

MEDICAL RESEARCH AT DALHOUSIE

ANATOMY

by Dr. R. L. DeC. H. Saunders

The research activity of the Anatomy Department includes problems of both an applied and fundamental nature, the major research interest being centred about x-ray microscopy and electron microscopy.

An x-ray projection microscope, the first of its kind in Canada, has recently been installed in the Anatomy Department. Built last year under grants from the National Research Council, it was assembled in the Electron Microscope Section of the Cavendish Laboratory, Cambridge University, and tested there by Professor R. L. de C. H. Saunders with the help of Miss R. M. Frye, B.A. Physics (Cantab.). Professor Saunders, head of the department, and Miss Frye are continuing studies with this instrument, which permits magnifications up to 1500 times with a resolution somewhat like that of the U-V optical microscope.

New angiographic techniques used with this instrument have made it possible not only to image all the vessels, including the capillaries, in both dead and living material, but also to observe vascular changes in living tissue under experimental treatment. Blood and lymphatic vessels have been imaged simultaneously in the rabbit's ear. Unstained tissue sections provide remarkably contrasty and detailed projection x-ray micrographs of not only bone and cartilage, but various soft tissues

(thyroid gland, spinal cord, tooth pulp, etc.). This is a technique which can reveal not only the internal structure of materials but also the location of particular elements, and further work is being done in this direction. The researches of Professor Saunders and his group have recently been published in the following books: "The Peripheral Circulation in Health and Disease" (Grune and Stratton, New York) and "X-Ray Microscopy and Microradiography" (Academic Press Inc., New York). Other x-ray microscope studies have also been reported in Britain, Sweden, Germany, Switzerland and America.

In addition, an electron microscope is being installed in the Anatomy Department this summer. Dr. C. Roland Leeson, (M.A., M.B., B.Chir. (Cantab.), P.A.R.C.S., P.A.R.C.P.), is at present carrying out electron microscope studies at Cardiff under a British Medical Association Research Scholarship. He will continue studies on salivary glands here this summer. Recent publications of his include, "Localization of Alkaline Phosphatase in the Submaxillary Gland of the Rat", *Nature*, vol. 178, p. 858, ('56).

Dr. S. S. Shulman, (M.B., Ch.B., F.R.C.S., F.A.C.S.), formerly of the University of Cape Town, is at present concerned with the effects of subtrochanteric osteotomy of the femur, and is carrying out experimental studies on rats and applying microradiographic methods. He joins the department this summer.



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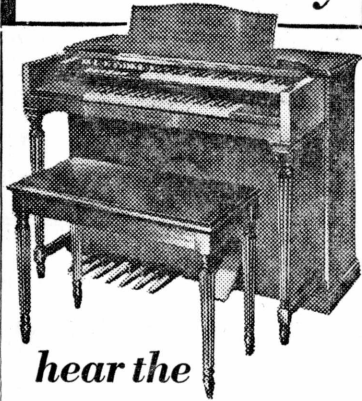
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Dr. R. B. Nichols has been engaged on a study of the internal mammary lymph nodes in view of their relation to carcinoma of the breast, and is preparing a statistical analysis.

In recent years a number of serious intestinal diseases have focussed surgical attention on the extrinsic and intrinsic innervation of the gut. As a result Dr. Nicholas I.E. Nemethy, Associate Professor, has been engaged in neurohistological investigations on the autonomic terminal innervation in the gut, both because of its theoretical importance and possible bearing on the management of certain clinical entities such as congenital megacolon and ulcerative colitis. This work recently reported (Proc. Amer. Ass. Anatomists, Anat. Rec. vol. 130, No. 2, Feb. 1958) and Dr. Nemethy now, under a N.R.C. grant-in-aid, is extending this work to histochemical studies of the synaptic mechanism of the neuroeffector system within the gut wall.

Dr. F. W. Fyfe, Associate Professor, has been studying calcification and ossification in the cricoid cartilage of the human larynx. This work was recently reported (Proc. Can. Ass. Anat. Oct., 1957) will be presented with additional confirmatory material to the Canadian Otolaryngological Society in June, 1958. It establishes certain general principles regarding the sequence of bony changes in the cartilaginous framework of the larynx which commence just before skeletal growth ceases. In addition to autopsy studies, over 350 students and other volunteers of both sexes have been x-rayed to provide statistical information as to the early in-

cidence and progress of these natural changes which were at one time thought to be typical only of old age.

Studies initiated by Dr. A. Trias (Licenciado en Medicina y Cirujia (Barcelona)), and concerned with the effect of pressure on the tibial epiphyses of rabbits are being reported shortly. This work is now being extended by Dr. Fyfe under an N.R.C. grant-in-aid to a study of the response of the growing skeleton to intermittent pressure and torsion using electrically controlled apparatus. The skeletal picture is one of rapid growth as opposed to the "slow motion" development of bone in the larynx which proceeds over many years.

BIOCHEMISTRY

by Dr. J. A. MacCarter

Three research programs are being actively studied in the laboratories of the Department of Biochemistry. Two of these are concerned with problems of the biosynthesis of proteins. The third is a study of epidermal carcinogenesis.

Dr. E. R. M. Kay, Assistant-Professor is studying the incorporation of amino acids into the proteins of sub-cellular fractions of cells, for example, isolated cell nuclei, and the relationship that nucleoproteins bear to protein biosynthesis. His work is supported by grants from the National Research Council and the National Cancer Institute.

