MEDICAL ASSOCIATION

Founded 1898 :: Incorporated 1906

GENERAL MEETINGS will be held on the first Tuesday of the month at 8:00 p.m.
CLINICAL MEETINGS will be held on the third Tuesday of the month at 8:00 p.m.
Place of meeting will appear on the Agenda.
General meetings will conform to the following order:

8:00 p.m.—Business as per Agenda.
9:00 p.m.—Paper of the evening.

Programme of the 42nd Annual Session

March 5—Dr. D. D. Freeze: "Anæsthesia and Analgesia."
March 19—Clinical Meeting.
April 2—Dr. H. H. Boucher: "Low Back Pain."
April 16—Clinical Meeting.
April 23—Annual Meeting.

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Iron is the *oldest* and still one of the most effective treatments for anaemia; but the *most potent form of iron medication* was not definitely known until recently.

In the past, hundreds of organic and inorganic compounds of iron have been tried clinically with widely varying results. This variation of result caused investigators to continue the study of iron absorption in anaemia. Their recent investigations confirmed the previously observed fact that ferrous salts are more readily absorbed than other forms of iron, and that all ingested iron is converted into the ferrous state before absorption. *cf. Journal C.M.A. March '33. Lucas and Henderson.*

F. Hendrych and K. Klimesch, Arch. Exptl. Path. Pharmakol 178, 178-88, 1935, regard ferrous chloride as the physiological form of iron. They find that it does not cause chronic poisoning when administered orally, but that ferrous carbonate and ferric citrate cause characteristic liver damage.

But ferrous chloride is unstable and so unpalatable that many patients refuse to continue treatment long enough to raise the haemoglobin to normal.

Former objections to the use of ferrous chloride have been overcome in Ferrochlor *E.B.S.* which presents ferrous chloride in permanent and palatable form. Each teaspoonful dose of Ferrochlor contains 2 grains of ferrous chloride, equivalent to 30 grains of reduced iron.

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THE EDITOR'S PAGE

The scheme worked out by the B. C. Medical Council's Committee on Economics, to provide voluntary Health Insurance for small groups in industrial occupations, has been presented to the public, and our readers have all had copies of the scheme.

It is, of course, largely based on the schemes already in force with certain large groups of employed persons, and the idea was to make this type of service on a group basis available to those who could not organise on a sufficiently large scale to make this possible. The scheme presents several options. It is, of course, tentative at present, and, we presume, open to modification and adjustment at any time. It will be very interesting to see what response comes from those who could benefit by such a scheme.

It is noteworthy that the only remarks on the subject, of a definitely hostile nature, came from a gentleman who was (or is?) on the Board of the Health Insurance Commission. His remarks were, we feel, hastily made, and very inaccurate. The Hon. G. M. Weir, Provincial Secretary, who also commented on the scheme, seemed to us to have taken a very fair and generous attitude. One can hardly compare the scheme, of course, with a compulsory one—which, even if all the benefits given by this scheme were granted, would still be cheaper and more economical to run.

None of us denies that an adequate scheme of Health Insurance, actuarially sound and satisfactory to both parties to it, would be the most generally acceptable scheme of all—but this is at least a step towards a wider scheme, and should, we think, be given due trial. It has the merit of aiming low at first, and not trying to do too much at one time. We wish the scheme all the luck in the world and feel that the College of Physicians and Surgeons deserves our thanks and congratulations for an excellent piece of work, which has been extremely well done.

* * * *

The BULLETIN regards itself as especially fortunate in having several valuable surveys to publish. These things are not essentially light reading: nor, to the man in search for direct information as to how to deal with a knotty case which has arisen in his practice are they apparently of very great immediate value: but they are the stuff out of which the true scientific structure of medicine is fashioned, and they represent accurate observation, and in many cases years of work.

Thus, take the review of sixty-eight cases of brain tumour, of which fifty-five are completely proven, presented from the Vancouver General Hospital records, and covering the years 1934-38. The compilers, Drs. D. P. Robertson and C. E. Gould, are to be congratulated on a very good piece of work. It is doubtful if more than two or three men in Vancouver realise that there had been sixty-eight cases of brain tumour in this city in these five years. Nor would the bare statement of this fact be of any value. But here we have histological and pathological classification, type incidence, age incidence, symptoms and signs, operative mortality, and so on. Rigid check is kept on the accuracy or otherwise of diagnoses made on admission. Eye-changes, the value of diagnostic X-rays, etc., are all dealt with: and the record is well made.

The same thing applies to Dr. Gee's very able report (soon to be published) on 2069 Aschheim-Zondek tests made in the last eight years, 1932-40. This is also a splendid piece of work. We applaud the reticence and truly scientific spirit which have kept Dr. Gee from publishing before this. She has here ample material for a considered judgment as to the value of this test, the degree of accuracy which can be attained, the extent to which it can be relied on, and a host of other details. The small percentage of errors is very striking, and shows this test to be one of very great value; twelve false positives and sixteen false negatives, some of which were later corrected, being an amazingly small number of incorrect results.

Another survey of real value is contained in the thesis we publish in this issue, written by Mr. J. H. W. Willard, M.A. Mr. Willard presents a survey that has taken weeks of careful study, as his very large bibliography will show. It deals with that wonder-working

drug, sulphanilamide, and, of course, a tremendous volume of literature is gradually being accumulated on this subject. The BULLETIN takes this opportunity of thanking Mr. Willard for giving us this survey. It was partly at our request that he undertook it—and it represents a great deal of work.

* * * *

The Greater Vancouver Health League, through its Executive Director, Mr. Edgar N. Brown, and the Venereal Diseases Section of the League, has been making a survey of the Venereal Disease situation in Vancouver. The object has been to obtain as accurate a record as possible of the number of cases under treatment by private physicians, and so by putting this with the number under clinic treatment to arrive at as accurate a result as possible.

The medical men of Vancouver co-operated very well indeed in this matter. That the report has a definite statistical value is indicated by the remarks of Dr. C. E. Dolman of the Provincial Laboratories, quoted in the survey.

One surprising feature of the report is the far greater number of cases of syphilis shown as compared to gonorrhœa. Of course, a great many cases of gonorrhœa are self-treated, but even so, we rather question the accuracy of this part of the report, and hope it will be either verified or corrected as some future date.

NEWS AND NOTES

VANCOUVER MEDICAL ASSOCIATION

The regular monthly meeting of the Association will be held on Tuesday, March 5th, in the Auditorium of the Medical-Dental Building. The speaker of the evening will be Dr. D. D. Freeze, who will speak on "Trends in Anæsthesia."

* * * *

Congratulations are extended to Dr. and Mrs. Donald H. Williams upon the birth of a son on January 29th, 1940.

* * * *

Dr. D. E. H. Cleveland recently addressed the Fraser Valley Medical Society on "Diagnosis and Treatment of Early Syphilis."

* * * *

Dr. H. McGregor of Penticton made a hurried business trip to Vancouver and New Westminster on February 9th.

* * * *

Dr. R. P. Borden of Penticton is back at his office after a recent indisposition.

* * * *

Dr. George Paine of Penticton is reported to be doing well and in better health.

* * * *

Dr. W. D. Higgs, formerly of Port Alberni, has returned from London, England.

* * * *

Dr. J. B. Swinden of Ucluelet has recovered from his recent illness.

* * * *

Dr. W. J. Knox of Kelowna was a recent visitor to Vancouver.

* * * *

Dr. B. de F. Boyce has returned to Kelowna after spending two weeks at Harrison Hot Springs.

* * * *

Dr. G. E. L. Mackinnon of Cranbrook has received the nomination as Conservative candidate for Kootenay East in the forthcoming Federal election.

* * * *

Dr. and Mrs. A. N. Beattie of Ioco are receiving congratulations on the birth of a daughter on February 1st.

Dr. and Mrs. E. J. Lyon of Prince George called at the office while in Vancouver recently.

* * * *

Dr. J. H. Carson of Prince Rupert is on an extended trip to Eastern Canada and the United States.

* * * *

Dr. A. Francis of New Denver attended the miners' bonspeil in Nelson recently.

* * * *

Dr. L. C. Steindel, who is associated with Dr. F. D. Sinclair of Cloverdale, will be married in Winnipeg.

* * * *

Dr. H. A. Whillans of Victoria is doing *locum tenens* during Dr. Steindel's absence.

* * * *

Dr. Stanley P. Findlay has taken over the practice at Fraser Lake.

* * * *

Lieut.-Col. Gordon C. Kenning, Officer Commanding No. 13 Field Ambulance, stationed at Victoria, has recovered from his recent illness and has returned to duty. Dr. and Mrs. Kenning spent a fortnight at Harrison Hot Springs Hotel.

* * * *

Major R. L. Miller of Victoria made another of his regular visits to Vancouver, spending the day effecting arrangements for recruiting and Medical Boards.

* * * *

Dr. W. E. Henderson of Chilliwack called at the office this week to discuss arrangements for Medical Services to indigents in that area.

* * * *

Lt.-Col. A. L. Jones, D.M.O., M.D. No. 11, is back at the office following a brief illness.

* * * *

Lt.-Col. Thomas McPherson of Victoria has been confined to hospital, and it is hoped he will soon be around again.

* * * *

Dr. W. T. Kergin, formerly of Prince Rupert, has taken up residence in Vancouver.

* * * *

The following doctors travelled to Vancouver to attend the meeting of the Board of Directors of the British Columbia Medical Association on January 24th: Drs. F. M. Auld, Nelson, President; P. A. C. Cousland, Victoria; W. A. Clarke, New Westminster; J. Stuart Daly, Trail; C. T. Hilton, Port Alberni; W. J. Knox, Kelowna; A. H. Meneely, Nanaimo; S. A. Wallace, Kamloops.

* * * *

Dr. J. Bain Thom of Trail, who was visiting in Vancouver, attended the meeting of the Board of Directors.

* * * *

Dr. R. Brynildsen has gone East to do post-graduate work in Chicago and Boston.

* * * *

PRELIMINARY ANNOUNCEMENT

A DINNER

Complimentary to

DR. G. F. AMYOT

Provincial Health Officer

THURSDAY, APRIL 4TH, 1940

YOU ARE REQUESTED TO RESERVE THIS DATE

CAMPBELL DAVIDSON

The sudden passing of Dr. Campbell Davidson of Qualicum Beach, Vancouver Island, on February 16th, removes from the ranks of the profession a member well known throughout the Province. Dr. Davidson had had previous warning of further attacks of coronary trouble and had been forced during recent years to lead a less active life.

During his twenty-three years at Qualicum he had contributed largely to all movements for the improvement of standards of medical service in the Upper Island District and had supported strongly the Upper Island Medical Association. He was a happy person to know and this was reflected in the atmosphere of his home.

Dr. Davidson served as Medical Officer of Health and Medical School Inspector during many years. He maintained a strong interest in matters affecting the health of the people and developed a fine organization in that area.

The late Dr. Davidson was born in Montreal, the son of Chief Justice Sir Charles Peers Davidson, and graduated from McGill University in 1898. During college days he played hockey on the McGill team when they won the Stanley Cup and was on the football team when McGill won the Allen Cup.

Before settling at Qualicum, Dr. Davidson had a wide experience as ship's surgeon, visiting all parts of the world.

To Mrs. Davidson and to his son and daughter the profession extends its sincere sympathy in their loss.

PAUL EWERT

The late Dr. Paul Ewert of Golden had just ended twenty-five years of faithful service in that district. He had endeared himself to the people as their physician and had made a fine contribution as a citizen. He possessed a personality admirably suited to his work on the C.P.R. in this mountain section. Among the members of his own profession he was well known and highly respected. He possessed a directness and honesty of purpose that had a strong appeal to men.

Dr. Carl Ewert of Prince George is a brother of the late Paul Ewert, and in the passing of years the name "Ewert" has occupied a deservedly outstanding place of honour in the professional life of this Province. The other surgeons serving the C.P.R. between Vancouver and Calgary held him in high respect as a man who knew his work and did it well.

Dr. Paul Ewert came, with his family, to Manitoba from Kansas at the age of eight. He graduated in Arts and obtained his medical degree from McGill in 1912. He served as interne at the Vancouver General Hospital and entered practice at Golden in 1914.

Dr. Ewert was active in practice during twenty-five years, and it was not until the evening of Sunday, February 4th, that he was suddenly stricken and died within half an hour. He was given a Masonic funeral on February 7th, and at the cemetery the returned men sounded "The Last Post."

It is unfortunate that Mrs. Ewert has been ill. Sincere sympathy is extended from the profession in the hope for her early recovery.

JOHN A. AMYOT

The passing of Dr. John A. Amyot in Ottawa will be mourned by the whole profession as a national loss. It is significant that one who was destined to make such an outstanding contribution to Canada should have been born in 1867. His lovable personality owed some of its natural charm to a distinguished French family of four centuries' standing in the Dominion.

Graduates of Toronto knew him; Medical Officers in the last war knew him; British authorities knew him; every doctor in Canada knew him through his position in Canadian Medicine; he was known internationally in the United States and in the League of Nations. It is not given to many to have so widely and so honourably served. To have achieved so much in one lifetime makes it possible to cease one's labours with the satisfaction of work well done.

The late Dr. Amyot retired in 1933 after forty-one years in Medicine. He graduated from the University of Toronto in 1891 and after a term as House Surgeon at the General Hospital entered practice in Toronto with a Lectureship in Pathology and Bacteriology, in which department he was Professor when the war took him overseas in 1914.

Dr. Amyot studied with Pasteur and other distinguished teachers, then really commenced busy years of service which have been partially recognized in his lifetime. He established and directed the Provincial Laboratory in Ontario; established the first post-graduate course in the University of Toronto leading to the D.P.H. qualification; was an active member of the International Commission to Study Pollution of the Great Lakes in 1912; worked widely for safe water supply and pasteurization of milk.

During the years 1914 to 1919 he served overseas. Lieut.-Col. Amyot was well known on the Western Front; in charge of sanitation in the Canadian Corps in war areas; later in command of these services with the Second Army, which embraced 260,000 troops; was a member of the Allied Health Committee in London and Paris; was later with London Headquarters as A.D.M.S. in charge of Health and Sanitation Services to the Overseas Forces of Canada.

Colonel Amyot was on three occasions Mentioned in Despatches. The C.M.G. was conferred by the late King. By the French he was made a Knight of the Legion of Honour.

Under his administration outstanding work was done in the prevention of "trench-feet," control of parasitic diseases, venereal disease and respiratory infections. Colonel Amyot applied his energy and effort to the development of the outstanding Laboratory Service of the Canadian Expeditionary Force.

