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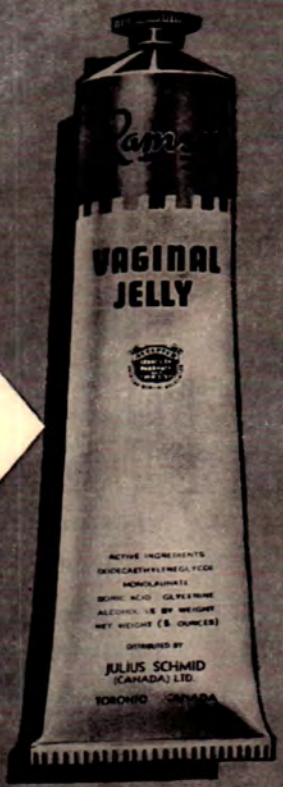

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CLINICAL ANGIOCARDIOGRAPHY

JAMES GORDON FRID, M.D., '50 *

WHEN the cardiac chambers, the aorta, and the pulmonary artery are serially visualized following the intravenous injection of a radiopaque substance, the procedure is known as angiocardiography.

The procedure aims to aid in diagnosis by delineation of large blood vessels and chambers of the heart and by recording the passage of the material with sufficient continuity to study the dynamics of the circulation involved.

Angiocardiography is a relatively new radiological technique which is limited now primarily by expense but which promises wider use in the light of frequent advances in equipment. Roentgenological visualization of the blood vessels in pathological specimens has been performed almost since the discovery of X-rays. However, until the development by Robb and Steinberg of angiocardiography in 1939, there had been no method of visualizing the superior vena cava and the left ventricle and no practical method of outlining the right chamber of the heart, the pulmonary circulation, and the thoracic aorta in man. Contrast roentgenography in the past had provided information about other portions of the body but until angiocardiography it had had limited success in the demonstration of cardiovascular structures of the thorax. Forssman in 1931 was unsuccessful in visualizing the chambers of the heart following insertion of a catheter at the ante-cubital vein and injection of an iodide preparation. In the same year Moniz *et al* were successful in visualizing the pulmonary blood vessels with Forssman's technique. Although reputedly harmless, the difficult nature of cardiac catheterization has precluded its general use. Another obviously unsuitable method tried has been the puncture of the left ventricle and the ascending aorta. In 1938 Costillanos *et al* successfully visualized the right side of the heart and pulmonary artery by peripheral intravenous injection of organic iodide compounds but only in children under six years of age. It was necessary to find a method of injection fast enough that sufficient opacification of the vessels could be obtained and also to find a material which was innocuous on injection. It was suspected that a large bore needle and syringe tip satisfied the first

* For the 1949-1950 Session the single award of $50 for The W. H. McGuffin Scholarship in Radiology was divided equally between James Gordon Frid and Howard Spencer Cameron.

criterion and that diodrast then used for intravenous pyelography would satisfy the second. In January, 1936, experiments on rabbits began to verify the above two suspicions. In January, 1937, the first clinical visualization of the right side of the heart and pulmonary circulation was obtained; in May, 1937, the left chambers and the aorta were successfully seen.

To give a proper account of the technique in this examination is somewhat difficult because of the newness of the field and because of changes in procedure coincident with frequent developments. The different methods, however, divide themselves fairly distinctly into two groups, the one in which only certain parts of the heart and major blood vessels are studied and the other in which the complete circuit of the contrast medium through the heart and its vessels is recorded. The preparation and manipulation of the patient, generally speaking, are the same however in both instances and will be discussed first.

Patients of all age groups can be examined by this procedure. This is stated to be a benefit of this technique by one writer who points out that in the previous diagnostic method of cardiac catheterization it was difficult to examine infants. For three to four hours previous to examination everything by mouth should be excluded to prevent aspiration of food particles in case of vomiting. Vomiting, however, is a very infrequent occurrence. It is generally considered best to give a general anaesthetic to children in order to insure co-operation during the examination; however, with recent developments rapid examination is possible and anaesthetic is not necessary The latest suggested management is to give phenobarbital to the older children plus some sweetened water in a bottle for the infant. Most adults are not premedicated. The blood pressure and pulse are recorded, and if hypotension, allergic tendency, or drug sensitivity is elicited, 0.3 to 0.5 c.c. of 0.1% epinephrine should be given just prior to the injection of diodrast. It is probably most advisable to fluoroscope the patient to determine the optimum position for the best visualization of the structures desired. The left anterior oblique position is most commonly used but the right anterior oblique and postero-anterior positions are also used, depending on what anatomy is to be intensively studied. The degree of rotation which is optimum is recorded by an angle meter, or by a special rotating stool marked in degrees. The solutions to be injected are warmed to body temperature and maintained there. Patients with cyanotic heart disease and polycythaemia are given fluids subcutaneously, pre-operatively, to prevent dehydration, and oxygen is given concomitantly with the anaesthetic, if used.