Dr. S. D. Wainwright, Associate Professor Research and National Re-

search Council Medical Research Associate is investigating the synthesis and genetic control of the formation of certain proteins by micro-organisms. His work is aided by grants from the National Research Council and the National Cancer Institute.

Mr. R. J. Hoyle, B.Sc., is also working on these problems while studying for the Ph.D. Dr. Wainwright wishes to make a detailed study of the biochemical mechanism and genetic control of formation of one well-defined protein. This represents the first step in a study of the factors controlling the production of a group of well-defined specific proteins. In turn, this would form the basis for further understanding of the general problems of cell growth, differentiation and quantitative differences observed in comparison of the metabolic activities of normal and "cancerous" tissues.

He has developed a system in which a sub-cellular fraction derived from the bread-mould *Neurospora crassa* produces an increase in the activity of tryptophan synthetase enzyme when incubated with a suitable mixture of amino acids and an energy source. It is believed that the increase in activity is due to a net synthesis of new enzyme protein, and Dr. Wainwright is in the process of procuring a highly specific anti-enzyme serum in order to further assess the validity of this conclusion. The system shows co-factor requirements and responses to inhibitors similar to those found by other authors. In particular, the system is totally inhibited by treatment with ribonuclease enzyme. Methods are

being developed for the isolation of highly-purified preparations of the nucleic acids of one strain of *N. crassa* and of pseudoallelic mutant strains unable to form active tryptophan synthetase enzyme. It is hoped that a study of the role of these nucleic acids in proteins synthesis and of their synthesis by sub-cellular preparations from *N. crassa* will shed light on the mechanism by which nuclear genes control the specificity of the protein synthesised by cytoplasmic organelles.

Dr. J. A. McCarter, Professor, aided by Miss J. K. Ball, M.Sc., who is studying for the Ph.D., and by Miss N. G. Eisner and Mr. T. Y. Huh, is studying some of the processes involved in the experimental production of skin cancer in the mouse.

It seems now to be commonly believed that the production of some cancers, particularly perhaps, those of the skin, takes place in two stages. The first of these is an initiating phase in which latent tumor cells are produced by the action of carcinogenic agents on normal cells. The second stage is one in which the latent tumor cells develop into visible tumors under the repeated and prolonged influence of a relatively non-specific 'promoting' agent, for example, croton oil.

Quantitative studies of dose and effect in the initiating phase of epidermal carcinogenesis have shown that the number of tumors produced in treated skin is directly proportional to the area of skin exposed and to the logarithm of the concentration and duration of exposure to a car-

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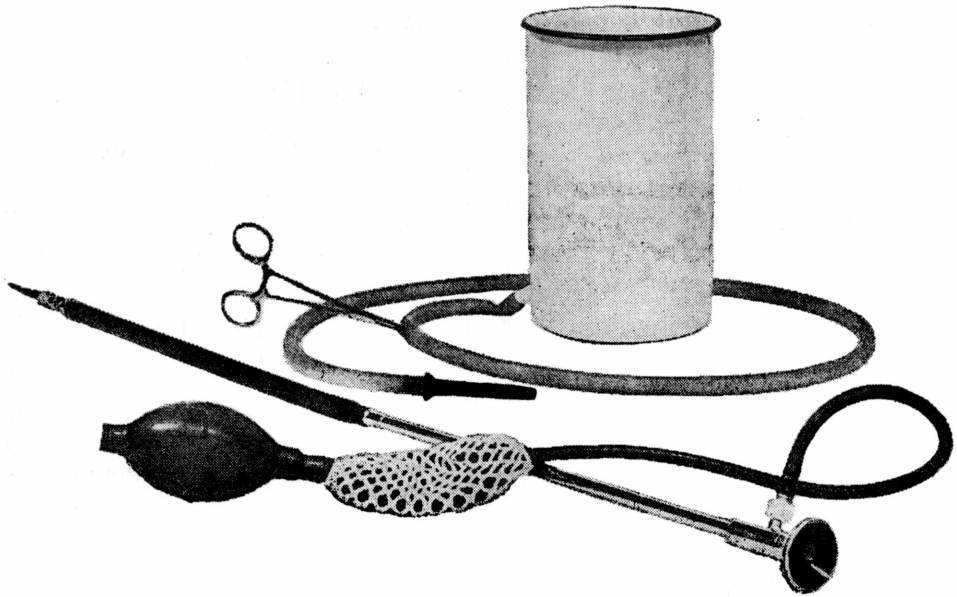
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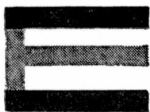
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cinogenic hydrocarbon applied in a non-volatile solvent. A different situation exists when the skin is exposed to a carcinogenic hydrocarbon in a volatile solvent because the solvent evaporates and leaves a deposit of the agent on the skin. Under these conditions a maximum biological effect is produced in a short time. The reason for this is not clear. Analysis of the skin shows that the amount of hydrocarbon in the skin increases steadily during the whole exposure period. Perhaps detailed fractionation studies that are in progress will reveal the reason for the saturation effect that has been observed.

Another observation that may be of interest is that at least one of the carcinogenic hydrocarbon forms with epidermal constituents a loose association that may be of importance in carcinogenesis. This work is supported by a grant from the National Cancer Institute.

MEDICINE

by Dr. W. I. Morse

I would like to describe briefly research problems being investigated by members of the Department of Medicine at Dalhousie University. A comment will also be ventured about clinical research in general indicating its scope and criticizing the concept that only specially trained individuals can undertake clinical investigation.