At the close of the war Dr. Amyot was asked to become the first Deputy Minister of the newly organized Federal Department of Health. Later, as Deputy Minister of the Department of Pensions and National Health, he was able to direct many new Acts designed to protect the health of the Canadian people. The Dominion Council of Health was organized.

Dr. Amyot was honoured in his lifetime, serving as President in many local, national and international Health Organizations. He represented Canada on several occasions in the Health Section of the League of Nations, which Section was able to build very definite world relationships.

The work of Dr. Amyot survives him and his memory will be constantly refreshed by those who will always be gratefully appreciative of the good things which have come to us out of his life.

The late Dr. John Amyot has left a challenge to Canadian Medicine to carry on the good work. In the Province of British Columbia we have a direct descendant and disciple in the office of Provincial Health Officer, Dr. G. F. Amyot.

In extending to our colleague, Dr. Amyot, our sincerest sympathy in the loss of his father, we would join him in supporting the traditions which are his heritage.

Vancouver Medical Association

A BRIEF DISCUSSION OF SOME NEWER LABORATORY PROCEDURES

H. H. Pitts, M.D.

I must first express my appreciation on behalf of the medical staff of the Laboratory of the Vancouver General Hospital for the honour of being asked to present papers to this Association this evening. When it was suggested that we present what might be termed "A Laboratory Evening" we were rather perturbed as to what we could provide that might be of general interest. Dr. Gee has been gradually gathering data as to the confirmation or otherwise of the Friedman modification of the Aschheim Zondek tests that have been done in the Laboratory during the past 7½ years, and we felt that a presentation of this rather large series, done in a local institution, together with a general discussion of the test, might be interesting and instructive. The compilation of these figures has been no small task but has been brought as nearly up-to-date as was possible and will be presented tonight by Dr. Gee.

Up to the present we have not compiled any statistics as to the percentage of malignancies or the relative percentage of malignancy of various organs or sites in our autopsy records. It was thought that these figures might be of some general interest, at least as a basis for discussion. To Dr. Creighton was allotted the rather formidable task of compiling these statistics from the autopsy records of the past 10 years, the results of which he will present to you this evening.

My own small part in the programme will take the form of a brief discussion of a few laboratory procedures that I hope will be of general interest. So, as ringmaster of our three-ring circus, I will crack the whip and ascend the podium.

While it is probably a fact that the finding of malignant cells in ascitic or pleural effusions means that the neoplastic process is a far-advanced one and hopeless, as viewed from a curative standpoint, nevertheless, from a diagnostic standpoint, valuable information may be gained and graver prognoses given, that otherwise might be more optimistic, with the erroneous conception that the effusion is of tuberculous, rheumatic, cardiac or cirrhotic origin. It must, however, be borne in mind that one does not always find these cells when they may be present and one also finds them when they are not present. I have been guilty on both counts. Some pathologists are in favour of centrifuging the fluid and making a direct smear from the precipitate, but we have felt somewhat safer in the procedure of coagulating the fluid with formalin and alcohol and a few drops of glacial acetic acid. Any cells present are usually carried down with the coagulum and then this is carried through the various stages of fixation as for tissues, mounted in paraffin and sectioned. One may also centrifuge the fluid and then subject the precipitate to coagulation with the subsequent steps as above. One can frequently make a fairly dogmatic diagnosis of the origin of the growth from the cells present, but probably, more frequently, one can state only that it is a malignant process of uncertain origin. I have found the greatest source of error in ascitic fluids from cases of hepatic cirrhosis, where large cells, apparently of endothelial origin, were present and which I considered to be malignant, only to be proven wrong at the autopsy table. My object in mentioning these ascitic and pleural fluids is to suggest that the routine examination of these fluids for malignant cells, whether malignancy is suspected or not, is a worthwhile procedure in conjunction with guinea-pig inoculation, culture, etc.

Pneumococcus typing is not an entirely new procedure, and was first suggested by Neufeld and perfected by Sabin in 1933. There are now 35 isolated types of pneumococci, types 33, 34 and 35 having been isolated in the past few months, and for all of these, with the exception of 34 and 35, antipneumococcic serum has been prepared. In the V.G.H. Lab. we have found the Lederle typing sera very satisfactory, although several of the large

biological houses manufacture a product probably equally as good. The Lederle sera are supplied in six Group Mixtures with methylene blue incorporated in them, as follows: Group A, Types 1, 2 and 7; Group B, Types 3, 4, 5, 6, 8; Group C, Types 9, 12, 14, 15 and 17; Group D, Types 10, 11, 13, 20, 22 and 24; Group E, Types 16, 18, 19, 21 and 28; Group F, Types 23, 25, 27, 29, 31, 32. Types 26 and 6 are the same or interchangeable, as are also Types 15 and 30. The rationale of using these group mixtures is similar to that of skin testing with group mixtures of proteins, pollens, etc., and very materially curtails and expedites the work required in ascertaining the specific pneumococcus responsible for this particular infection. A drop of the sputum to be tested is first examined for the presence of pneumococci, and if they are found a drop or two of the sputum is placed on each of 6 coverslips or slides, to each of which is added a drop or two of Group Mixtures A to F respectively and each slide so labelled. Generally, within a few minutes, at room temperature, or after incubation for a few minutes, one will note, on examination under the microscope, swelling of the capsules of the pneumococci in one of the slides and none in any of the other five. We will say, for example, that this occurs in Slide C. This means that the specific organism in this case belongs to either type 9, 12, 14, 15 or 17. The same procedure is now carried out using a drop or two of sputum mixed with an equal quantity of each of these typing sera. After the usual time it will be found that there is swelling of the capsules of the pneumococci in the slide labelled, say 17, and no swelling in any of the other slides. Therefore this particular organism is Pneumococcus Type 17, and the attending physician may immediately institute specific antipneumococci serum therapy or Dagenan therapy, a combination of both, or whatever method of choice. The earlier the sputum is typed, the sooner the specific therapy may be instituted, and while it is claimed by a number of writers, reporting large series of cases, that Dagenan ingestion does not interfere with typing, our experience, in a considerable number of cases, has not supported this tenet and that probably within 12-24 hours after fairly intensive Dagenan therapy typing is impossible. A clean receptacle without preservative or antiseptic should be used to receive the sputum, and if possible the specimen should be from the bronchi and not merely salivary secretion. In infants, swabs from the laryngopharynx may be used for typing. The value of liver function tests is a very controversial question, and of the several that have been elaborated it would seem that the Bromsulphalein Test is the one productive of the most information. Experimentally 85% of the amount of the dye injected intravenously into normal rabbits is excreted in the bile within one hour. The liver cells rapidly absorb it from the blood stream, as proved by extirpation of the liver when the dye is retained in the bloom stream almost to 100%. Two mgm. per kilo of body weight or the body weight divided by 55 gives the exact amount in c.c. of a 5% solution required. This is injected intravenously very slowly, and, 30 minutes after, 4-5 cc. of blood are withdrawn from the other arm and placed in a dry test tube without preservative. It is allowed to coagulate, and, after centrifuging, the serum is pipetted off and equally divided in two tubes. To one is added 1 or 2 drops of a 10% solution of NaOH to bring out the rather violet color of the dye, and to the other 1 drop of 5% HCl to clear it of any hæmolysis. The alkalinized tube is compared in a special comparator box against tubes of known standards which give the exact percentage of the dye present in the serum. Normally the dye is removed from the bloom stream within 30 minutes, but in liver disease varying amounts from almost 100% downwards may be retained, due to the inability of the damaged liver cells to absorb it, and the percentage retained expressed directly the degree of impaired liver function. Several of the larger institutions throughout the United States and Canada use this test almost exclusively, and our own Laboratory is equipped to carry out this procedure.

During the past two or three years considerable has been added to the literature concerning vitamin K in hæmorrhagic diatheses and more especially in the jaundiced patient in whom surgical intervention is indicated. Vitamin K is a fat-soluble vitamin obtained chiefly from alfalfa and marketed either in the form of a concentrate in gelatine capsules or liquid extract. It is usually prescribed in conjunction with bile salts. A test which developed from the experimental work with this vitamin is the Prothombin Time. Quick was one of the first to elaborate a test for measuring this, as it was felt that a truer and more delicate index of the coagulability of the blood than the clotting time was needed and

especially to follow the effect of the vitamin K, which has been found to definitely shorten the prothrombin time and expedite coagulation. It is generally agreed that four agents are necessary for the clotting of blood—prothrombin (which has been termed a pro-enzyme) plus thromboplastin or thrombokinase plus calcium which produces thrombin. This acts upon the fibrinogen to produce fibrin, the basis of clot formation. It has been determined that there is no appreciable deficiency of calcium and fibrinogen in jaundice that would account for the tendency to hæmorrhage, and Quick reasoned that, by keeping the thromboplastin and calcium constant, the rate of coagulation must be dependent on the prothrombin and could serve as a direct means for estimating this. He obtained his thromboplastin or thrombokinase by macerating a fresh rabbit or guinea-pig brain, after carefully dissecting away the blood vessels, in a mortar with acetone and extracting it down to a fine powder. Five cc. of physiological NaCl containing 0.1 cc. of sodium oxalate solution are mixed with 0.3 gm. of this powder and incubated at 45 degrees C. for 10 minutes, then centrifuged at slow speed for 3 minutes and the supernatant milky fluid is pipetted off. One-tenth cc. of the plasma of oxalated blood is mixed with an equal quantity of the thromboplastin solution and to this is quickly added an equal quantity of a slightly over 1% solution of calcium chloride. The time required for the formation of a clot after this final step is called the prothrombin time and has been found to lie usually between 12 and 13 seconds. Quick has compiled a graph and curve from which one may readily read off the percentage of normal for the completed test. Quick states that as much as 80% of the prothrombin in the blood may be lost before serious hæmorrhage results, but that a prothrombin time of 15 to 20% of normal is a very critical level and should be treated by immediate transfusion or transfusions, depending on the decrease of the prothrombin time. Higher but still subnormal values are found to respond to vitamin K therapy in conjunction with bile salts, especially in jaundiced patients, although Quick found that the prothrombin time was normal in more than 50% of such cases in his series. Likewise in hæmophilia it is normal.

We have tried Quick's method on several occasions with rather unsatisfactory results even in normal controls, and one objection is the instability of the thromboplastin, which retains its potency for only one week. Smith has recommended a rather simpler, although, he claims, as informative a method using a thromboplastin made by grinding up fresh ox or rabbit brain or lung with saline 10 gm. to 10 cc. and extracting it for two hours, then straining through gauze. This keeps for several weeks in the refrigerator. 0.1 cc. of this plus 0.7 cc. of a known normal blood are mixed in a test tube, and this is inverted every 5 seconds until clotting occurs. If clotting occurs before 25 seconds or later than 60 seconds the thromboplastin is too concentrated or too weak, respectively, and should be diluted or a new lot prepared as the case may be. Normally it should clot by this method in approximately 35 seconds. Blood from the patient to be tested is treated as above described and the result is given by the following formula: $\frac{35}{\text{C.T. of unknown}} \times 100$. Hæmorrhage occurs, according to Smith, when the prothrombin falls to the 30-50% of normal range. There are several other tests, somewhat more complicated, to measure prothrombin time, but it is stated that none actually measure it directly, as many factors may alter it besides variations of the prothrombin itself, so that these tests on the same patient may vary at different times under the same condtiions.

Our own experience with these tests, i.e., Quick's and Smith's, have not been particularly successful, chiefly because of difficulty with the thromboplastin. However, we hope to perfect these tests gradually to a point in which we feel some degree of confidence in the result, as they are apparently of definite value in certain instances of hæmorrhagic diathesis.

I fear that this presentation may have been rather boring and dry, but its purpose was to briefly describe a few of the newer procedures and suggest that they might be more frequently used, to advantage.

In conclusion, may I again express my deep appreciation for the honour of addressing you this evening.

British Columbia Medical Association

(Canadian Medical Association, British Columbia Division)

President ..... Dr. F. M. Auld, Nelson
First Vice-President ..... Dr. E. Murray Blair, Vancouver
Second Vice-President ..... Dr. C. H. Hankinson, Prince Rupert
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Executive Secretary ..... Dr. M. W. Thomas, Vancouver

BRITISH COLUMBIA MEDICAL ASSOCIATION THE 1940 ANNUAL MEETING WILL BE HELD IN NELSON IN SEPTEMBER

At its last regular meeting the Board of Directors of the British Columbia Medical Association definitely decided that it would accept the invitation of the West Kootenay Medical Association to hold the 1940 Annual Meeting in Nelson, the home city of Dr. F. M. Auld, President.

Dr. J. Stuart Daly of Trail, President of the West Kootenay Medical Association, attended the Board meeting and reaffirmed the wish of the West Kootenay Medical Association to be host to the provincial association this year.

Members are requested at this date to make plans which would allow their attendance at the 1940 Annual Meeting in Nelson.

INCOME TAX

The Provincial returns from doctors must be made on or before March 31st.

Dominion returns fall due on April 30th.

If claims are made for car expenses it will be necessary to keep records that you may be able to produce actual documentary evidence. Records are not necessary if claims are based on mileage, which for 1939 is allowable at the rate of 8c per mile.

MEDICAL SERVICES TO INDIGENTS

For the information of all concerned it is noted that the arrangement whereby all municipalities may receive 33c per capita governmental grant is applicable for all cases whether employable or unemployable.

The 33c contribution by the Government is contingent upon the provision of a like or larger amount by the municipality to build a 66c per capita minimum medical service fund.

These monies are for medical services only. The medical service fund is not to be used to purchase medicines or other supplies.

Some municipalities have made a larger contribution than the required 33c in consideration of the needs of persons who do not fall under the above classifications.

The inclusion of the unemployable persons widens the scope of the scheme. At present those in receipt of Old Age Pensions and Mothers' Allowances do not fall under this plan.

It is urged that members of the profession in all municipalities assure themselves that the local authority is making provision for the available governmental grant of 33c per capita. This applies to all heads of families and single persons in each municipality. Practically all municipalities have completed arrangements for thus providing medical services for this part of their indigent population. All municipalities may provide such a fund.

Doctors are urged to read the above and use it.

COLLEGE OF PHYSICIANS AND SURGEONS OF B. C. MEDICAL SERVICE PLANS

The plans of the larger associations, such as the Telephone Employees and the B. C. Electric Office Employees, are operating satisfactorily in providing Medical Services to members and dependants on a prepayment basis through deductions from pay-roll.