Local novocaine anaesthetic is applied to the site of the cut on the right or left ante-cubital vein. The distal end of the vein is ligated and a number 13 or 14 cannula is tied into the proximal end. A slow intravenous drip of normal saline is commenced through a three way stopcock to insure patency of the cannula. Some workers test the adequacy

of the location of the needle by the rapid injection of 50 c.c. of saline. To prevent diffusion 20 c.c. of blood are drawn into the syringe containing the diodrast. Since blood is lighter than diodrast it is on top and follows the diodrast into the vein. To test for sensitivity to diodrast most inject a few minims of 70% diodrast through the cannula. If after several minutes no reaction has occurred then the final injection is made. Some also test for sensitivity by either intracutaneous or conjunctival application and any allergic symptoms are noted. It is claimed however that these latter tests are inadequate and serve only to satisfy medico-legal needs. In order to obtain sufficient opacification, the following dosages according to age have been found satisfactory:

3 mos. to 2 yrs. of age	— 10 to 18 c.c.
2 yrs. to 10 yrs. of age	— 20 to 30 c.c.
11 yrs. to 15 yrs. of age	— 30 to 40 c.c.
15 yrs. and over	— 40 c.c.

An injection period of longer than two seconds will seldom give sufficient contrast for diagnostic visualization of the heart and great vessels.

Some workers claim that it is necessary for the patient to be inspiring forcibly following complete expiration in order that the diodrast will reach the superior vena cava soon enough. This point of technique is based on the aspiration effect of the negative pressure in the thorax. If the patient is emphysematous one must wait one-half to one second after the beginning of the inspiration before injection to get the aspirating effect of the thorax. Some commence the injection immediately after the first exposure has been made; others make the first exposure when the last 5 to 10 c.c. of diodrast are entering the vein. As soon as possible after the injection the cannula is removed, the vein is tied off and the wound is closed with silk suture.

Most claim that the erect posture is the best as there is least distortion of the heart. In this position the arm is raised from the side to an angle of 135 degrees, during injection and examination. The tautograph, a recent development to be discussed, employs an ordinary radiographic table and hence allows prone and semi-horizontal positions.

The main difficulty in this examination has been of course to provide apparatus which will supply unexposed film rapidly enough since the opaque material traverses the vascular circuit concerned in approximately 8 seconds. This difficulty has created the two different types of examination previously mentioned. In the first where only conventional equipment is available the circulation time to the particular part to be studied is pre-determined and the exposure made at that time. Multiple anatomical studies therefore require multiple injections. This type of examination was the first used since standard equipment only was employed, the best for the purpose being a stereoscopic film changer. In the latter, two exposures can be made at an interval of three seconds. The

disadvantages here are great: *1.* Circulation times; arm to lung (ether), arm to carotid sinus (sod. cyanide) must be done and these at times are not accurate due to the pathology to be studied. *2.* Multiple injections must be made. *3.* Single exposures are of the momentary state only and may therefore give rise to serious misinterpretation. For detail a single exposure is best but for physiological structure continuous recording is required. All radiological departments can employ this first method; the second type of examination to be described, however, is as yet too expensive.

In the second type of examination the whole circuit of the opaque material is recorded. Here many types of apparatus have been tried some of which will be mentioned. They are based on one of three principles:

1. Rapid movement of cassettes by a moving rack or by a rotating cassette holder.
2. Rapid still photography of the fluoroscopic screen.
3. Movie photography of the fluoroscopic screen.