Professor R. C. Dickson aroused our interest in a new drug, potassium perchlorate, which prevents the formation of thyroid hormone. A study of this drug for the treatment of

hyperthyroidism was initiated with the aid of several members of the resident staff of the Victoria General Hospital, Doctor J. Stapleton of the Radiotherapy Department and the author. Potassium perchlorate has in our hands proved effective in controlling hyperthyroidism and at the time of this preliminary report no patient has shown the serious side effects occasionally observed with other anti-thyroid drugs. Doctor S. J. Shane in collaboration with other members of the Department of Medicine is making a preliminary study using potassium perchlorate for the relief of intractable angina pectoris. It has previously been observed that the susceptibility to angina can be lessened by the induction of hypothyroidism and it is hoped that potassium perchlorate will significantly reduce thyroid function in such patients.

Doctor Allan MacLeod, working as a research fellow with Doctor C. E. vanRooyen of the Department of Bacteriology, is making a study of virus infections of the central nervous system and respiratory tract. Among other contributions, they have made a careful study of an epidemic of aseptic meningitis due to Echo nine virus and also of an epidemic of respiratory tract infection in children.

Doctor C. A. Gordon is making a study of pulmonary function with the aid of a specially equipped laboratory at Camp Hill Hospital. He has conclusively demonstrated that pulmonary ventilation is increased when a person lies with the head tilted downward (by comparison with the horizontal or head raised position). Dr.

Gordon and Dr. R. M. MacDonald have made studies of pulmonary function in the cough syncope syndrome and obtained evidence that the syncopal attacks are associated with over ventilation with its effect on the blood gas concentrations. They also have evidence that this syndrome is not uncommon in hospitalized veterans, a fact which has not been appreciated in the current literature on the subject.

The author, in collaboration with Professor Dickson has initiated a study of the etiology and treatment of obesity. Doctor J. W. MacIntosh, Jr., and Doctor Donald Dodds have participated in this study as research fellows, and Doctor Myer Mendelson from the Department of Psychiatry has interviewed the patients currently under treatment. In an attempt to demonstrate a metabolic abnormality in obesity, loading doses of glucose and sodium succinate (an intermediary compound in the oxidation of food stuffs) have been administered and the changes in blood glucose and pyruvic acid concentrations measured. Differences between obese and normal persons were observed but these were most readily explained by errors in dosage of glucose and succinate to the obese group resulting from use of "ideal" weight for dosage calculation. A study is currently underway in which the dosage of glucose and succinate to obese patients and their controls is based on the weight of body cells or protoplasm, as derived from measurements of total body water. It is thought that the data now being collected will indicate with greater ac-

curacy the true glucose tolerance in obesity.

In addition to the technically difficult determination of total body water in obesity (using a dilution method with deuterium oxide as indicator) Professor C. B. Weld of the Department of Physiology and the author have collaborated in another approach to the measurement of human fat and protoplasm content. This approach is to measure human density which of course involves the measurement of human body volume. After consulting with Doctor A. D. MacDonald of the Physics Department an apparatus to measure volumes by air displacement was built to our specifications. As might be expected with a new technique, many difficulties have been encountered in making sufficiently accurate measurements with this apparatus. If it can be made sufficiently reliable human density values will be obtained in conjunction with those of total body water content and the mass of fat and protoplasm will be derived with greater confidence than would be possible if either density or water content were used alone.

Doctor D. J. Tønning has carried out a study of urinary pepsin excretion in various endocrine disorders. He has observed some correlation in diabetes mellitus between the urinary pepsin excretion and responsiveness of the blood sugar concentration to the administration of sulphonylurea compounds. With the aid of Surgeon Lieutenant Commander Donald Brooks as a part-time research fellow, Doctor Tønning and Doctor John

Aldous of the Department of Pharmacology have been studying the effects of sodium succinate including its therapeutic usefulness in barbiturate poisoning. Doctors Tanning and Brooks are also observing the effect of tolbutamide in the treatment of diabetes mellitus. A study of screening methods for the detection of mild diabetes mellitus has been initiated by Doctor Max Gorelick, a resident at the Victoria General Hospital, with the aid of Doctors Tanning, Morse and Woodbury.

Doctor Tanning has also collaborated with Doctor G. Bethune and Doctor W. Stevenson in a study of hypophysectomy as a palliative measure in advanced metastatic breast carcinoma. About half of their hypophysectomized patients have been helped.

A study of corticosteroid therapy in the syndrome of sterility, amenorrhea, and hirsutism in young women has been undertaken by the author in collaboration with Doctor M. G. Tompkins of the Department of Gynecology, Mrs. L. Stewart of the Provincial Biochemistry Laboratory and Doctor S. Hirsch of the Psychiatry Department. Doctor C. Brennan has been part-time research fellow on this project. We have confirmed the observation of other investigators that this treatment usually re-establishes a normal menstrual pattern in women with this syndrome but evidence has also been obtained from our study that intermittent use of corticosteroids may also accomplish the desired result.

Doctor J. O. Godden with the aid of Doctor J. Filbee from the Department of Radiotherapy and Mr. W. L. M. King, a third year medical student, has made a survey of the occurrence of pain after ingestion of alcoholic beverages in malignant and non-malignant disease. To date they have observed this symptom only in association with Hodgkin's disease. Doctor Godden is also collaborating with Doctor Kurland, United States Public Health Service, and Doctor R. S. Allison from Belfast, Ireland, in a study of the incidence of chronic neurological disease in Halifax County. They have been assisted in this work by Mssrs. E. G. Ellis, H. O. Nason, R. V. Snow and P. J. Kavanagh from the third year medical class. The findings will be compared with observations from the United States, Ireland, Scotland and Japan, which were obtained by similar techniques.