The new "Medical Services Association" is now being actively promoted. Sufficient interest has been shown by many groups of employees in various industries to make it necessary to proceed with incorporation.

The object of the Association is:

> "To provide or arrange for the provision to members and their dependants of any or all services required in the prevention, diagnosis or treatment of illness on a non-profit, prepayment and voluntary basis."

Small groups of employees are thus enabled to co-operatively join in securing through this new association a comprehensive Medical Service.

The patient will be given "Free Choice of Doctor."

Normal Patient-Physician Relationships will be preserved.

This plan has been developed to meet the needs of employees earning less than $2400.00 per annum.

The Committee on Economics of the Council of the College of Physicians and Surgeons of B. C. has worked out the details and the terms of service, which were accepted at the Annual Meeting last September.

At its inception the plan is being introduced in the Greater Vancouver and New Westminster areas.

CANADIAN MEDICAL ASSOCIATION MEMBERSHIP

The Committee in charge, under the Chairmanship of Dr. W. E. Ainley, is pleased to report that the effort to increase the membership in the Canadian Medical Association as from British Columbia has been successful in adding fifty-five new members. The enrolment for 1940 at this date totals 300. New memberships are being received daily at this office.

Cheques for membership are made payable to the College of Physicians and Surgeons of B. C. The fee for membership in the C.M.A. for 1940 is $8.00. In order that no numbers of the *Canadian Medical Association Journal* are missed, early remittance is urged.

CANADIAN MEDICAL ASSOCIATION ANNUAL MEETING JUNE 17-21

The following are the representatives from British Columbia on General Council of the Canadian Medical Association: Drs. E. Murray Blair, Vancouver; W. A. Clarke, New Westminster; W. Allan Fraser, Victoria; Gordon C. Kenning, Victoria; H. H. Milburn, Vancouver; G. F. Strong, Vancouver; S. A. Wallace, Kamloops.

At the last meeting of the Board of Directors it was decided that an attempt would be made to discover members who will be able to attend the Sessions of the General Council of the Canadian Medical Association at the meeting in Toronto in June. Members are asked to notify the office well in advance of the Toronto meeting of their possible attendance.

THE CHEMOTHERAPY OF SULFANILAMIDE AND ITS DERIVATIVES

By J. H. W. Willard, M.A.

The wealth of clinical reports on chemotherapy of the sulfanilamide derivatives seems at this time to merit a review. This may clarify the nomenclature and conflicting notions as to their efficacy. New and more practical derivatives are appearing rapidly and consequently the preventative and curative value of this field of drugs is enlarging. The subject will be discussed under (1) Various derivatives, (2) absorption and distribution in the body fluids, (3) mechanism of action, (4) administering the drug, (5) comparative values, (6) diseases and organisms against which they are effective, (7) toxic effects.

The many derivatives of sulfanilamide were synthesized in an attempt to reduce toxic effects, increase absorption and retention, and to improve their efficacy: they are not specifically used against certain organisms or diseases. The most popular of these drugs are Sulfapyridine (Dagenan, M and B 693) and sulfanilamide, although recently the derivatives sulfathiazol and sulfamethylthiazol, which are closely related to sulfapyridine, have been shown to possess greater curative powers and to be less toxic.

Among other members of this increasingly large family are prontosil (prontosil flavum), neoprontosil (prontosil soluble), benzyl sulfanilamide (septazine, proseptazine), sulfanilyl sulfanilamide (disulon), sulfanilyl dimethyl sulfanilamide (uliron or uleron), 4, 4 diaminodiphenylsulfone, di-(acetylamino) diphenyl-sulfone, and para-benzyl-aminobenzene sulfanomide.

Dr. C. A. H. Buttle divides the derivatives of sulfanilamide into two groups: (a) Those with substituents in the amino group and (b) those with them in the amide group. Included in the first group are prontosil rubrum, prontosil soluble or neoprontosil, rubiazol, proseptasine and soluseptasine. The activity of this group is probably due to their breakdown within the body to sulfanilamide. Drugs of this group have no advantage over sulfanilamide in the range of infections which could be dealt with, and although some were less toxic they were also less active than sulfanilamide. In the second group were uleron abucid, ethanol sulfanilamide, disulfanilamide, sulfapyridine or dagenan, rodilone, benzylsulfanilamide and sulfathiazol. These drugs probably do not break down into sulfanilamide within the body but are themselves active agents against bacteria.

The Absorption and Distribution of Sulfanilamide in the Body Fluids

Dr. Ellison of Manhurst clinic outlined the absorption and distribution of sulfanilamide in the body fluids as follows: (1) Sulfanilamide and acetyl sulfanilamide are found in equal quantities of each in both the blood and urine; (2) the spinal fluid contains 25 to 30% less than the blood; (3) sulfanilamide is also found in prostatic and amniotic fluids and breast milk; (4) Dr. W. W. Spink finds that the free sulfanilamide level of the synovial fluid tended to approximate the level in the blood.

Mechanism of the Action.

There are many theories regarding the mechanism of the action of this class of drugs. Edna R. Main, Lawrence E. Shinn and R. R. Mellon point out that peroxide accumulation is associated with retardation of growth observed in pneumococcus culture containing sulfanilamide or structurally related compounds which have anti-catalase activity. The concentration of peroxide per unit of growth may be from two to ten times as great in the presence of the compounds as in the control culture. P. A. Shaffer believes the drugs provide a mechanism by which the sterilizing oxidation intensity of molecular oxygen is applied nearly at its maximum to bacteria and unavoidably also to some extent to host cells.

Some interesting facts regarding the action of this drug are:

1. Relative ineffectiveness of sulfanilamide against a strain of bacteria in vitro, while in vivo or if reinforced by human serum the bacteriostatic action is tremendous.
2. Reports of cases where very small doses were given and where concentrations of the drug were as low as 1 in 10,000 or 1 in 18,000 and still effected the miraculous cures.
3. Various strains of some organisms respond differently and may or may not be killed even when the drug is administered in large doses.

4. The fact that though there is no regular effect on phagocytosis or increase in leukocytosis, or evidence of definite opsonic effect to enhance phagocytosis, sulfanilamide therapy is apparently potent as shown by no direct bacteriostatic action in saline media but a marked one in human serum, even in dilutions of 1 in 100,000 sulfanilamide. Apparently bacteriostasis and phagocytosis reinforce each other to promote cure. Recently bacteriologists claim to obtain equal bacteriostatic effect with sulfanilamide, in normal saline as in human sera, if the incubation temperature is raised to 40 degrees Centigrade.

5. Some writers suggest that sulfanilamide exerts a restraining power on bacteria and holds them in check until the body has a chance to build up its own antibodies to promote cure. Sulfanilamide probably makes the organisms less virulent, and hence more phagocytized.

6. The so-called resistance factor of the host has been shown to be of importance, especially in experiments done on rabbit pneumonia. Here sulfanilamide decreases the pneumonia proper but the host will not survive unless the so-called resistance or fitness factor is up to a certain minimum level so that the rabbit can remove the germ from the blood stream and in this way take advantage of the sulfanilamide action which has held them in check and probably rendered them less virulent. This fitness factor can be supplied or raised by administering liver extract or vitamin C or suprarenal extract. This would suggest enzyme and coenzyme action with vitamin C as the hydrogen acceptor and bespeaks a mechanism of biological oxidation. Perhaps some of the failures can be cured with the addition of high vitamin C and liver concentrates.

A few words must be said regarding the administration of these drugs, and their comparative values.

In most cases it is administered orally, although topical administering of sulfanilamide has been used at the Minneapolis General Hospital in a series of compound fractures with good results. Hypodermoclysis, except in cases of severe nausea, vomiting or coma, is of very limited use. Rectal administration is unsatisfactory due to the uncertain absorption, in the opinion of Dr. W. Wright of Minneapolis; whereas Professor Campbell of the British Medical Association believes that rectal administration of the drug suspended in saline and alkalinized to bring it into solution, should be used as an alternative to parenteral injection where severe vomiting rendered oral administration impossible. Dr. E. K. Marshall and W. C. Cutting state that very little increased absorption occurs with a large dose of the very insoluble compounds (for example, disulfanilamide) as compared with a small dose. Sulfanilamide, when given in solution by mouth, is absorbed much more quickly than when given in solid form. Absorption is very slight from the stomach, but very rapid from the intestine. Professor Campbell of the British Medical Association maintains that a concentration of sulfanilamide in the blood of 4 mg. per 100 cc. is probably as effective as a concentration of 10 mg.

E. G. Lucas and D. P. Mitchell find, from a study of eleven patients given sulfanilamide by mouth, that 1 to 2 mg. doses produce a maximum rise to 5 to 10 mg. per cent in blood sulfanilamide in 2 to 6 hours, and higher values cannot be obtained by larger doses or repeated administration unless there be renal damage. The output of sulfanilamide in urine is directly proportional to dose, 45 to 60 per cent being excreted in twenty-four hours, and in two to four days output equals intake. After about twelve hours the majority of sulfanilamide in both blood and urine is in the conjugate, inert form. E. K. Marshall, Jr., states that a concentration of 10 per cent in the blood stream seems to be necessary for full effectiveness. This could be obtained by a dosage of 1 gm. per day for every twenty pounds of body weight; children, however, needed fifty per cent more, and infants about three times as much per unit of body weight. Dr. W. Harry Feinstone finds that the concentration of sulfanilamide in blood of patients remains at a curative level for longer periods when given in oil than when given in water or gum arabic. According to Dr. Sara E. Branham, of the United States Public Health Service, the combination of these drugs with serum gives better protection than either the drugs or the serum alone.

Comparative Value.

There is no evidence that different members of the sulfanilamide group were more effective for one type of bacterial infection than for another, and a development of a drug resistance in a virulent strain had not been established. The drugs were relatively ineffective in localized infections of some duration and exo-toxin diseases, for example, diphtheria. M & B 693 (Dagenan or sulfapyridine) was effective in infections with pneumococcus of all types, whereas sulfanilamide acted only against Type 3. It was more effective than sulfanilamide in staphylococcal and gonococcal infections and equally effective in streptococcal and meningococcal diseases. Albucid, which appeared to be completely non-toxic, was effective in gonorrhœa, especially in females. Dr. Sara E. Branham, of the United States Public Health Service, fiinds that, weight for weight, sulfapyridine seems more effective than sulfanilamide. The experience of Drs. E. N. Cook and E. B. Sutton, of the Mayo Clinic, is that M & B 693 is more effective in gonococcal infection and sulfanilamide.

Benzylsulfanilamide is regarded by Dr. Hans Molitor and Harry Robinson as practically non-toxic although its anti-streptococcal activity was quite pronounced. Their report culminated a large number of acute, accumulative and chronic toxicity experiments in mice, rats, rabbits and dogs.

Dr. E. K. Marshall finds that ethanol sulfanilamide is absorbed and excreted very rapidly, while disulfanilamide is absorbed slowly and excreted rapidly in comparison with sulfanilamide. Sulfanilamide derivatives do not all pass into the spinal fluid as readily as do sulfanilamide. Up until recently the best of these derivatives seems to have been sulfapyridine. The most recent and effective of the sulfanilamide derivatives are "sulfathiazol" and "sulfamethylthiazol." They are chemically related to sulfapyridine. They combine with acetic acid to a much smaller extent than sulfapyridine. Sulfathiazol has a very low toxicity. It has been shown to be better for pneumonia treatment than even sulfapyridine. Pus-forming staphylococci are also yielding to it, especially those that have hitherto not responded well to chemotherapy, as larger doses can be given over longer periods (less toxic). Nausea is practically absent with its use. Sulfamethylthiazol is proving to be even superior to sulfathiazol for staphylococcus and at least as effective for pneumonia. Drs. W. E. Herrell and A. E. Brown of the Mayo Clinic report on an experiment showing the comparative effect of some of the more popular sulfanilamide derivatives. The drugs were added in equal concentration to broth cultures containing 12-15 colonies per cc. After seven hours: Controls had 21,360 colonies; sulfanilamide, 2,760 colonies; sulfapyridine, 2,820 colonies; sulfathiazol, 2,400 colonies; sulfamethylthiazol, 15 colonies. The germs were completely unable to multiply in the presence of the newest chemical remedy.

Efficacy.

These drugs have now the enviable reputation of curing, and in some cases preventing, some thirty-four diseases. Following is a list of diseases and organisms against which sulfanilamide, sulfapyridine or sulfamethylthiazol have enjoyed marked success: Type a organisms of the B. hæmolytic streptococcus, gonococcus, meningococcal meningitis and the pneumococcus, trachoma, staphylococcus, cerebrospinal meningitis, gas gangrene, streptococcal puerperal infections, undulant fever, peritonitis, pneumococcus meningitis, lobar pneumonia. It has been of aid in recoveries from the Sonne strain of dysentery bacillus, E. typhi, E. paratyphi, Clostridium Welchi, influenzal meningitis, actinomycosis, erysipelas, Hæmophilus influenza bacillus, tonsillitis, filarial elephantiasis, plague, acute salpingo-oöphoritis, acute gonorrhœal cervicitis, acute parametritis, bacterial endocarditis, due to streptococcus viridans, lymphogranuloma, chancroid, some non-specific urinary tract infections, chronic ulcerative colitis, pemphigus, and Lupus erythematosus. There are conflicting reports regarding its effect on malaria and smallpox, and its value has yet to be proved. It shows promise, however, in the fight against rheumatic fever. It seems to be unsuccessful in scarlet fever and human tuberculosis, although it has been shown by Arnold R. Rich that it inhibits the development of experimental tuberculosis in the highly susceptible guinea pig.

Diseases and Organisms Against Which It Is Effective.

Pneumonia: Some conspicuous examples of the efficacy of the drug appears in 627 cases

of lobar pneumonia with a mortality rate of only 5.4%, as reported in August, 1939, at a meeting of the British Medical Association (by Dr. W. F. Gainsford).

Dr. W. A. MacCall reports that with the use of sulfapyridine this drug was effective in pneumococcal infections and improvement was noted within 24 hours. The total leucocyte count seems to be the best indicator of progress. Resolution and spread of the process are delayed when the count remains high, suggesting that specific antiserum may be of value when the patient's antibody response is slow. In bronchopneumonia the drug seems promising, and it has been of benefit in cases in which other treatment failed. In almost all cases temperature fell on administering of the drug. This has been so constant that an antipyretic effect is suggested.

O. E. Romcke reports from Norway on the use of sulfapyridine in 342 cases of pneumonia, from October, 1938, to May, 1939, that mortality was 5.8%. For 245 cases of lobar pneumonia the mortality was 4.3%. For patients under fifty years the mortality was 1.6%. The most frequent complications were pleurisy, otitis and empyema. The average dose of sulfapyridine in persons older than ten years was 22 grams (total).