The most recent development in the group with moving cassettes is the tautograph. It obtains rapid serial roentgenograms by utilizing a chain conveyor system for standard cassettes, by the incorporation of a self-cocking synchronized Potter-Bucky grid, and by the complete automaticity of the entire equipment. The details of this device were released in July, 1949, by Wendell Scott of St. Louis. It produces a sequence of up to 10 cardiograms at 1 second intervals and thereby gives a continuous picture of the bolus of diodrast as it circulates through the chambers of the heart, lungs and aorta. It eliminates the necessity of forecasting circulation time in order that exposure may be made at the proper second. One injection is all that is necessary. It gives added clarity and contrast since it incorporates the Potter-Bucky diaphragm. The device also reduces the hazard of excessive Roentgen ray exposure since fluoroscopy is not employed.

In the September, 1949, issue of *The American Journal of Roentgenology and Radium Therapy,* Dotter *et al* have published their preliminary paper on rapid photographic recording of roentgenoscopic images. This method had previously been hampered by the small film size and the distortion resulting from short target-screen distances. This new apparatus is more economical than others promoted in that it can also be used for routine chest photo-fluorographic examinations. The equipment consists of a roll-film magazine in which only the roentgen-ray film is transported. The magazine is mounted upon a motor base plate which is attached semi-permanently to a regular radiographic table or other suitable support. It is snapped in and out of the base plate for loading and unloading. The magazine is light in weight, and contains 75 feet of approximately 9.2 inch square film with capacity for approximately 90 exposures. The motor base also mounts two high speed intensifying screens and a horizontally moving parallel grid in front of the magazine. If the motor

base plate and magazine are mounted on a pedestal Bucky stand unlimited positioning is available. A stretcher can be positioned over the film in the case of the debilitated patient. This technique gives high quality, clearly defined roentgenograms. Exposure every half second can be made The apparatus is now available commercially.

The third group, i.e., where movie photography of the fluoroscopic screen is employed is as yet not perfected. However, by this method all phases of the circulation are recorded and frequently the aortic or pulmonary valve is recorded in one frame. A coarse grain film is needed and therefore detail is sacrificed to some extent.

To return to the medium injected, diodrast is very satisfactory for angiography. It causes lttle venospasm, and systemic reactions are usually minimal. Ten to twenty seconds after injection most patients sense a metallic taste in their mouth and a wave of heat from mouth to lower extremities. It has been found that coincident with these sensations there is a drop of not more than 30 millimeters of Hg in arterial blood pressure and a decrease of heart rate of 30 beats per minute approximately. Transient nausea, vomiting, urticaria, pruritus, sneezing and a sense of laryngeal constriction occur very occasionally, but are rarely of sufficient moment to cause any concern. In the few instances where reaction has occurred, 0.3 to 0.5 c.c. of 0.1% epinephrine affords prompt relief. Toxic reactions supposedly occur principally in cases where renal damage is present. It is inadvisable to inject diodrast into those with: severe renal damage, marked jaundice, hyperthyroidism, circulatory failure and those who are critically ill. Personal and family history should be checked carefully for allergy. If it is positive, review the need for examination. Occasionally, epinephrine is used prophylactically and with success. There are very few delayed reactions such as urticaria and angioneurotic oedema. They too, are relieved by epinphrine. Mild thrombophlebitis developed at the site of injection in 33 of 127 patients of one series, but was of no consequence. No toxic effect on the heart, lungs, kidneys or the blood was discovered. Diodrast is freely miscible with blood, rapidly excreted and relatively non-toxic but it is slightly irritating at the site of injection in some patients. The discomfort of the examination to the patient is comparable to that caused by gastric lavage, bronchography, or spinal puncture. Reaction, if any, does not hinder visualization as it occurs after the roentgenograms have been made.