Professor R. C. Dickson is studying the flora of the small intestine and the effect of various antibiotics on the intestinal tract. Doctor J. F. L. Woodbury has undertaken a study of the value of chloroquine in the treatment of rheumatoid arthritis and related diseases. Doctors Crossman Young, Austin MacDonald and Joseph Cairns of the resident staff are making a study of the effect of anticoagulants in myocardial infarction under the supervision of Doctor L. C. Steeves. Doctors Robert Anderson and Cairns of the resident staff are studying the significance of pericardial friction rubs occurring in patients with myocardial infarction under the supervision of Doctor D. L. Roy.

Doctor R. L. Aikens has been making a study of sarcoidosis. Doctor Woodbury with the aid of Doctor Murray Snow and Morse is observing the effect of several uricosuric agents in gout.

A study of symptoms following gastrectomy by Doctor R. M. MacDonald has recently been broadened to include the findings from gastroscopy performed by Doctor Dickson. Doctor J. A. Noble of the Department of Surgery and Doctor J. F. Nicholson of the Department of Psychiatry have also collaborated in this project.

Doctors H. C. Read, R. D. Drysdale and R. L. Aikens, with the aid of Mr. H. Thistle, a third year medical student, have been studying the effects of treating the lymphoma group of diseases and carcinoma of the lung with nitrogen mustard. Dr. Walter Leslie has reviewed our experience with polyneuritis with the aid of Mr. K. Seamans, a third year student.

From present trends one can predict with some confidence that research will play an increasingly important role in the activities of the Department of Medicine. Significant new knowledge is almost certain to come from the cardio-pulmonary unit which is being established and also from the Department's research laboratory which has just started operating in the Dalhousie Public Health Clinic. The first assignment which has been undertaken in the research laboratory by Miss E. Bennett, Schering Research Fellow in Biochemistry attached to the Department, to study

and obtain experience with a new and improved estrogen method. It is hoped that this method can be used to measure urine estrogen excretion in women with sterility, amenorrhea or hirsutism and in men with prostatic carcinoma.

The variety of clinical research projects described in the foregoing paragraphs provides ample evidence that clinical research may require complicated exacting techniques which must be performed by a highly trained laboratory staff or in other instances may require nothing beyond a carefully taken history and physical examination on a sufficient number of patients. It is incorrect to assume that significant contributions to knowledge can no longer be made by physicians whose training and experience has been largely gained at the bedside. Their contributions, however, may sometimes be enhanced by consultation or collaboration with statisticians or experts in other fields.

OBSTETRICS

by Dr. H. B. Atlee

The following research projects are currently being carried out in the Department of Obstetrics and Gynecology:

1. A multidisciplinary investigation into the causes of spontaneous abortion under a Federal Grant headed by Dr. Carl Tupper, out of which several papers have already been produced and which have been read before scientific

bodies in Canada and the United States.

2. An X-Ray investigation into the architectural structure of the female pelvis with reference to previously unstudied angles being conducted by Dr. I. A. Perlin under a Federal Grant.
3. A study of Post-Maturity and its effects being conducted by Dr. I. A. Perlin at the Grace Maternity Hospital under a Federal Grant.
4. A combined study of menstrual anomalies being conducted by Drs. W. I. Morse and M. G. Tompkins under an N.R.C. Grant.

The following are projected studies for which grants are either in the process of being asked for or will, we hope, shortly be asked for:

1. The study of amnionitis to be carried out by Dr. J. McD. Corston and Dr. C. E. van Rooyen.
2. A study of the possible effects of *Trichomonas vaginalis* in producing infections of the newborn.
3. A multidisciplinary approach into the causes of Prematurity.
4. A multidisciplinary approach into the causes of so called functional uterine bleeding.

PATHOLOGY

by Dr. William A. Taylor

Dr. Ian D. Maxwell, who came to us as Associate in January, has been re-establishing here his colony of rats with transferable liver carcinoma. This tumour has properties which

make it suitable for investigation of the immunology of cancer cells. Dr. Maxwell has meanwhile been applying anti-body-detection techniques to human serum in those diseases which are now suspected to have an auto-immune basis and has had positive results in various thyroid disorders.

Dr. Rucbner and Dr. Bramhall are doing work on hepatitis in mice. They are using a virus which produces a disease in mice similar to acute infectious hepatitis in man and have been investigating the effect of various dietary factors on the extent of the liver damage. One rather surprising finding is that the grossly fatty liver of choline deficiency does not increase liability to fatal liver damage. They have found also that mortality is unaffected by varying the amount of fat in the diet. On the other hand, the severity of the infection is greatly increased when the dietary protein is low.

While devoting special attention to autopsies on neonatal deaths and in particular to infants unexpectedly found dead in bed, Dr. C. P. Handforth has conducted animal experiments elucidating the role of nerve reflexes, blood-gas changes and circulatory changes in producing the morbid anatomical changes seen in asphyxia. The results to date suggest that in sudden death in infancy there acute obstruction of the airway, that the level of obstruction is in the larynx, and that in small animals obstruction of the airway may itself initiate reflex apnoea. Bacteriological and virological studies in these infants are done by Miss

Ruth Faulkner in Professor van Rooyen's department. So far, no significant bacteria or viruses have been isolated.