Dr. Maxwell Finland of Thorndyke Memorial Laboratory, Boston, states that serum can be used and will be successful in about two-thirds of the cases of pneumonia due to pneumococcus. Sulfapyridine is probably useful in all types of pneumococcus pneumonia and is probably as successful if not more so than sulfanilamide, and less toxic. Typing and other tests to determine the kind of germs causing the pneumonia should be done, Dr. Finland believes, even if the doctor expects to treat the patient with a chemical remedy instead of the serum. If the patient, then, cannot stand the toxic effect, the serum may be administered without further delay.

Dr. F. G. Smith reports on 50 cases of acute lobar pneumonia in adults treated with sulfapyridine, stating that of 50 unselected consecutive cases these had a mortality rate of 8% contrasted with previous mortality series of 678 cases of 32%.

Dr. W. Barry Wood, Jr., presents evidence that type-specific antibodies play an important rôle in the process of recovery from pneumococcal pneumonia following treatment with sulfapyridine. The lateness of the appearance of circulation antobodies is offered as a possible explanation for the relapses which frequently occur when sulfapyridine therapy is discontinued too soon.

Dr. E. N. McDermitt (Galway) said that he had gained the impression that in lobar pneumonia treated with sulfanilamide resolution of the consolidated area was slower, and in empyema the pus was thin in consistence. These changes might be due to the leucopenia which so often accompanied administration of the sulfanilamide.

Gonorrhœa: Dr. F. J. T. Borvie of Aberdeen reports that sulfanilamide gave cures in 70 to 80% of the cases, uleron in 70 to 90% of the cases, and sulfapyridine (M & B 693, and Dagenan) in 85 to 95%. Sulfapyridine appeared to be the drug of choice since it could be given at once, whereas optimal results with sulfanilamide and uleron were obtained only if the treatment were postponed for about ten days from the onset of the disease. After the treatment with sulfapyridine there was a very low incidence of complications (1.5%) as compared with the high figure (25 to 30%) which was the rate before chemotherapy. A total of 20 gm. of sulfapyridine was sufficient. This could be given in daily 3 gm. doses for six or seven days, or 4 gm. could be given at once, then 2 gm. four times a day until the total amount reached 20 gm. When the latter method was used nausea lasting from twelve to twenty-four hours was common, but otherwise there appeared to be no danger and the results were better. In a series of seven cases of gonococcal ophthalmia neonatorum treated with sulfapyridine all became bacteriologically negative within thirty-six hours; the confinement to hospital was reduced to about seven days as compared with the much longer periods needed for older methods of treatment.

Dr. R. E. Gillett reports that acute gonorrhœal cervicitis was markedly helped but it was of little value when the disease became chronic. Acute parametritis was likewise markedly benefitted.

Drs. E. N. Cook and E. B. Sutton of the Mayo Clinic state that sulfapyridine is better than sulfanilamide for gonococcus infections. It shows apparent cures in 1 to 8 days, with no failures in 18 acute and chronic cases. They add it is not long enough time yet to be

sure there will be no relapse. The chemical is most effective when combined with "mild local treatment."

Dr. W. Wright of Minneapolis reports on their results using sulfanilamide. They considered it the best therapeutic agent to date. This was two years ago. The regular course of treatment by them in the average adult male or female consists of the following: 80 grains per day for 4 days; 60 grains per day for 3 days; 40 grains per day for 7 days; 20 grains per day for 7 days. This was administered in four equally divided doses throughout the day, with equal amounts of sodium bicarbonate to decrease acidosis and toxic symptoms. 140 males and 49 female cases were under observation till a definite cure was established. Their test of a cure consisted of the following in the male:

1. Negative smears from prostate.
2. Negative smears after sound.
3. Urine absolutely clear, or if persistent shreds, then multiple negative smears of shreds.
4. Negative smears after 1% silver nitrate (1% Ag. No_3).
5. No reaction after injecting 30/100 gonococcus filtrate intracutaneously.

A cure for female cases was complete after the following:

1. At least 10 to 20 consecutive smears showing negative instead of the required 3 consecutive negative smears.
2. Clinically negative for discharge.
3. Absence of pain or masses in the pelvis.

A good result meant negative smears, clear urine, and absence of discharge within two weeks after beginning the sulfanilamide treatment. A fair result means definite improvement with sulfanilamide, but in these cases additional medication such as neosilval, protargol irrigations or Corbus-ferric filtrate was used. These apparent cures must be within a month after chemotherapy is started.

Out of 140 males 68% were good results, 12% were fair results, 20% were failures—some couldn't tolerate the drug (10%). The 40 females showed 80% cure. Of 2,672 cases from various clinics they have found 80.9% cure. Possibly failures are due to certain strains that are sulfanilamide resistant.

They have noted that a patient treated with sulfanilamide and not responding usually responds less to filtrate, protargol and irrigations than those not previously given the drug. This may be due to a drug idiosyncrasy or lack of immunity built up in the patient, or an increased resistance of the gonococcus.

The question of contra-indication of other drugs to sulfanilamide is as yet not settled. They have used sulfanilamide along with other drugs such as bromides, luminal and other sedatives with no unusual effect.

In gonorrhœa of pregnancy it can apparently be used with safety to mother and child and prevent gonorrhœal ophthalmia. Dr. Speert found that by giving sulfanilamide to mothers in labour and checking the blood in the cord after delivery, the sulfanilamide concentration in the fœtal circulation approaches the concentration of sulfanilamide in maternal blood. He has observed no ill effects on the newborn child.

Bacterial endocarditis due to streptococcus viridans is reported on by Drs. S. R. Kelson and P. D. White. They employed sulfapyridine along with the blood clot-dissolving heparin. Of three patients, three recovered and two of these remained well from 1 to more than 5 months. The sulfapyridine checks the growth of the germs if it doesn't kill them outright, while the heparin can, it is believed, prevent further development of clumps by reducing the ease with which the blood clots. This also prevents the danger of an artery getting plugged by one of the germ blood clumps that so often gets free from its location. The growth of more vegetations is checked. They believe this treatment gives more promise than any method they have used or heard of in the past. Patients should be watched and diagnosis certain. The treatment can do no harm and the benefit outweighs the risk.

Drs. Meyer Friedman of San Francisco and W. W. Hamburger and L. N. Ratz of Chicago also believe in this heparin treatment.

Sulfanilamide and sulfapyridine have both been previously tried in this fatal heart disease with a few cases of recovery.

Drs. W. W. Spink and F. H. Crags report on 11 persons suffering from subacute bacterial endocarditis due to streptococcus viridans and on one person showing staphylococcus albus infection whom they treated with sulfanilamide. Except for two patients, the bactericidal effect was only temporary and dependant upon continued use of the drug. One of the two who improved was well nine months afterward but the other eventually died of the disease. All subjects had bacteriæmia. The drug rendered the blood temporarily sterile in 6 of the 12. Several took the drug over a long period, with a marked erythrocyte fall in only one and without a depression of leukocytes in any instance. A relation between the amount of free blood sulfanilamide and its effect on the bacteriæmia was not apparent. The doctors believe that the drug is of doubtful value in the treatment of bacterial endocarditis because the proliferating mass of bacteria situated deep in the vegetations are probably too well protected for the drug, although those on the surface and in the circulating blood may be destroyed.

Peritonitis and sulfanilamide therapy is reported on by Drs. W. E. Ladd, T. W. Botsford and E. C. Curnen of the Harvard Medical School. They find that the death rate at the Children's Hospital, Boston, is cut from 73% to 20%. Their treatment consisted of making a small surgical incision into the abdomen, usually under local anæsthetic, and drawing out a bit of the pus for examination to determine the germ causing the trouble. A drain is left in the wound to draw off more of the pus, and sulfanilamide is immediately given by hypodermic injection until the patient is able to take it by mouth. If examination of the pus shows that the germ is pneumococcus (in most of these cases it is either the pneumococcus or the streptococcus), sulfapyridine is given instead of sulfanilamide and anti-pneumonia serum of the correct type is also given.

Acute Suppurative Arthritis due to hæmolytic streptococcus treated with sulfanilamdie is reported on by W. W. Spink. A patient with severe streptococcic infection (sepsis), including tonsillitis, pneumonia, acute glomerular nephritis with nitrogen retention and suppurative arthritis of the knee joint, was treated with sulfanilamide. There was complete restoration of joint function. A study of the exudate from the joint cavity obtained before the sulfanilamide therapy showed short chains of cocci, mostly extra-cellular. After sulfanilamide administrations large numbers of cocci were intracellular and the extracellular organisms were pleomorphic and stained poorly. These abstracts confirmed the experimental studies of others. The free sulfanilamide level of synovial fluid tended to approximate the level of the blood.

Streptococcal puerperal infections are reported on by Dr. N. Kenny of London, who finds the death rate reduced from 28% to about 5% by sulfanilamide therapy. An early series of cases had received an average of 18 gm. of prontosil rubrum and the mortality rate in this series (5.3%) had not been improved upon by much larger doses of sulfanilamide in subsequent series. There was now a tendency to give too large doses, and a return to moderate doses of prontosil rubrum would produce less toxic effects. In sulfanilamide treatment of B. coli pyelitis of pregnancy the smallest possible dose should be used in view of the labile character of the hæmopoietic system at this time. Usually 1.5 gm. in 24 hours was sufficient and more than 3 gm. had never been necessary. The proper prophylaxis of puerperal infections by strict attention to asepsis should not be relaxed. The sulfanilamide drugs should be used as a prophylactic measure only when there is reason to suspect the presence of pathogenic streptococci in the atmosphere, and in such cases the drug should be given in full curative doses.

Dr. W. E. Herrell and Dr. A. B. Brown of the Mayo Clinic report that the *pus-forming staphylococci* are being controlled by the new derivative sulfamethylthiazol. They have found this effective in cases of blood-poisoning and pneumonia, and mention a five-day cure in one case of pus-forming staphylococci as well as laboratory tests showing the new chemical completely stopped the growth of such germs. They found it less toxic than sulfapyridine and very effective in pneumonia treatment, as patients showed striking recovery in forty-eight hours. They believe it promises success in controlling a whole new group of diseases due to the staphylococci. They mention one case of staphylococci blood infection where the temperature from from 104 to 100 degrees in the first 24 hours after administration. In forty-eight hours the temperature was down to 99 degrees F., and in

five days was normal. The patient had no gastro-intestinal irritation and was able to take meals regularly, although, with sulfapyridine treatment, which was first tried, she became so sick the medicine had to be discontinued.

Dr. L. G. Carroll of St. Louis reports that he has had great success using sulfamethylthiazol against staphylococcus. *Hæmophilus influenza bacillus* infection was treated by Dr. J. H. McLeod of Washington with sulfapyridine. The subject was an 8-months-old baby with conjunctivitis, followed by an ear infection and subsequently pneumonia. There were a few pneumococcus germs present but lots of the hæmophilus influenza bacillus. Twenty-four hours after sulfapyridine administration, the baby was much improved and recovered completely in a short time.

Dr. Margaret Pitman paralleled Dr. McLeod's work on hæmophilus influenza bacillus with mice. She found that 70-100% of the mice were protected against 100 M.L.D. of the germ with 8 mg. of sulfapyridine given in one dose before infection. The drug did not prevent blood-invasion but retarded increase of bacteria in the blood. Many of the mice that survived developed a massive bacteriæmia.

Influenzal meningitis treated with sulfapyridine is reported on by Drs. T. R. Hamilton and S. C. Neff of the University of Kansas Hospital. A two-year-old baby girl suffering with influenzal meningitis was received in a prostrate condition and high fever. She was much better after 4 days of sulfapyridine treatment and well enough to return home in one week, and completely recovered 16 days after contracting the illness.

Cerebrospinal meningitis, which claims to be 60-90% fatal, is enjoying 95% cures when treated with sulfapyridine, according to Drs. J. Bryant and H. D. Fairman. They saved 20 of 21 patients treated with sulfanilamide and 160 of 168 treated with sulfapyridine.

Dr. S. Stanley and Dr. S. S. Schneierson find that sulfanilamide and prontosil have a marked bactericidal and bacteriostatic effect upon meningococci in vitro, depending upon the concentration of the drug.

Meningococcal meningitis and sulfanilamide therapy is reported on by Dr. H. S. Banks of London. He states that in a series of 28 cases treated with sulfanilamide alone no deaths had occurred, and of 34 cases given sulfapyridine only one had died. Relatively high mortality rates occurred when serum alone was used, and when serum was administered in conjunction with insufficient doses of sulphanilamide. It was a good plan to change the drug used from sulfapyridine to sulphanilamide when mental depression became marked, usually after thirty-six hours. Four cases had been treated in this way with good results. The concentration of the drug in the cerebrospinal fluid had been found to follow closely the blood level and was approximately half as high.

Gas gangrene and meningitis are effectively treated with sulfanilamide, according to Dr. Thomas M. Rivers of the Rockefeller Institute. Drs. Long and Bliss of Johns Hopkins Medical School also report that gas gangrene is effectively treated with sulfanilamide.

Trachoma, according to a paper by Dr. James G. Townsend, Health Director for the U. S. Indian Service, is being effectively treated with sulfanilamide. Eight hundred and fifty school children have been treated, besides many adult patients. The drive was started amongst children because they can be reached through schools and watched. According to Dr. Townsend, sulfanilamide is the best therapy doctors have had so far for fighting trachoma among the Indians. There is no question but that it brings about a marked improvement. Best results appear in acute rather than chronic cases. Trachoma gets between 2000 to 3000 new eye victims every year and is very contagious. The disease was arrested in 105 of 167 children treated at the Chemawa, Oregon, School. Twenty-three patients treated 18 months ago have had no relapse. The patients feel better immediately after the treatment is started and the pain and soreness in their eyes begin to abate on or about the third day. The sulfanilamide is given three times a day by mouth every day for five days. Then after two days of rest the treatment is resumed for another five days. At the end of this time the eyes are much better and the condition arrested. After another month, during which there is no improvement, the eyes begin to improve very rapidly, suggesting an accumulative effect of the drug.

Typhoid fever treated with sulfapyridine is reported on by Drs. E. H. R. Harries, Robert Swyer and Noel Thompson of Northeastern Hospital, London. Good results in severe cases of typhoid fever are reported by them. The most striking example was a case of "walking typhoid" and for whom any experienced doctor would have predicted a long period of illness. Within ten days after entering the hospital the patient was in the recovery or convalescent stage. He was given both sulfapyridine and the serum. The doctors suggest that this combination is probably the best thing to use for treatment of other cases.