This specialized technique is utilized in the following clinical conditions:

1. Differential Diagnosis of Aortic Aneurysm and Mediastinal Tumour.

The fact that mediastinal tumours closely approximate the heart and great vessels occasionally makes it very difficult to differentiate the tumours from vascular structures when examined conventionally. The tumour may be so close to the pulsating structures that if it is examined

by fluoroscope, and especially if it is cystic, it may appear to be pulsating actively. Indeed, a murmur may be heard over the appropriate part of the chest and a diagnosis of aneurysm seem justified. On the other hand, aneurysms do not always pulsate because the wall may be fibrotic, the communication with the artery may be too small or the blood in the aneurysm may be clotted. In the Mount Sinai Hospital, where angiocardiography seems well established, angiographic studies are done routinely in such cases except where conventional roentgenologic examination shows the mass to be clearly separate from the heart and great vessels. When the mass is a mediastinal tumour the great vessels are sharply and continuously outlined and decrease gradually and uniformly in diameter when traced from their origin. However, when an aneurysm is present, it becomes opaque at the same time as the parent vessel, a dehiscence, i.e. a process of splitting, in the wall of the vessel may be seen, and there may be local dilatation of the vessel at the aneurysm. This observation is not infallible for clotting in the aneurysm, too small an opening into the aneurysm, or too low a concentration of dye in the aneurysm, may prevent its visualization.

2. Obstruction of Superior Vena Cava.

This examination has provided only rarely information which could not have been anticipated clinically. At times it is stated that the precise site and extent of the obstruction is required in which case angiocardiography is useful. Sussman and Grishman are at present investigating the possibility of demonstrating pressure on, or infiltration of, the vena cava by enlarged mediastinal nodes; it is hoped that this may provide information regarding the operability of primary carcinoma of the bronchus. The method may prove useful in the study and treatment of constrictive pericarditis, when basal adhesions result in elevated venous pressure.

3. Congenital Heart Disease.

The usefulness of angiocardiography in these lesions depends on the severity of the anatomical lesion, the ease with which the affected structure is visualized, and the changes which have taken place in the circulatory dynamics.

Angiocardiography is not essential in the diagnosis of most cases of congenital heart disease in adults. Careful clinical examination, electrocardiography, conventional roentgenologic investigation and such simple tests of circulatory dynamics as blood pressure recordings in all extremities, pulse tracings and blood circulation times ordinarily permit reasonably accurate diagnosis. But in infants, multiple lesions are the rule and diagnosis is aided greatly by this procedure.

(a). Abnormality of a Large Vessel or Cardiac Chamber Outlet.

Precise portrayal of the anatomic findings in dextrocardia, right aortic arch, coarctation of the aorta, stenosis of left subclavian artery and

stenosis of the pulmonary artery are given by angiocardiography. Aortic or sub-aortic stenosis is not often demonstrable but associated unsuspected deformities of the aorta are fairly frequently visualized. Stenosis at or near the pulmonary valve, on the other hand, is usually clearly visualized. Congenital aneurysm of the aorta or pulmonary artery is well defined ordinarily and in a few instances an anomalous pulmonary vein can be seen.

While coarctation of the aorta can be diagnosed by clinical and laboratory means, the precise location, length and configuration of the coarctated segment have become a matter of practical concern since it has been discovered that the condition is apparently operable.

Angiocardiography may also be helpful where multiple lesions produce murmurs or where a conventional roentgenogram is difficult to interpret. For example, coarctation of the aorta occasionally occurs with aortic stenosis and this would account for an inexplicable dilatation of the ascending aorta. Again a systolic and early diastolic murmur in the pulmonary area in the presence of coarctation of the aorta might indicate a patent *ductus arteriosus* but angiocardiography will settle this question.

Stenosis of the left subclavian artery causing the absence of a left radial pulse is explained by angiocardiography. It has also demonstrated association of this condition with coarctation of the aorta or with a generally small aorta.

In the November, 1949, issue of *The American Journal of Roentgenology and Radium Therapy,* Grishman *et al* report the diagnosis of the aberrant insertion of a pulmonic vein into the right atrium with an associated inter-atrial septal defect. It also occurs that *both* veins have aberrant insertions but only three such cases have lived beyond infancy. It is stated that if veins appear in the conventional roentgenogram of the chest, they require identification which is possible only by angiocardiography. Also reported in this article is a group of three patients with arterio-venous aneurysm of the lung which the writers claim to be a frequently recognized anomaly. Since often severe haemodynamic disturbances can be corrected by lobectomy the diagnosis is important. The common signs and findings of the condition are cyanosis, clubbing, pulmonic mass and occasionally signs of circulatory insufficiency.