Dr. C. M. Harlow continues his investigation of atherosclerosis with particular attention to changes in serum chemistry in that condition. He is at present feeding marine oils and other products to volunteers and looking for changes in the blood lipids.

Dr. C. D. Chipman is investigating the staining properties of mucopolysaccharides in tissue-sections and has developed a method for rapid identification of mucin information in tumours as an aid to diagnosis. Dr. N. Kerenyi is continuing here, work which he began in Budapest on the pathology of the kidney in the newborn.

Grants in aid of research have been received from Lederle of Canada, the Department of Veteran Affairs and the National Research Council.

PHARMACOLOGY

by Dr. John Aldous

The program of research in pharmacology is particularly directed toward the training of students registered in the Faculty of Graduate Studies. At the present time one student is completing work for the M.Sc. degree and one for the Ph.D. (Division of Biological Sciences).

Financial support for the research programs has been received from the

National Research Council, the Defence Research Board and Hoffman-La Roche, Ltd.

Work which has been concerned with the mechanism of toxic action of various agents has been conducted by Dr. Aldous during the past twelve years. At the present time, interest is focussed on the actions of fluoroacetic acid. This is an interesting agent because its toxicity only appears if it is metabolized by the cell to fluoroacetic acid. In view of its peculiar characteristics, fluoroacetic acid is proving to be a useful tool for investigating the physiological and biochemical functions of the living cell.

Dr. Szerb is carrying on a program which is concerned with the actions of narcotic drugs and their antagonists. The importance of serotonin in sympathetic nerve transmission is currently under study, and toward this end, Dr. Szerb is employing a biological technique which will allow him to detect as little as 1 nonogram⁹ (10- gm.) of nor-adrenaline in his preparations.

Dr. Reynolds is directing the research work of the first Ph.D. student in this department. The project entails an analysis of the various factors involved in cardiac arrhythmias, particularly in auricular fibrillation. As a result of this study, Dr. Reynolds hopes to be able to contribute to the knowledge of the mechanism of action, and desirable properties of anti-arrhythmic drugs.



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PHYSIOLOGY

by Dr. C. B. Weld

1. Dr. Weld, on a grant from the National Research Council, has been for several years studying the mechanisms of transport of lipids in the blood. In particular this has meant the studying of the lipemic condition, the formation, disappearance, and the composition of the chylomicron. This work has been presented at numerous scientific meetings and, by invitation, at an International Conference on blood lipids in Brussels.

Currently the study has been extended to similar particles found in the intestinal lumen. Though similar in appearance to chylomicrons it has been found that the intestinal particles are not the same chemically and it would seem that they are cytoplasmic particles, the nature of which is now being investigated.

2. In conjunction with Dr. Morse of the Department of Medicine, on another N. R. C. grant he is also associated with the study of the obese state and is attempting to develop a practical clinically applicable method of determining the body volume.

3. With Dr. Dickson of the Department of Medicine and a grant from the Defence Research Board, a Cardio-Pulmonary research unit is being set up. The purpose is to obtain exact functional measurements in health and in disease states, under normal atmospheric conditions and in high and in low pressure states. Definitive standards are not at present available and are greatly needed.

Dr. Kaplans' interests lie in the field of cellular physiology and, with a grant from the N. R. C., he is working on the differences in the state and activity of enzymes inside the cell as compared to the same enzyme outside the cell. This study involves surface chemistry techniques, which is almost a separate field of study in itself, and the researches are of a very basic character.

Dr. Josenhan's interest lies in the field of physical exercise and the development and training of muscles. He has developed a unique method of measuring muscle strength, and plans to use this device together with electromyographic recordings to study the relative value of varying training procedures in strengthening normal and diseased muscles.

SURGERY

by Dr. Ian MacKenzie

The activities of any department, pre-clinical or clinical, in a Faculty of Medicine are not complete unless they include active research either of a clinical or experimental nature, or a combination of both. Facilities for experimental work in this department have hitherto been lacking but it is hoped that this deficiency will be remedied within the next few months.

As a result of the reorganization of the Forrest Building, consequent upon the removal of the Dental Faculty to their new building, three rooms have been made available to the department of Surgery for the

formation of an experimental laboratory. Plans for the modification and furnishing of these rooms as a laboratory have been drawn up and the necessary structural work will, it is hoped, be completed very shortly. The University authorities have kindly made a sum of money available for the basic equipment necessary for such a laboratory and once the necessary alterations have been made and the equipment installed it will be possible to embark on a programme of experimental research. Another aspect of such work involves the housing and care of experimental animals and, while it is unfortunately not possible to do this within the Forrest Building, it is hoped that arrangements for this purpose can be made elsewhere.

Obviously it will not be possible to embark on a very ambitious or diversified programme of research in the first instance, owing to the restricted space available, but it is hoped that the facilities which we shall have will enable us to embark on a modest programme. In time it is to be hoped that, as the demand for research space outruns the available facilities, the necessity for a larger laboratory will become apparent.

To begin with, experimental work on some aspects of Hodgkin's disease (lymphadenoma) and of Mammary Cancer is contemplated and it is hoped to establish close relations with some of the pre-clinical departments in the pursuance of this programme.