Filarial elephantiasis, according to Dr. G. A. H. Buttle, is helped by the action of sulfanilamide due to the killing of the secondary streptococci.

Plague, according to Dr. Buttle, is also helped by treating with sulfapyridine.

Brucella (undulant fever) infections respond markedly to sulfapyridine treatment, is the experience of Dr. Buttle.

Lymphogranuloma, trachoma, smallpox are all virus diseases, yet are directly influenced by the sulfanilamide derivatives, according to Dr. Buttle.

Smallpox is apparently treated with some success by sulfanilamide, Dr. W. O. McCammon claims. Seven cases of smallpox came to his attention and sulfanilamide was used on four of them. In these four there was only a slight eruption that soon disappeared. He believes the eruption was prevented by the sulfanilamide therapy. These four patients were back at work a week sooner than were the other three cases, which were treated symptomatically and in which the typical eruption of smallpox developed. He hesitates to draw any radical conclusion from so few cases.

Malaria in man is unaffected by sulfanilamide treatment, although it acted like a charm in Plasmodium knowlesi malaria in monkeys, points out Dr. P. H. Manson-Bahr of London. He also states that the results in undulant fever in man had been on the whole favourable but not dramatic.

Actinomycosis when treated with sulfanilamide has shown favourable results, reports Dr. Mahnson-Bahr.

Pneumococci meningitis (type 15) was treated by Dr. E. T. Lisansky with para-aminobenzene-sulmonamide. A case of type 15 pneumococcic complicating the right antrum sinusitis recovered when treated with this drug and radical drainage of the sinuses.

Tonsillitis treated with sulfanilamide is reported on by W. R. Snodgrass of Glasgow. In his opinion, although there is general agreement regarding the efficacy of sulfanilamide therapy in tonsillitis, there was actually a scarcity of properly controlled studies. It is his experience that acute widespread and invasive infections respond best, and poorest results were found in single walled-off lesions such as quinsy.

Erysipelas is also treated by Dr. Snodgrass with sulfanilamide. He states that in a carefully controlled study of this treatment he had found the drug was of great value and suggested that a suitable dosage in adults was 1.5 gm. of prontosil rubrum or 1 gm. of sulfanilamide every four hours until the lesion had ceased to spread and the primary pyrexia and toxæmia had ceased; thereafter 1 gm. thrice daily should be given for 14 days to prevent relapse. He also adds that in scarlet fever sulfanilamide therapy had no significant effect on the initial symptoms or signs, or on the incidence or duration of complications.

Chronic ulcerative colitis shows prompt improvement when treated with neoprontosil (oral), is the experience of Drs. A. E. Brown and W. E. Herrell. This prompt improvement, which has occurred so frequently and uniformly after the use of neoprontosil seems to indicate that the drug is of definite benefit in this disease. The lack of toxic manifestations associated with the use of neoprontosil in general makes this drug especially adaptable to the treatment of chronic ulcerative colitis.

Toxic Reactions of Sulfanilamide

According to Dr. Ellison of Lymanhurst Special Clinic, these vary from fatigue and anorexia to the less common reactions of methemoglobinemia and sulphemoglobinemia.

1. Malaise: This varies from mild fatigue to almost exhaustion and prolonged deep sleep, the patient often being too tired to eat.

2. Anorexia: Very frequently the patient loses all taste for food and frequently loses five to ten pounds while being treated.

3. Nausea and vomiting: This varies from mild nausea to severe vomiting. Drs. E. N. Cook and E. B. Sutton of the Mayo Clinic find that when the drugs are given with a small quantity of milk the stomach and intestinal distress is sometimes relieved. Also, the administering of equal weight of sodium bicarbonate is also effective in minimizing nausea.

4. Fever is rather uncommon. It usually ranges from 100 to 101 or 102 degrees and is accompanied with other toxic signs such as cyanosis, nausea and vomiting.

5. Dermatitis: This is also quite rare, but sometimes appears after ten days or one week administration. It may appear after the drug has been discontinued.

Rash: Maculo-papular, most frequently on forearm, face, legs, buttocks. Quite often it is unilateral. It usually appears 24 to 48 hours after the sulfanilamide is discontinued, and requires no other therapy except local treatment for itching. Even if the drug is continued the rash will fade in about 72 hours. Sunlight or ultra-violet light will tend to bring on a sulfanilamide rash.

6. Edema: This occurs infrequently.

7. Leucopenia: Agranulocytic anæmia and hæmolytic anæmia are all rare. Agranulocytosis is about the only fatal complication and occurs usually late in the treatment. It is very important to do white cell counts after treatment has been continued for ten days and every third to fourth day thereafter. Dr. H. Myhre mentions a case and suggests that the drug should never be used for more than seven to ten days at a time. If a second course is needed, the blood count must be watched, especially if the temperature rises. Dr. Nathan Rosenthal and Peter Vogal mention three cases of granulocytopenia found in children after the use of sulfapyridine. They say sulfanilamide is also causing the trouble. They stress the necessity of watching the blood for danger signs. Dr. Saeton Sailer reports a case of subacute bacterial endocarditis due to a streptococcus viridans infection. The patient was treated with 282.6 gm. of sulfanilamide over a period of 23 days, resulting in granulocytopenia. Sections of the bone marrow showed areas of aplasia, which predominated, and of myeloid and lymphocytic hyperplasia; areas of focal necrosis were present in the intermediate zone of the liver. Pneumonic lesions were free from leucocytic infiltration.

8. Methemoglobinemia and cyanosis in a mild degree has been quite common, espcially during the first few days of treatment when the dosage of the drug is high. Unless it is marked or accompanied by more severe toxic signs it is perfectly safe to continue with the regular doses of sulfanilamide together with equal amounts of sodium bicarbonate. Recent work explains cyanosis on the basis of blue pigmentation derived from sulfanilamide, and picked up by the red blood corpuscles to give the cyanotic-like colouring.

Drs. A. F. Hartman, A. M. Perley and H. L. Barnet report on methemoglobin formation and its control: "In the majority of patients receiving 0.1 mg. or more of sulfanilamide per kilogram per 24 hours, cyanosis develops, and so far we have been able to demonstrate the presence of methemoglobin in every case of cyanosis. There is marked variation in both the rate and the degree of methmoglobin accumulation. Methylene blue causes a very rapid disappearance of cyanosis with simultaneous reduction in the methemoglobin concentration, when given intravenously in single doses of 1.0 to 2.0 mg. per kilogram, or when given orally in doses of 1.0 to 2.0 grains (65 to 130 mg.), repeated every four hours. The latter method also prevents any appreciable formation of methemoglobin if started simultaneously with sulfanilamide administration.

9. Sulphemoglobinemia is uncommon, usually associated with a history of recent medication with sulphate cathartic, such as magnesium sulphate dressings. It can be prevented by (1) warning the patient to take no cathartic other than one ordered by the doctor, (2) use of mineral oil and enemas if necessary, (3) limiting eggs on diet to two a day, (4) giving enema before sulfanilamide is instituted if the patient has taken sulphate cathartic the past day or so.

The best treatment of complications is transfusions and intravenous glucose. Oxygen therapy is of little and questionable benefit, but is usually used in conjunction with other treatment.

10. Hæmaturia sometimes appears, due to the deposition of the acetyl derivative in the renal tract.

11. Mental depression and vomiting: Mental depression is more common with M & B 693 than with sulfanilamide.

12. Nervous symptoms, such as atopia, atonic convulsions and paralysis were often produced by large doses of sulfanilamide but not with benzylsulfanilamide.

13. Depressant: Dr. Ellison of Lymanhurst Clinic says that sulfanilamide is a depressant and the occasional deaths that can be attributed to the drug are caused by respiratory and cardiac paralysis.

14. Formation of uroliths of acetylated sulfapyridine in rats and rabbits but not in dogs or mice, are reported by Dr. Hans Molitor and Harry Robinson.

15. Acidosis is reported by Dr. T. Goodier to be one of the complications caused by sulfanilamide therapy.

16. Dr. F. G. Smith reports that acute toxic nephritis and focal necrosis in the adrenal appeared, and was confirmed by autopsy.

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Vancouver General Hospital

VERIFIED BRAIN TUMOUR CASES, VANCOUVER GENERAL HOSPITAL, 1934-1938

By Drs. D. P. Robertson and C. E. Gould.

During the five-year period, 1934-1938 inclusive, there were sixty-eight cases of brain tumour at the Vancouver General Hospital. Of this number, however, twelve cases were not proven by operation, biopsy or autopsy. The diagnosis in the remaining fifty-six cases was definitely established by one or more of the above-mentioned methods, and it is this series of fifty-six proven cases that is summarized below.

1. *Type Incidence*:

Table I.

		V. G. H.			V. G. H.
Glioma	about 41 %	66.07%	Tuberculoma and Granuloma	2.5%	
Meningioma	13 %	12.50%	Blood vessel tumour	1.7%	
Auditory Nerve Tumour	10 %	3.5%	Choroid plexus tumour	1.0%	
Hypoduct Tumour	7 %		Cholesteatoma	1.0%	1.7%
Sarcoma	7 %		Pineal body tumour		3.5%
Secondary carcinoma	5 %		Chordoma, speno-occipital		1 case
Pituitary adenoma*	4.6%	5.3%	Suprasellar cyst		1 case
Pituitary adenoma†	19.2%		Septum pellucidum cyst		1-case
			Lindau's disease		1 case

* National Hospital figures. †Cushing's figures.

The left-hand column in Table I represents the averages combined from two large series of cases—that of the National Hospital for Nervous Diseases, Queen's Square, London, and that of Harvey Cushing. The type incidence percentages were nearly identical in both series, with a single exception, viz., the pituitary adenomata, Cushing's figure being about four times as high as that of the National Hospital.

The right-hand column gives the comparative percentages in this five-year series at the Vancouver General Hospital. In a series as relatively small as this one is, it is not to be

expected that the figures will be comparative with the averages arrived at with the larger series. It is to be noted, however, that of the total fifty-six cases, thirty-seven cases, or 66.07%, were malignant gliomas—a figure significantly above the average. The meningiomas, seven cases out of fifty-six, or 12.50%, represent the average. The pituitary adenomata total, at 5.3%, is comparative to the National Hospital figure rather than to Cushing's.

The two pineal body tumours, the chordoma, suprasellar cyst, septum pellucidum cyst and case of Lindau's disease represent lesions that total less than 1% in a larger series of cases.

2. *Location of Tumours*:

TABLE II.

	Frontal	Temporal	Parietal	Fronto-Parietal	Temporo-Parietal	Third Ventricle	Temporo-Occipital	Parieto-Occipital	Occipital	Cerebellar
GLIOMAS—										
Glioblastoma Multiforme	1	3	3	2	4	--	2	--	1	--
Astroblastoma	2	--	--	--	--	1	1	1	1	--
Astrocytoma	--	--	3	--	--	--	1	--	--	2
Spongioblastoma	1	2	--	--	--	--	--	1	--	--
Medulloblastoma	--	--	--	--	--	--	--	--	--	3
Oligodendroglioma	--	--	--	--	1	--	--	--	--	--
Ependymoma	--	--	--	--	--	--	--	--	--	1

MENINGIOMAS—

1 overlying Rolandic fissure.
1 left parasellar region
1 right frontal lobe
1 midline, frontal region
1 left temporal and frontal lobes
1 right parietal parasagittal area.

Others speak for themselves, except:
Cholesteatoma—right frontal area.

Table II shows the variety of distribution and emphasizes the lack of a site of predilection as far as the gliomas are concerned, with the single exception of the medulloblastoma, which ran true to type, and were found in the cerebellum in all three cases.

3. *Age Groups*:

TABLE III.

	Youngest	Oldest	Average	Cases
GLIOMAS—				
Glioblastoma Multiforme	13	72	49.0	16
Astroblastoma	10	60	47.8	6
Astrocytoma	5	52	26.3	6
Spongioblastoma	28	60	44.0	4
Medulloblastoma	5	33	20.3	3
Oligodendroglioma	54			
Ependymoma	49			
MENINGIOMAS	6	78	37.8	7
Chromophobe adenoma of pituitary	49, 45, 61			
N. VIII neurofibroma	48, 23			
Pineal body tumours	11, 13			
Chordoma	13			
Suprasellar cyst	32			
Septum pellucidum cyst	23			
Lindau's disease	28			
Cholesteatoma	59			

Table III shows the wide spread in the age incidence of the gliomas, the widest spread being in the glioblastoma multiforme group, while the medulloblastomata, characteristically, are limited to younger individuals. The meningiomas are shown also to have a wide spread in age incidence, and the pineal body tumours, as is usually the case, accurred in children.

4. *Operative Mortality*:

TABLE IV.

	Operation	No Operation	Post-Operative Deaths
Gliomas	26	11	18
Meningiomas	5	2	1
Chromophobe adenoma of pituitary	3	0	1
N. VIII neurofibromas	1	1	0
Pineal body tumours	2	0	2
Chordoma	1	0	1
Suprasellar cyst	1	0	0
Septum pellucidum cyst	1	0	0
Lindau's disease	1	0	0
Cholesteatoma	1	0	0

Table IV shows the operative mortality of all the cases operated upon in this series. Operation mortality is reckoned as a death occurring subsequent to operation, and prior to discharge from hospital, and may occur many weeks post-operatively.

Study of this table shows the martality rate in the different types of tumour to be comparable to the rates obtained in other centres.

5. *Incidence of Headache, Vomiting and Papillœdema*:

TABLE V.

Headache as the first subjective symptom:

Gliomas	16 out of 34	3 no history.
Meningiomas	3 " " 6	1 no history.
Other tumours	7 " " 12	
	20 " " 52	51.9%

Vomiting:

Gliomas	12 out of 34
Meningiomts	3 " " 6
Other tumours	5 " " 12
	22 " " 48 — 38.5%

Papillœdema:

Gliomas	15 out of 32
Meningiomas	4 " " 7
Other tumours	3 " " 9
	12 " " 47 — 45.8%

All three (headache, vomiting, papillœdema) were absent in:

Gliomas	9 out of 32
Meningiomas	0 " " 6
Other tumours	3 " " 9
	27 " " 52 — 25.5%

Table V takes up the incidence of headache, vomiting and papillœdema—the cardinal triad of increased intracranial pressure—in this series.

Headache is shown to be the most consistent first subjective symptom, occurring as such as roughly one-half of all cases.