(*b*). *Pulmonary Stenosis.*

In the presence of a septal defect a right or left shunt ordinarily occurs if there is a lesion raising the pressure in the right auricle or ventricle or in both. Pulmonary stenosis is the lesion in most cases. In a few instances, as in the Eisenmenger complex, pulmonary stenosis is not present and there is dilatation of the pulmonary artery. The outstanding sign of such a shunt is cyanosis. Diodrast follows the same path as the blood when injected hence the diagnosis of right to left shunt. In the typical case of Tetralogy of Fallot, the opaque material passes into the right ventricle at about the end of two seconds, and the pulmonary

artery and aorta are then visualized in three seconds rather than in five to six seconds. The pulmonary stenosis and the size of the pulmonary artery are clearly seen. These findings by angiocardiography are important due to the recent development of surgical techniques for the alleviation of this condition.

Angiocardiography is also helpful in cases of transient cyanosis where the right ventricular pressure is only slightly raised. In such a case the sudden injection of 40 c.c. of diodrast may elevate the right auricular and ventricular pressures sufficiently to demonstrate the right to left shunt, even though it is not present ordinarily. Angiocardiography is also helpful in those cases in which the inter-ventricular septal defect is so large that there is no murmur. (*Cor triloculare*).

The procedure is invaluable in elucidating the anatomic status in those cases of congenital cyanosis in which the pulmonary artery appears dilated. This occurs in the Eisenmenger complex. Simultaneous and rapid visualization of the aorta and the large pulmonary artery and the absence of pulmonary stenosis are the radiological features. In the cases observed by Sussman and Grishman, the diodrast passed from the right ventricle to the two great vessels directly, only a little passing through the septal defect.

(*c*). *Patent Ductus Arteriosus.*

In nearly all cases of this condition an apparent localized dilatation of the aorta was seen which is not encountered in normals or in other cardiac abnormalities. The dilatation occurred in the descending aorta on its anterior aspect just beyond the isthmus. This changed segment varied in size from a slight bulge to a uniformly dilated segment. This appearance is probably due in most cases to the infundibulum of the ductus, or occasionally it may represent a traction aneurysm of the aorta caused by the ductus. The appearance is not pathognomonic. Following ligation of the ductus (during surgical alleviation of the condition) clips were placed at the site of ligation to prove the cause of dilatation. Direct visualization of the ductus or prolonged renewed visualization of the pulmonary artery due to the patent duct's connection were not observed probably due to dilution of the material by the time it was to pass back to the pulmonary artery.

(*d*). *Left to Right Intra-cardiac Shunt.*

This entity is not satisfactorily visualized due to dilution of diodrast by the time the dye reached the left ventricle. Sussman has demonstrated conclusively several cases of inter-atrial shunt probably made possible by increased pressure in the right atrium due to rapid injection.

4. Vascular Pattern in the Lungs.

Since both inflammatory and neoplastic diseases of the lungs are associated with a disturbance in the vascular pattern it would be anticipated that angiocardiography would be useful here. Robb and Steinberg

refer to pressure on and displacement of the hilar vessels by enlarged glands. They observed these changes in both primary and secondary tumours of the mediastinum as well as in tuberculosis. In pulmonary tuberculosis they describe pulmonary circulation changes of three types: (1) *diminished vascularity* resulting from the narrowing and obliteration of blood vessels in exudative tuberculosis and from fibrosis in the productive type. (2) gross displacement of the intra-thoracic cardiovascular structures by extensive pulmonary fibrosis, and (3) *displacement and stenosis* of the pulmonary artery by tuberculous adenitis. In tuberculous fibrosis, emphysema, chronic pulmonary suppuration and pulmonary cyst or neoplasm there is a decrease in the vascularity of the involved regions, while in other portions there appears to be an increase in size and number of blood vessels. Arterial occlusion in lung cancer is of particular diagnostic value.

In concluding this brief discussion of the uses of angiocardiography, it may be stated that some interesting studies have been made on the cardiac silhouette and cardiac physiology, the first of which will be discussed briefly.

Analysis of the cardiac topography in various conditions by means of angiocardiography has considerably simplified the teaching of cardiac roentgenology. There is little doubt as to the identity of individual segments of the cardiac silhouette following this procedure. It is dynamic material studied and it is also individualistic.