BACTERIOLOGY, VIROLOGY and IMMUNOLOGY

by Dr. C. E. van Rooyen

Following the departure of Professor R. W. Reed to occupy the Chair of Bacteriology at McGill University, Professor C. E. van Rooyen, of the University of Toronto School of Hygiene replaced Dr. Reed in March, 1956 and so it was possible to continue the teaching and research duties of the Department, without interruption. Through the co-operation of Dr. D. J. Mackenzie of the Provincial Public Health Laboratories, an immediate start was made on the setting up of a laboratory to meet the demands for teaching routine and research in virus field, so urgently desired in Eastern Canada. We were greatly assisted in our attaining our objective by grants of funds for purchase of equipment from the Defence Research Board of Canada, the Provincial Health Research Grants and the Nova Scotia Chapter of the Canadian March of Dimes. With the exception of an electron microscope which we lack for need of funds, all other equipment has now been installed and operating satisfactorily.

Dalhousie graduate members of the first virus laboratory consisted of Dr. Alan J. MacLeod, M.D. (formerly of Moser River) Miss Ruth Faulkner, M.Sc., and Mr. Kenneth Rozee, M.Sc. Subsequently we were fortunate in being able to secure the services of an enthusiastic group of technicians, consisting of Miss Elizabeth Petite, B.Sc., Miss Boussey, Miss Virginia Ritcey, B.Sc., Mr. Joseph Burke and Mrs. Wanda Tenderenda.

The year 1956 was occupied in establishment of the basic routines, methodology and techniques of virology. These included acquiring knowledge of the practice and principles of tissue culture, animal inoculation, and the bioassay of virus growth and neutralization techniques. Simultaneously the support of the Victoria General Hospital and Children's Hospital staff and the surrounding physicians, was enlisted and the new facilities available at Halifax for virus studies, were brought to their notice.

During the summer of 1956, an outbreak of acute non-bacterial respiratory tract disease occurred among the infants of Nova Scotia. Material was duly collected and a determined effort was made to isolate Adeno or other viruses from such cases. No agent was however recovered, but valuable technical experience was gained. The negative laboratory results coupled with the practical importance of the clinical problem reveal the great need for planned and aggressive research into the aetiology of infant bronchiolitis.

The year 1957 saw the scope and field of the Virus Laboratory enlarged to extend their services to include Newfoundland, Prince Edward Island and New Brunswick through the Atlantic Provinces Joint Medical Advisory Committee, under the direction of Dr. J. S. Robertson, Nova Scotia Deputy Minister of Health.

From March 1957 to September 1957, a widespread outbreak of aseptic meningitis occurred in Eastern Canada. From suspected cases, approximately specimens were forward-

ed to the Virus Laboratory. Likewise Dr. A. O. D. McDermott, Chief Medical Health Officer of Newfoundland and Dr. J. W. Davis of St. John's Fever Hospital reported in the Canadian Medical Journal that a similar epidemic affected Newfoundland and that probably 1,000 cases occurred. From our studies it has been possible to designate the clinical picture of Echo 9 virus infection, a hitherto unrecognized disease in Eastern Canada.

Symptoms and Signs of Echo 9 Infection

40 patients from whom Echo 9 virus was isolated were studied clinically. 33 of these were under 15 years of age, 27 were male and 13 female. Of the females, two were in the first trimester of pregnancy and one in the second.

The onset in most cases was insidious but a few patients gave a clear-cut history of a 24 hour period of complete remission early in the disease. The course of the illness was variable being most severe in young adults and teen-agers.

Headache, nausea and vomiting were the outstanding symptoms and were present in all patients old enough to state their complaints. Other common complaints were stiff neck, feverishness and muscle pains. A rash was seen in ten of the patients studied. This was maculopapular, pink in color and distributed chiefly on the face, neck and trunk. The lesions varied in size from 1-3 mm. in diameter and were present from 24-48 hours. Less frequent complaints were chills, dizziness, photophobia and constipation.

Physical findings in most cases were few and consisted of a moderate elevation of temperature and stiffness of the neck. Spasm of the hamstrings and the presence of Kernig's sign were noted in about 25% of cases. The deep reflexes were normal and there was no evidence of cranial nerve palsies. Muscle tenderness was present in 2 patients who represented the most severely ill members of the series. One was a youth of 14, the other a man of 50; both presented with severe throbbing frontal and occipital headache, photophobia, nausea and vomiting, and pain and stiffness of the neck, back and limbs.

This disease was clinically indistinguishable from severe pre-paralytic poliomyelitis. In contrast to this, there were 3 young children in a small localized epidemic who had no complaints whatsoever. The average duration of illness in the series was 9 days and there were no complications or unfavourable sequelae.

The average of 26 white blood counts was 9,500 and only 2 were over 15,000. A cerebrospinal fluid pleocytosis featuring mononuclear cells was seen in nearly all cases. The average of 35 determinations was 389 with a high of 2240 and a low of 8. The chlorides were normal or very nearly so in all cases. The protein was normal or slightly elevated with an average of 41 mg.% in 29 determinations. Table II contains a summary of Echo 9 virus isolations in Eastern Canada.

Discussion on Findings

141 cases of aseptic meningitis observed in the Atlantic Provinces have been subjected to clinical and viro-

logical studies. From two patients we recovered Coxsackie A 9 virus, from one patient Coxsackie B4 virus, from three patients Poliovirus. From 36 patients unidentified agents were obtained. From 40 cases Echo 9 was obtained and thus clinical and laboratory accounts of Echo 9 infection form the bulk of the present studies.