Vomiting occurred, although not necessarily as a first symptom, in 38.5% of all cases. In only a few cases was it recorded as being of projectile type, although extracranial causes were not found to account for the non-projectile cases.

Papillœdema was found in 45.8% of all cases in which the ophthalmoscopic examination was recorded—a total of forty-eight cases.

Perhaps the most interesting figure in this table is the number of cases in which all three of the cardinal triad of headache, vomiting and papillœdema were absent—twelve out of forty-seven cases, or 25.5%, and it is to be noted that this triad was absent in nine out of thirty-two gliomas, but in none of the meningiomas.

Note: Totals in this table are less than the total number of cases since only those records which definitely stated the presence or absence of the symptoms in question were included.

6. *Correct and Incorrect Admission Diagnoses:*

TABLE VI.

	Correct	Incorrect	Not Noted
	27	9	1

Gliomas

Of the 9 incorrect diagnoses:

1. J. C., male, 60 ..... Old right hæmiplegia. Spongioblastoma.
2. A. B., female, 51 ..... Menopausal depression. Astroblastoma.
3. R. C., female, 72 ..... Old cerebro-vascular accident. Glioblastoma multiforme.
4. J. W., male, 62 ..... Cerebral thrombosis. Glioblastoma multiforme.
5. E. K., male, 54 ..... Sinusitis. Glioblastoma multiforme.
6. W. A., male, age ? ..... Mental observation. Glioblastoma multiforme.
7. E. S., female, 54 ..... Hæmorrhage, right internal capsule. Oligodendroglioma.
8. M. R., female, 16 ..... Subacute appendicitis. Astrocytoma of cerebellum.
9. M. H., female, 5 ..... Meningitis. Medulloblastoma.

Meningiomas 5 1 1

1. L. E., female, 78 ..... Cerebral hæmorrhage.
2. K. T. L., male, 58 ..... No diagnosis.

Others

Chromophobe adenoma of pituitary	3 correctly diagnosed.
N. VIII neurofibroma	1 cord tumour.
	1 correctly diagnosed.
Pineal body tumours	1 cranial tumour, adequct of Sylvius.
	1 correctly diagnosed.
Chordoma	1 cranial tumour, cerebellar.
Suprasellar cyst	1 suprasellar tumour.
Septum pellucidum cyst	1 cranial tumour.
Lindau's disease	1 cranial tumour, cerebellar.
Cholesteatoma	1 cranial tumour, frontal.

Table VI shows the correct admission diagnoses. In the glioma and meningioma group only the incorrect diagnoses are listed.

Some of the pertinent circumstances concerned in these mistaken diagnoses are listed:

1. J. C., male, 60—Old right hæmiplegia. Admitted semi-conscious. No history. Died ten days after admission. Pathological diagnosis: Left temporal spongioblastoma multiforme.
2. A. B., female, 51—Depressive state, diagnosed as menopausal depression. Went progressively downhill to death about one month after admission. Pathological diagnosis: Left frontal astroblastoma.
3. R. C., female, 72—History of ataxia of one year's duration. Right hæmiparesis on examination. Diagnosed as old cerebro-vascular accident, and transferred to convalescent home, where she died three yeeks later. Pathological diagnosis: Left temporo-parietal glioblastoma multiforme.
4. J. W., male, 62—Symptoms of dizziness and weakness of about one month's duration. Diagnosed cerebral thrombosis. Pathological diagnosis: Glioblastoma multiforme.
5. E. K., male, 54—Because of severe headaches of one month's duration was diagnosed as sinusitis on admission, but diagnosis was changed to brain tumour. He was operated upon and died six weeks post-operatively. Pathological diagnosis: Temporo-parieto-occipital glioblastoma multiforme.
6. W. A., male, age ?—Symptoms of depression, with childish conversation and disorderly habits. Admitted for mental observation, but diagnosis later changed to brain tumour. Operated upon, died two days post-operatively. Pathological diagnosis: Right temporo-parietal glioblastoma multiforme.
7. E. S., female, 54—Admitted in coma, died thirty minutes after admission. Diagnosis, hæmorrhage into right internal capsule. Pathological diagnosis: Right temporo-parietal oligodendroglioma, with hernia cerebri.
8. M. R., female, 16—Symptoms of vomiting and headaches for two months, and abdominal pain for ten days. Slight tenderness to deep pressure in both lower quadrants. Diagnosed as subacute appendicitis. Died one hour after appendectomy. Pathological diagnosis: Astrocytoma of cerebellum.

9. M. H., female, 5—No history obtainable in this case. Brought in with moderate degree of opisthotonos, stiff neck, and positive Kernig's sign. Diagnosis, meningitis. Died one day after admission. Pathological diagnosis: Medulloblastoma, left cerebellum, with marked internal hydrocephalus.

Note: None of the above cases were admitted under or seen by the Department of Neurology.

In the meningioma group:

1. L. E., female, 78—Admitted comatose. No history available. Complete left-sided hæmoplegia. Diagnosis, cerebral hæmorrhage. Died shortly after admission. Pathological diagnosis: Dural meningioma, mid-line, frontal.

In the remaining tumours, adequate localization was accomplished in all cases but one, viz.:

R. T., male, 48—History of difficulty in walking for five years, pain in neck for one year, radiating to jaw for last four days. Tentative diagnosis, spinal cord tumour. Patient died suddenly on third day of hospitalization. Pathological diagnosis: N. VIII neurofibroma, with hernia cerebri.

7. *Occurrence of Primary Optic Atrophy*:

Primary optic atrophy: TABLE VII.

G. D., female, 33	Dural meningioma, left Left parasellar region.
H. F., male, 32	Suprasellar cyst.
J. M., female, 45	Chromophobe adenoma of pituitary.

Table VII shows the incidence of primary optic atrophy in this series. Tumour arising sufficiently near the optic foramen so as to cut off the sub-arachnoid space of the optic nerve from the cerebral sub-arachnoid circulation will cause optic atrophy of the so-called primary type, and not necessarily preceded by papillœdema.

The three cases in this series come within this category, two being parasellar, the third being in the pituitary itself.

8. *Occurrence of Herniation through the Foramen Magnum*:

TABLE VIII.

M. H., female, 5	Medulloblastoma, left cerebellar lobe.
E. S., female, 54	Oligodendroglioma, right temporo-parietal area.
S. B., male, 37	Glioblastoma multiforme, left fronto-parietal area.
M. W., female, 48	Astroblastoma, temporo-parieto-occipital lobes.
R. T., male, 48	N. VIII neurofibroma.
E. R., female, 23	N. VIII neurofibroma.

This almost invariably fatal process occurred six times in this series, and death was averted in one case.

1. M. H., female, 5—Medulloblastoma, left cerebellar lobe. Moderate degree of opisthotonos, stiff neck, and positive Kernig's sign. Diagnosis, meningitis. Died one day after admission. Autopsy showed marked hydrocephalus, with cerebellum and medulla herniated into the foramen magnum.
2. E. S., female, 54—Oligodendroglioma, right temporo-parietal area. Severe occipital headaches every three months for five years, with vomiting at night, followed by unconsciousness for a few hours. Felt well up until three days prior to admission, and was able to do her housework the day before admission, but developed a severe headache that night and had to be carried to bed. Did not awaken the following morning, was brought to hospital, and died thirty minutes after admission. Autopsy showed a duck-egg-sized tumour in right temporo-parietal area, and herniation of cerebellum through the foramen magnum.
3. S. B., male, 37—Glioblastoma multiforme, left fronto-parietal area. Diagnosed as brain tumour. Died one day post-operatively. Autopsy showed intracystic hæmorrhage and herniation through the foramen magnum.
4. M. W., female, 48—Astroblastoma, right temporo-parieto-occipital area. Diagnosed as brain tumour. Lumbar puncture done on ward. Respiration ceased. Taken to operating room, burr hole made over anterior pole of left lateral ventricle and bloody fluid withdrawn, but patient failed to revive. Autopsy showed a large tumour, and hæmorrhage into the ventricles, with a pressure cone at the base of the brain.
5. R. T., male, 48—N. VIII neurofibroma. Bizarre symptoms suggestive of cord tumour. Diagnostic measures pursued, but patient died suddenly on third day of admission. Autopsy showed a cerebellopontine angle tumour with the brain stem herniated through the foramen magnum.
6. E. R., female, 23—N. VIII neurofibroma. Cerebellar decompression and removal of the tumour done, but because of the downward herniation of the cerebellum, extension of the decompression down to the fourth cervical vertebra was done on the twentieth day post-operatively. Recovery uneventful.

9. *Size of Pupils in relation to Side of Lesion*:

TABLE IX.

Noted in seven cases—

2 ..... midline.
2 ..... dilated same side.
3 ..... dilated pupil opposite side.

Relative differences in the size of the pupils was noted in seven cases. In two of these cases the tumour was in the midline, while in two the dilated pupil was on the same side as the lesion, and in three on the opposite side to the lesion. As a localizing sign, therefore, it would appear to be of no value in itself.

10. *Occurrence of Intracystic Hæmorrhage*:

Intracystic hæmorrhage: TABLE X.

1. S. B., male, 37 ..... Glioblastoma multiforme.
2. J. C., male, 60 ..... Spongioblastoma.
3. A. B., female, 51 ..... Astroblastoma.
4. G. H., female, 16 ..... Astrocytoma.
5. M. W., female, 48 ..... Astroblastoma.

Table X shows the incidence of intracystic hæmorrhage, in all cases producing a rapidly fatal outcome. In two cases, Numbers 1 and 2, the hæmorrhage produced herniation cerebri, which was the immediate cause of death, while in the remaining three the death might be said to be due to cerebral shock, without pressure cone formation.

11. *Localizing Value of Diagnostic X-Ray*:

TABLE XI.

Diagnostic X-Ray:	Flat plates		18
	Definite evidence of tumour location	5	
	Gliomas	0	
	Meningiomas	2	
	Pituitary tumour	1	
	Suprasellar cyst	1	
	Cholesteatoma	1	
	Evidence of intracranial lesion	3	
	Gliomas	2	
	Pineoblastoma	1	
	Negative findings	10	
	Gliomas	8	
	Pinealoma	1	
	Septum pellucidum cyst	1	
	Ventriculograms		16
	Definite location of tumour	8	
	Gliomas	4	
	Meningiomas	1	
	Pinealomas	2	
	Chordomas	1	
	Evidence of intracranial lesion	5	
	Gliomas	5	
	Unsuccessful (but location diagnosed clinically)	2	
	Thorotrast		
	1. Intra-arterial—showed location—glioma.		
	2. Intraventricular—showed hydrocephalus—glioma.		

Table XI summarizes the diagnostic X-ray that was done in this series. It is notable that flat plates of the skull were of little diagnostic value as far as the gliomas were concerned. Of ten cases, local evidence of tumour was revealed in none, and only two showed evidence of intracranial lesion.

Ventriculography was done in sixteen case, intraventricular thorotrast being used in one case, and cranial arteriography with thorothrast was one in one case.

Of the fifteen cases in which routine air ventriculography was done, evidence of tumour location was afforded in eight cases, of which four were gliomas, while thorotrast in one case revealed hydrocephalus.

Evidence of intracranial lesion was afforded in five additional cases, while only two were entirely negative.

The intra-arterial injection of thorotrast in one case revealed the location of a glioma.

Public Health Section

THE PREVALENCE OF VENEREAL DISEASE INFECTIONS IN VANCOUVER

By

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The Greater Vancouver Health League, working in co-operation with the Division of Venereal Disease Control, has made considerable progress in an educational way in the control of venereal disease in Vancouver, but it had been handicapped in previous years by the absence of any reliable statistics as to the prevalence of syphilis and gonorrhœa in the community.

Various estimates had been offered, ranging from the statement that one in seven of the population were infected to other statements that the diseases were of negligible importance, and the result had been a confusion in the public mind which made educational work difficult.

It was felt, therefore, that a survey of prevalence was justified and would serve a useful purpose. The Board of Directors of the Health League authorized the study in December, and the following committee was appointed to conduct it:

Dr. A. M. Menzies, unit director of the Metropolitan Health Board, chairman; Dr. A. M. Agnew, president of the Vancouver Medical Association; Dr. M. W. Thomas, executive secretary of the British Columbia Medical Association; Dr. W. W. Simpson, and the authors.

The procedure followed was similar to that of comparable surveys conducted by the Health League of Canada in Toronto in 1929 and 1937[1]. The object was to learn the number of cases of venereal disease which were under treatment on any one day, in this case, on December 31, 1939. Since the enquiry was limited to practising physicians, hospitals and clinics, the results show only such cases as were under medical supervision and, therefore, fall short of indicating the total of all cases of venereal disease on the given date.

A confidential printed form and a covering letter were sent to each of 338 practising physicians in Vancouver City. The outlying suburbs usually included in Greater Vancouver were omitted. Within three weeks, 193 doctors had responded and a second letter and form were sent to the others. Later it was necessary to send a third letter and, in the case of a few men, to follow this with telephone calls.

The co-operation of the medical profession was generous and excellent. Of 338 names on the list, only 13 were not accounted for, so that 96 per cent of returns were made. Additional returns were obtained from the Vancouver Clinic of the Division of Venereal Disease Control, the Division of Tuberculosis Control, the Provincial Mental Hospital, the Marpole Infirmary, and similar institutions.

Under these circumstances, a total of 2054 cases of venereal disease in Vancouver were reported. This represents an incidence of 7.75 per thousand of the population. The total was divided into 1549 cases of syphilis (5.84 per thousand) and 483 cases of gonorrhœa (1.83 per thousand), plus 21 additional cases which were not classified.

Private physicians (96 per cent of the profession) reported a total of 782 cases of venereal disease, of which 528 were syphilis and 254 were gonorrhœa, as shown in Table I.

1. *Canadian Public Health Journal*, March, 1930, and December, 1937.

TABLE I.
CASES OF VENEREAL DISEASE REPORTED BY PRIVATE PHYSICIANS.

SYPHILIS

	Early Syphilis				Late Syphilis				
	Male		Female		Male		Female		
Total Syphilis	Under 14	Over 14	Under 14	Over 14	Under 14	Over 14	Under 14	Over 14	Not Classified
528	5	43	7	23	10	265	6	159	10

GONORRHŒA

	Early Gonorrhœa				Late Gonorrhœa				
	Male		Female		Male		Female		
Total Gonorrhœa	Under 14	Over 14	Under 14	Over 14	Under 14	Over 14	Under 14	Over 14	Not Classified
254	3	114	2	32	2	67	3	20	11

A certain number of physicians noted that they did not treat venereal disease, and, in addition, the list included technicians, internes and retired doctors, but of the total, 45 per cent reported one or more cases. The largest number of cases reported by an individual was 46.

As compared with institutions, private physicians were treating fewer cases of syphilis but slightly more cases of gonorrhœa, as shown in Table II.

TABLE II.
SYPHILIS AND GONORRHŒA TREATED BY PHYSICIANS AND INSTITUTIONS.

	SYPHILIS		GONORRHŒA		
	Number Treated	Per Cent	Number Treated	Per Cent	Not Classified
Private Physicians	528	34.08	254	52.48	----
Clinics and Institutions	1021	65.92	230	47.52	21

The majority of the cases classified under clinics and institutions were patients of the Vancouver Clinic of the Division of Venereal Disease Control. The returns from this treatment centre are shown in Table III.

TABLE III.
SYPHILIS AND GONORRHŒA TREATED BY THE VANCOUVER CLINIC OF THE DIVISION OF VENEREAL DISEASE CONTROL.

SYPHILIS.

— Male —		— Female —		Total
Under 16	Over 16	Under 16	Over 16	Syphilis
25	692	22	219	958

GONORRHŒA.

— Male —		— Female —		Total
Under 16	Over 16	Under 16	Over 16	Gonorrhœa
1	160	9	60	230

To what extent this statistical study represents a true picture of the situation must remain a matter of conjecture. The number of reported gonorrhœa cases seems surprisingly low, as compared with generally accepted estimates elsewhere, even when the shorter treatment period and the excellent results obtained by the use of sulfanilamide are taken into account.

The proportion of venereal disease in Vancouver which is treated by private or public medical agencies cannot be estimated. In other words, the committee had no way of determining whether the 2054 cases reported in the survey include the vast majority of venereal infections or merely a small fraction of them. Self-treatment and treatment by druggists and quacks undoubtedly are carried on, and certainly a considerable number of cases, particularly of latent syphilitics, are not diagnosed or treated by anyone. It may be possible at a later date to make a study of such extra-medical treatment, as was done in 1939 in the United States by the American Social Hygiene Association and the U. S. Public Health Service.

However, insofar as medical treatment is concerned, the findings of the Vancouver Laboratory of the Provincial Board of Health have provided an interesting comparison. Dr. C. E. Dolman, director of the Division of Laboratories, reviewed the results of the survey and made the following comment in a letter to one of the authors:

"Although the figures you have obtained in your survey are undoubtedly on the low side, since all sources of error tend in that direction, your findings are not very discordant

from those which we have been able to deduce to some extent from our laboratory work. Thus in 1939 the total number of positive Kahn blood specimens obtained from physicians and hospitals within the city of Vancouver, and from the Vancouver Clinic, was 3881. The total number of positive smears for gonococcus obtained from the same sources during 1939 was 1968. Of course our own figures under both headings are subject to correction in the opposite direction from your own, since these figures would include a goodly proportion of repeat tests. However, if *all* positive specimens related to separate individuals, we should still have an incidence of the combined diseases of slightly under 2 per cent, which is far different from the figure of 10 per cent of the population suffering from syphilis which has been bandied about in recent years.

"I might add, for your interest and that of members of the League, that the incidence of congenital syphilis in Vancouver, as shown by over 11,000 tests routinely done on infants born in Vancouver hospitals over the past seven years, is at the maximum possible rate of 0.9 per cent."

It is the hope of the Greater Vancouver Health League to conduct similar surveys at future dates, possibly annually, in order to arrive at some conclusion as to the trend of syphilis and gonorrhœa infections in Vancouver. Such conclusions would be an interesting corollary to the vigorous preventive and treatment programme of the Provincial Board of Health.

SUMMARY.

A survey by the Greater Vancouver Health League to determine the prevalence of syphilis and gonorrhœa in Vancouver as at December 31, 1939, resulted in a tabulation of 2054 cases under medical treatment on that date, an incidence of 7.75 per thousand of the population. There were 1549 cases of syphilis (5.84 per thousand) and 483 cases of gonorrhœa (1.83 per thousand) reported, plus 21 cases which were not classified. The medical profession co-operated generously and 96 per cent of practising physicians responded, of which 45 per cent reported one or more cases.

The incidence rate represents only known cases under medical treatment and it is incomplete to an unknown degree because the tabulation did not include those cases treated by quacks, druggists, or under self-treatment, or the cases which have not been diagnosed. However, insofar as medical treatment is concerned, the results obtained in the survey were confirmed in a general way by the findings of the Division of Laboratories, Provincial Board of Health.

St. Paul's Hospital

THE INTRAVENOUS FEEDING OF AMINO ACIDS

By IRIS CORBOULD, R. H. CLARK and R. E. MCKECHNIE, II, M.D.

Reprinted from the *American Journal of Digestive Diseases*, Vol. VI, No. 3, May, 1939.

In medical practice the feeding of human beings by other than oral means has long been recognized as a necessity under certain conditions. Up to the present certain salts and glucose have been the only materials injected. Patients decline fairly rapidly in the absence of tissue-building proteins.

Aberhalden[1] has established that proteins in the process of digestion are completely hydrolyzed. Moreover, Van Slyke[1] has shown, by examining the blood before and during digestion, that it is in the form of amino acids that protein synthesis begins, since polypeptides when introduced into the blood stream are excreted unchanged.

It is not known in what proportion the various amino acids are absorbed by the tissues from the blood. Moreover, the present price of individual amino acids would prohibit their general use for such a purpose. In the experiments described below an inexpensive pure protein was hydrolyzed and the resulting mixture of amino acids utilized.

Considerable work has been done on feeding animals orally with mixtures of amino acids, but very little on their intravenous injection. Buglia[2] found by injecting hydrolyzed

proteins that a considerable proportion of the amino acids was taken up by body and suggested that the animal could probably be fed that way.

Ackroyd and Hopkins[3] have shown that if hydrolyzed casein is administered orally as the sole source of protein, the animal loses weight and ultimately dies. But that if tryptophane, which is destroyed by acidhydrolysis, is added in small amounts to the hydrolyzate, normal growth is maintained. This seems to be due to the inability of the animal to synthesize the indol ring.

Casein was selected as the source of amino acids and hydrolyzed by means of sulphuric acid. Enzyme hydrolysis was not considered, since ti would be difficult to separate enzymes completely before injection, while hydrolysis by bases racemerizes the amino acids. Of the ten indispensable animo acids it has been shown that tryptophane, histidine, phenylalanine and methionine can be replaced for growth purposes by their antipodes. On the other hand, only the natural forms of valine, isoleucine, lysine and threonine are available for the use of the growing organism[4]. Arginine has not yet been investigated.

Experimental.

One litre of 15% sulphuric acid was used for each 100 grams of casein, and the mixture was digested on a sand bath under a reflux condenser for several hours after a portion withdrawn first gave a negative biuret test. The extra digestion was to ensure complete hydrolysis to amino acids. The mixture was then boiled with animal charcoal until colourless and filtered. Sufficient solid barium hydroxide to almost neutralize the sulphuric acid was added and the solution again filtered. The mixture was then diluted to two litres for each original 100 grams of casein, since it was found that in a more concentrated solution the more insoluble amino acids such as tyrosine and leucine tended to precipitate out on standing. The mixture was adjusted to a pH of about 7.4 by means of sodium hydroxide solution. Then sufficient Ringer's salt to make the solution isotonic and about 10% glucose were added, and the pH was readjusted when necessary.

The solution was next filtered through a Seitz filter to sterilize it, although it was found to be just as efficient to autoclave the solution before adding the glucose, and then to add the glucose which had been sterilized in the dry form.

Rabbits were selected as experimental animals; each was fed approximately 80 cc. of the mixture as calculated on their energy and protein requirements, depending on their weights. At first the injections were made through a vein in the ear, but this method was found to consume too much time, so intra-peritoneal injections were carried out twice a day. The animals absorbed the food slowly from the peritoneal caving. A few rabbits were run as controls, being fed the same amount of glucose solution without the amino acids. Fresh drinking water was always available. After each experiment the animals were sacrificed and the kidneys and liver as well as other internal organs were examined for signs of strain, but they appeared quite normal in each case.

The rabbits lost weight slowly after the first few days, although those that were fed amino acids as well as glucose lost more slowly than those which had only the glucose. It was then decided to add about 0.5 grams of tryptophane per litre of solution to the same mixture. Rabbits fed this diet were found to keep up weight fairly evenly for about a week, then to decline at a fairly steady rate. This loss may have been due to several causes: inadequacy of the protein mixture, to improper balance among the various amino acids, or to absence of other factors, such as Vitamin A. To test the latter supposition a Vitamin A concentrate, "Avalon," was obtained, and one drop was injected intravenously each day in addition to the regular intraperitoneal injections of the usual mixture plus tryptophane. This was found to lengthen the time before the animals lost weight. Probably other growth factors might be added advantageously.

In conclusion, rabbits fed intravenously or by intraperitoneal injections on a mixture of amino acids from hydrolyzed casein, supplemented with tryptophane and Vitamin A, lose practically no weight over a period of two weeks, and remain in normal physical condition.

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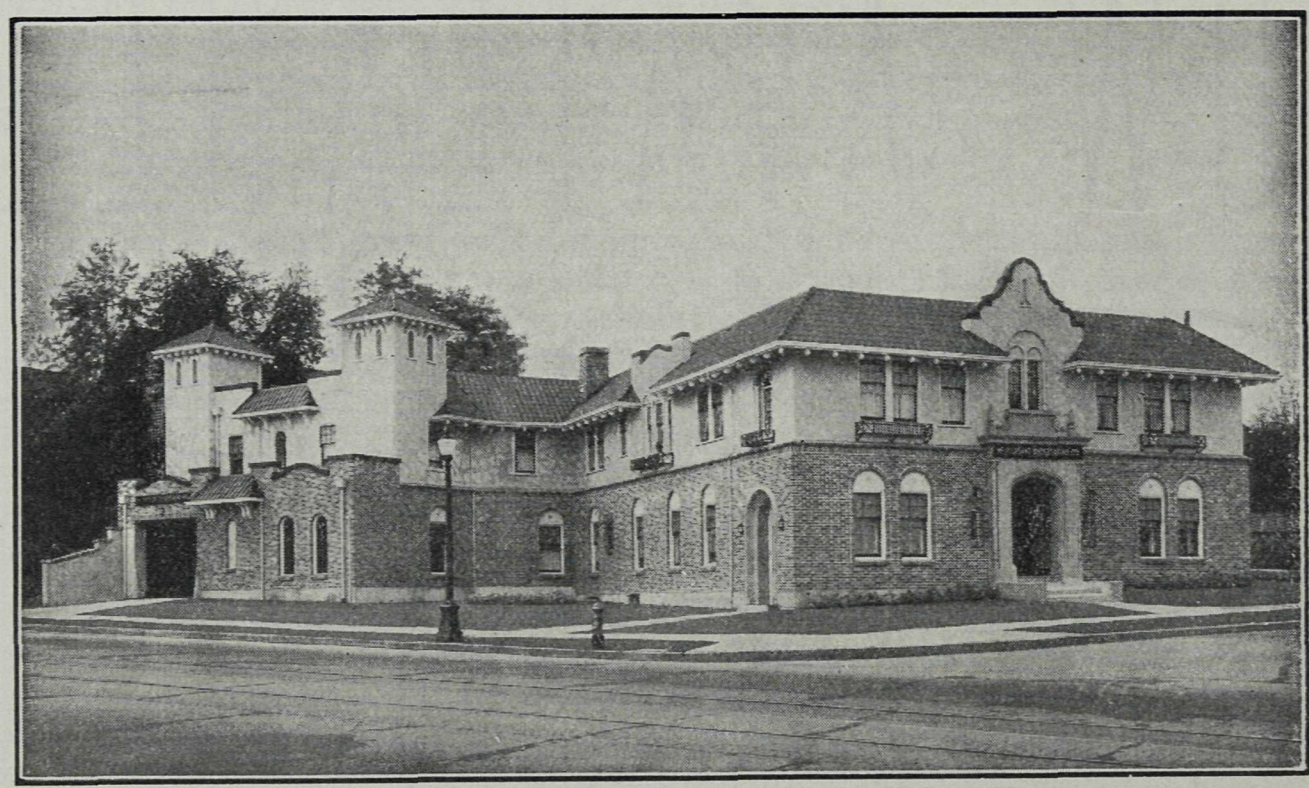

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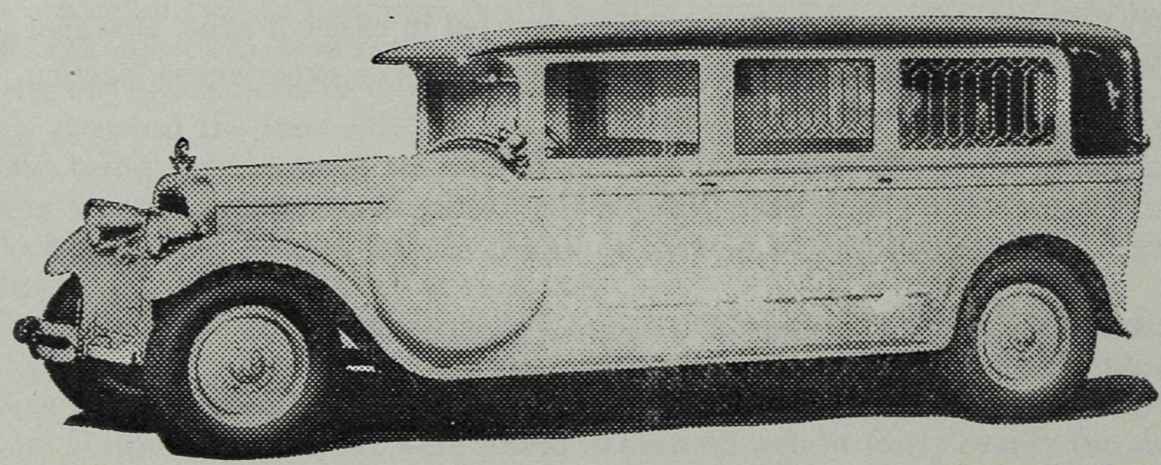