In considering the clinical syndrome of Echo 9 infection, a variety of interesting possibilities worthy of further investigation arise. Thus, many of our cases could have passed unnoticed as example of severe headache, save for the fact that the attention of local clinicians had been focussed on the disease and a search for cases was conducted. The frequency with which isolation of virus was possible from the CSF has emphasized the value of virological examination of the CSF in all cases of severe headache of idiopathic character.

The relationship of Echo 9 diseases with rash to rubella is worthy of future scrutiny. The lack of a suitable laboratory test for rubella virus has proved a major handicap to the accurate identification of rubella. The rash observed in Echo 9 bears a close similarity to that of rubella and it is not improbable that the two conditions could have been confused in the past. But whether or not the two diseases are identical etiologically remains open to conjecture and further research alone can decide. It should also be mentioned that the conditions designated Roseola Infantum and Boston Exanthem (Neva and Enders, 1954), (Neva and Zuf-

fante, 1957) merit similar consideration. It is hoped that the continued efforts of clinical and laboratory personnel will help to establish etiological diagnoses for some of the exanthemata and fevers of unknown origin so frequently encountered in medical practice. In view of the correlation between rubella and congenital deformities, we believe that a search for Echo 9 virus should be conducted in the pregnant female in the event of any patient developing such signs and symptoms as we have described in a sociation with Echo 9 infection.

The growth of Echo virus in tissue convenient and perhaps more readily cultures of human amnion provides a available laboratory medium for recovery of the agent than monkey kidney tissue. From three women pregnant, we isolated Echo 9 virus in primary culture on human amnion cells, but it is also interesting to record that pregnancies continued uninterrupted to date. The growth of Echo 9 virus in human amnion at present would appear to be of academic importance, but the existence of Echo 9 virus amnionitis during pregnancy is a possibility which should not be ignored.

Observations on the pathogenicity of Echo 9 virus to suckling mice which were originally reported by Boissard et al (1957) have been confirmed and extended by us. Histological changes seen in the skeletal muscles of infant mice bear the closest resemblance to those first described by Dalldorf and Sickles (1948). There are pathognomonic of Coxsackie A virus infection and manifest clinically as perperangina of

the infant, but the counterpart of this disease in the adult is however obscure. Another apparent difference seems to be that whereas Dalldorf and Sickles were able to induce changes in suckling mice by direct inoculation of fascal materials, the authors and others have only succeeded in doing so by injection of monkey kidney or human amnion culture material.

Resume of Present Researches

1. Echo 9 virus has been isolated from 40 cases of aseptic meningitis which have been studied clinically.

2. Headache, nausea and vomiting, stiffness of neck, feverishness and muscle pains were prominent symptoms. Moderate fever, nuchal rigidity and normal reflexes were cardinal physical findings.

3. A maculo-papular rash was noted in some 25 per cent of our cases.

4. A CSF - Pleocytosis featuring mononuclear cells was a constant finding.

5. Virus was readily isolated from CSF, stools and throat washings on monkey kidney and human amnion cells in primary cultures.

6. The viruses isolated were antigenically similar, serologically typed as Echo 9 virus, and shown to be pathogenic to infant mice.

7. Some implications of our findings have been discussed in relation to the etiology of severe headache, roseola infantum and rubella.

PREVENTIVE MEDICINE

by Dr. J. O. Godden

The major research project in this Department at present is a study of BCG Vaccination and the effectiveness of antimicrobial therapy in tuberculosis patients. Dr. C. J. W. Beckwith, who is directing this study, has completed the tuberculin testing of all Halifax school children during the past three years. "Tuberculin converters" are divided into two groups, one being untreated and the other receiving anti-tuberculosis therapy. A follow-up study is being maintained to determine the incidence of clinical tuberculosis in both groups.

The children in Grades 9, 10 and 11 who are tuberculin negative are offered BCG vaccination and a follow-up study is being conducted to determine the incidence of tuberculosis in the vaccinated and unvaccinated following graduation from high school. More than one-third of the new cases of tuberculosis in Halifax in recent years has been in this age group.

Studies on BCG vaccination of nurses and medical students are also being continued. A very effective reduction in tuberculosis has been established. Special interest is being taken in a small group of students who do not develop tuberculin hypersensitivity following vaccination, but who give some indication of developing immunity to tuberculosis.

A study is also being carried out on the optimum period of hospital care for patients with tuberculosis. A comparison is being made of the

rates of reactivation of patients following discharge from the Nova Scotia Sanatorium and the Halifax Tuberculosis Hospital with a view to determining the relationship of length of hospitalization and reactivation rates.

The Department also has some interest in research projects in Aviation Medicine, particularly the factors affecting the incidence of decompression sickness. A low pressure chamber is available in the Department.

Members of the Department of Preventive Medicine have been active in local research projects and have contributed a number of papers to the literature.

1. Epidemiology in the Service of Clinical Medicine, Nova Scotia Medical Bulletin, about July, 1957.

2. The Chronic Neurological Disease Survey, Halifax County, 1957. Nova Scotia Medical Bulletin, March, 1958. Dr. John O. Godden.

These papers describe a joint project of the National Institutes of Health (U.S.) and Dalhousie University, a survey of the incidence of chronic neurological disease in Halifax County, Nova Scotia, and Charleston County, South Carolina.

3. The Symptoms of Alcohol Pain—John O. Godden, Nova Scotia Medical Bulletin, August, 1957.

This is a preliminary report of a study done in the summer of 1957 with Dr. John F. Filbee and Mr. W.