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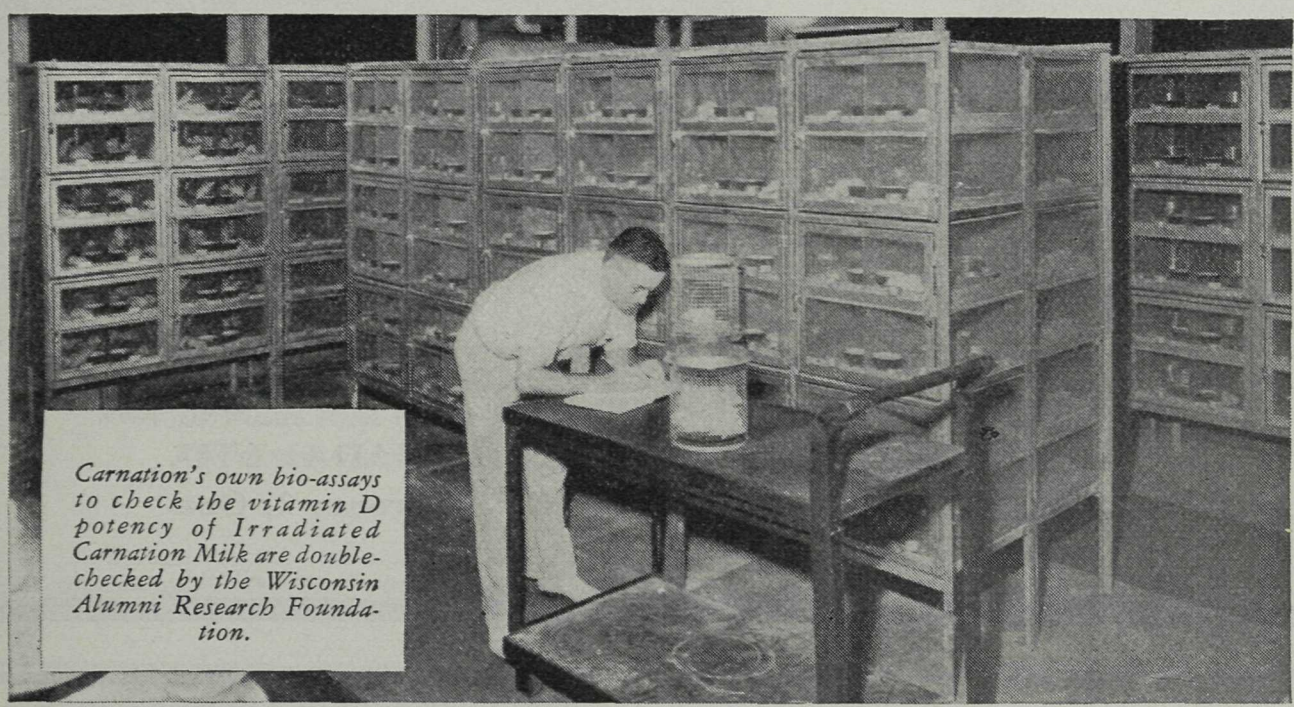

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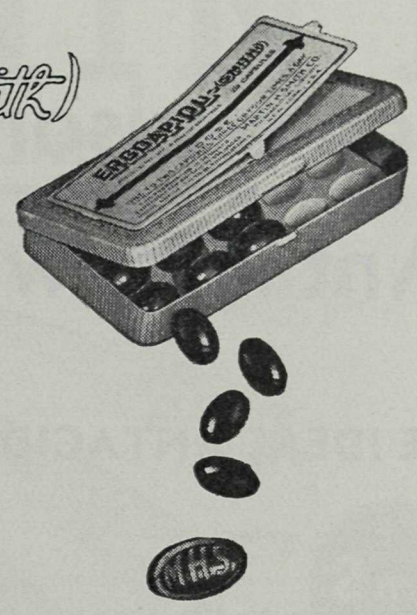

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*H. Beckman: Treatment in General Practice. 3rd Edition: 1938, p. 395.

[1]ANNOUNCING Amphojel with Mineral Oil—For those isolated cases where constipation is associated with the reduction of gastric acidity by Amphojel (Wyeth's Aluminum Hydroxide Gel).

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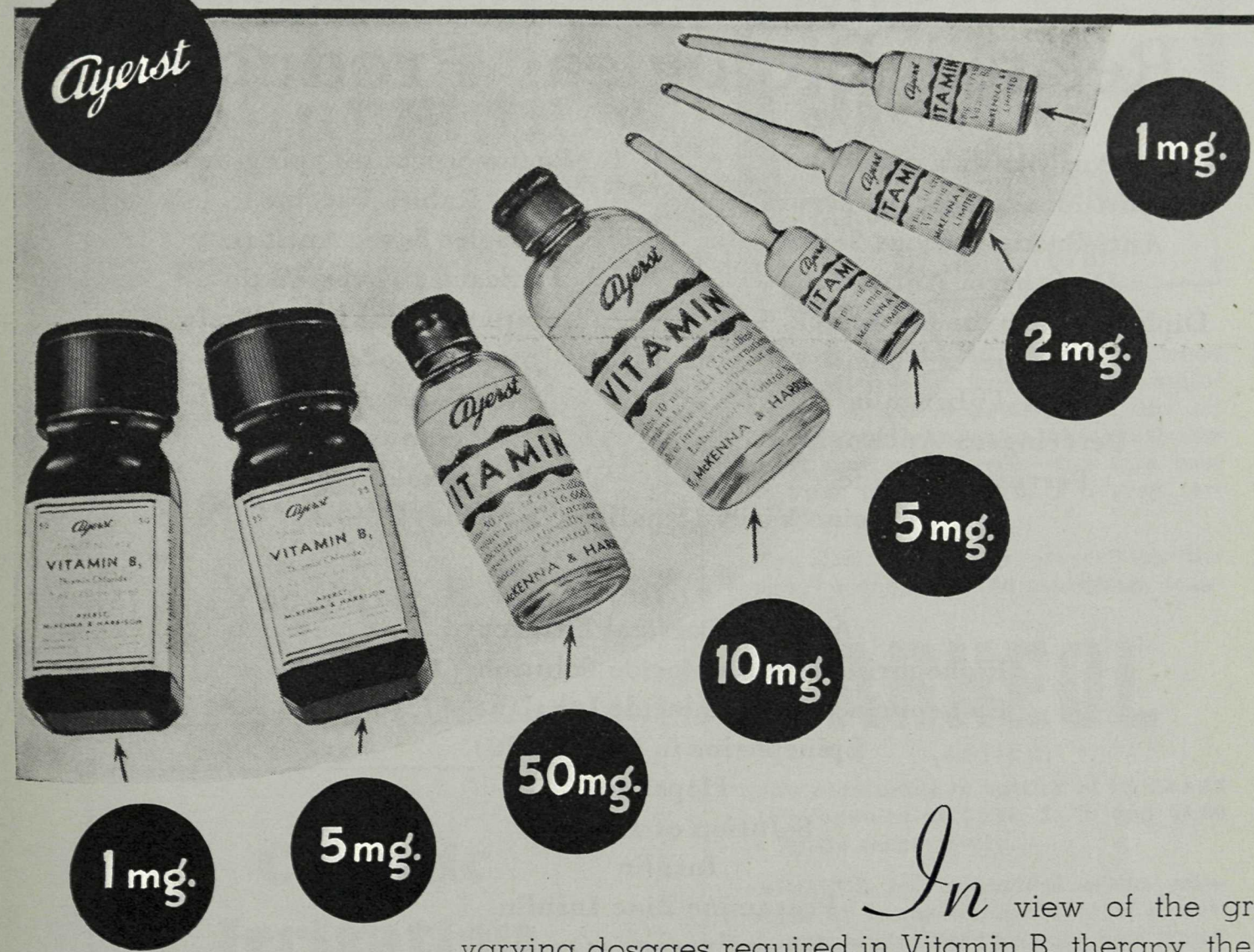

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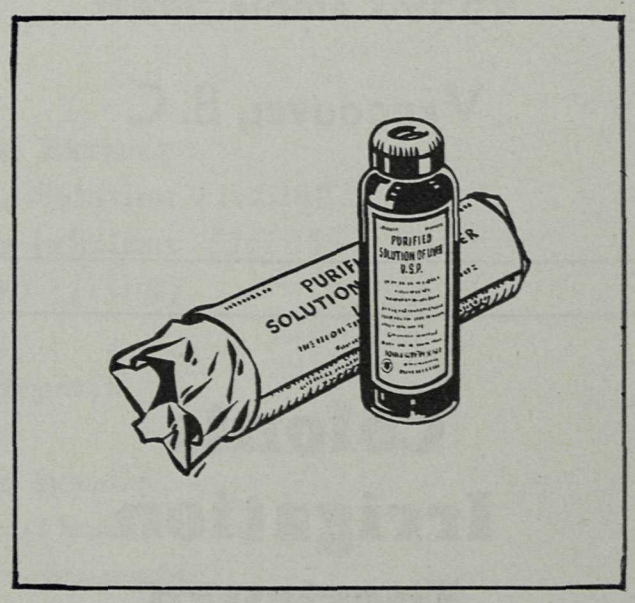

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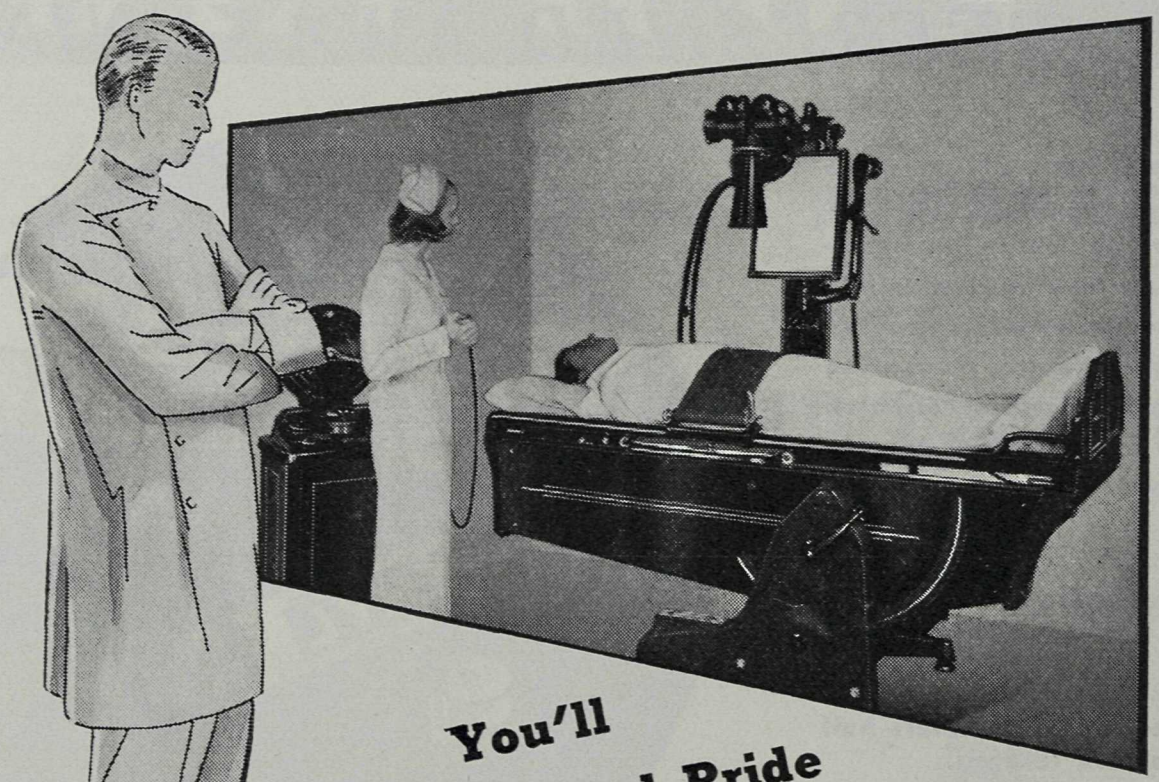

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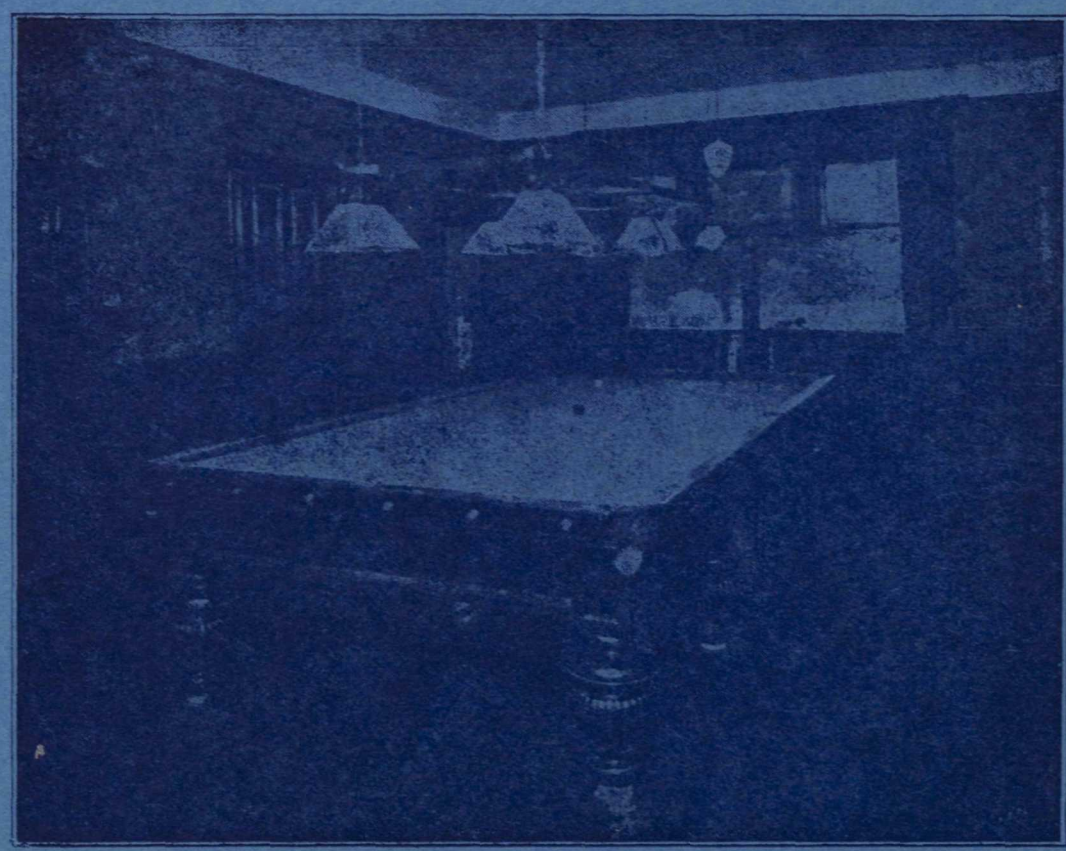

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