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L. M. King on the incidence of alcohol pain and various diseases (to be published in the future).

4. The Prevention of Cancer of the Lung—John O. Godden, Canadian Journal of Public Health. To be published June, 1958.

5. A Comparison of Organic and Psychiatric Symptoms in a Small Town—Wm. Longaker, M.D., and John O. Godden, M.D. To be published.

This was a co-operative project between the Department of Psychiatry, Cornell University and the Department of Preventive Medicine, Dalhousie University.

The Department of Preventive Medicine is currently at work on:

1. A Scientific Exhibit on the Prevention of Carcinoma of the Lung, to be presented at the annual meeting of the Canadian Medical Association, June 16-20. Participating in this are Dr. C. B. Stewart, Dr. John O. Godden and Mr. John Merryman.

A study of the characteristics of smokers and non-smokers is underway under the sponsorship of the Medical Faculty Research Fund. This is a co-operative effort between the Department of Psychology, Dalhousie University and the Department of Preventive Medicine. Dr. H. D. Beech and Dr. John O. Godden.

We are looking forward to the successful completion of the Chronic Neurological Disease Survey which is now in its final stages under the direction of Dr. R. S. Allison of Belfast, Northern Ireland and Dr. Milton Alter of Bethesda, Maryland.

PSYCHIATRY

by Dr. R. O. Jones

Since the inception of the Department of Psychiatry in September, 1941, we have always had a considerable urge to be involved in research activities particularly so since we feel that it is difficult to keep staff academically oriented and interested and to develop research interests in students if the example of research in the Department is not very obvious. However, I am sorry to say we have not been terribly successful in this objective because there has been such a rapid development of the teaching program, both at the undergraduate and graduate level plus a parallel demand for increased services. There has, of course, been a rapid increase in the man power of our Department; but the other demands have more than used our resources, and research by and large has fallen by the board.

We have, however, managed to make some slight beginnings on a research program; and there is good reason to hope that in the next two or three years this will be very widely expanded. To date the following have been the research activities of the Department.

(a) In 1948 with the advent of the Federal Mental Health Grants which took care of a number of teaching and service activities of the Department, the Rockefeller Foundation which had actively supported these activities prior to the Health Grants agreed to allow their money to remain for the next few years in the University to initiate

studies between the Department of Psychiatry and the Department of Obstetrics and Gynaecology with the stimulation status by the fertile brain and the tremendous energy of Dr. H. B. Atlee, we were happy to co-operate with his Department; and Dr. H. K. Hall became involved in a study of the attitudes of pregnant women attempting to predict their behaviour during labour and their subsequent behaviour as mothers. This culminated in a paper presented at the American Psychiatric Association a few years later. Dr. Sol Hirsch also was supported for two years on this project and worked in the Pre-Natal Clinic. Here he spent a good deal of time studying the personality dynamics and motivation of illegitimately pregnant girls and has contributed at several programs of national societies on this subject. I think that he has conclusively demonstrated the value of psychiatric aid in a Pre-Natal Clinic and that the observation which he has made and which we hope will be added to in the near future will be of aid in understanding the problems of illegitimacy.

(b) The research activities of the Department were very much stimulated by Dr. R. J. Weil when he became a staff member in the early 50's. Dr. Weil has had a very excellent research background, and at the time of his coming to Halifax he was just completing a major research study in collaboration with Dr. Joseph Eaton of Wayne University in Detroit on mental illness in the Hutterite culture. There were many publications on this subject, and Dr.

Weil brought a great deal of honour both to himself and to the University by the quality of the work that these studies included. This culminated in the book published in 1955, "Culture And Mental Disorders" by Doctors Joseph W. Eaton and Robert J. Weil. Since that time Dr. Weil has been actively engaged in one or more research projects all the time. Most recently he has collaborated in the multi-disciplinary project on Spontaneous and Habitual Abortion. The other members of the team are rD. Carl Tupper, Obstetrician and Gynaecologist (Director of project); Dr. James Gray, Pathologist; Dr. Horace Beach, Psychologist; and Mrs. Lucille Stewart, Bio-Chemist. This has been a very intensive study of a large group of women who spontaneously abort and has resulted in a number of presentations at national meetings of psychiatric and obstetrical societies. In June of 1958 further papers will be presented for the Canadian Psychiatric Association and the Canadian Association of Obstetricians and Gynaecologists. This study is still going on, thanks to the generosity of John Wyeth and Brother Limited, Canada.

(c) The Department of Psychiatry has received a grant for the past three years to be used in teaching and research from John Wyeth and Brother (Canada) Limited, in collaboration with other departments of the hospital. This has largely been used in teaching activities in the medical services of the Victoria General Hospital but some small amount has been devoted to the provision of psychiatric aid in medical research

problems. It has led to collaboration between Drs. Myer Mendelson and W. I. Morse on the etiology and management of obesity. We are sorry that this project had to temporarily discontinued with Dr. Mendelson's departure from the city. However, I am glad to say that the psychiatric aspect of this project has now been taken over by Dr. Doris Hirsch and is proceeding in a satisfactory way.

In conclusion, I hope that the research program of the Department of Psychiatry at Dalhousie University is only in its infancy. From the above-mentioned studies, it is obvious that here we have a very excellent opportunity for inter-disciplinary research; and it is our hope that we will be able to develop this opportunity over the years so that the particularly valuable opportunities which exist in this medical centre may no longer remain unexploited.

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