It has helped to re-evaluate the diagnostic criteria in cardiac roentgenology. In the normal heart for example, it has shown that the *conus arteriosus* from which the pulmonary artery arises, does not reach the left cardiac contour in the postero-antero projection. The middle left segment consists of the pulmonary artery and its bifurcation. Between this and the left ventricle lies a portion of the left auricular appendage the length of which varies with the habitus of the patient and the angle of inclination of the heart.

Angiocardiography has made it possible to study the inter-ventricular septum, its position and particularly its direction. In the normal heart the convexity of the septum is to the right when the right ventricle is opaque. This procedure has also shown that the first 2-2.5 inches of the ascending aorta can not be seen in the conventional cardiogram.

In most cases of pulmonary heart disease it is impossible to diagnose right ventricular enlargement on the basis of roentgenograms. While dilatation of the pulmonary artery (considered by some to be a sign of right ventricular enlargement) is frequently associated with right ventricular enlargement, it is actually only an indirect sign of the latter condition.

In many cases of obstructive emphysema where right ventricular failure is suggested clinically, the transverse diameter of the heart is normal, but with angiocardiography it is found that the septal wall is

convex to the left rather than to the right, signifying the right ventricular dilatation. Only in cases of right heart failure advanced to right auricular enlargement is enlargement of the right side of the heart shown by its contour. In associated hypertension or coronary sclerosis the left ventricle is dilated and hypertrophied and the septum is not only reversed back to normal but is again convex to the right. Predominant right heart failure with the misleading cardiographic picture of primary left heart failure can thus be explained.

In this paper the history, technique and clinical uses of angiocardiography have been discussed. It is interesting to note that of the recently developed radiological techniques angiography is receiving most attention at current roentgenological meetings. Advances in equipment for this examination are relatively frequent and may herald its general use.

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ABSTRACT: PRURITIS VULVAE DUE TO AUREOMYCIN

H. T. BEHRMAN,

J.A.M.A. 144: 995, Nov. 18, '50

The increasing use of the various antibiotics has increased the incidence of side reactions to these drugs. Workers have recently reported urticaria, erythema multiforme and eczematoid dermatitis of the groin after the use of aureomycin.

The author has noticed several cases of *pruritis vulae* following aureomycin therapy in the treatment of various diseases .The complaint is characterized by itching of the vulva and the vaginal introitus, with superficial excoriations and slight erythema within several days to one week following aueromycin therapy. Scrapings and cultures of these minute vesico-pustules demonstrated *Monilia albicans* in one case.

The several case reports presented were all typical. A possible explanation of the lesion may be the effects of aureomycin on normal vaginal flora. The normal flora is destroyed with the exception of the members of the yeast family. The destroyed organisms seem to exert a restaining influence and once removed the *Monilia* proliferate and give rise to typical Monilia vulvo-vaginitis. *Pruritis ani* may also be encountered as a side reaction to the drug.

The associated pruritis generally subsides spontaneously but can be relieved by bland lotions, antihistaminics, sodium propionate douches, and/or a local application of 15 per cent sodium propionate ointment.

—CHARLES SPURGEON, '52.

THE LIFE OF SANTIAGO RAMON Y CAJAL * (1852-1934)

ROBERT ARTHUR JAMES HAGGAR, M.D., '50

SANTIAGO RAMON Y CAJAL — artist and scientist, author and teacher — is the most outstanding name in Spanish medicine. Born when the science of general histology was in its infancy and the science of neurohistology still in the embryonic stages, Cajal devoted his life to making important discoveries in these two fields.

He also made valuable contributions in histological pathology and colour photography.

Santuagi Ramón y Cajal was born on May 1st, 1852, in Petilla de Aragon, a small town in the province of Zaragoza in northern Spain. His father was Justo Ramón Casasus, a 2nd class surgeon, industrious, conscientious and very successful in his rural practice. From this stern parent, Cajal seems to have inherited his strength of will, love of industry and vigorous mentality. Early cruel encounters with poverty and obscurity made the elder Ramón ambitious for his son and he wanted Santiago to have a classical education in medicine. This was such an obsession with the father that it resulted in considerable interference with the son's progress and development.

Cajal's mother has been described as a beautiful and robust mountain girl. Her beauty was not passed on to any of her five children who, instead, received from the male parent an unusual physiognomy consisting of a high broad forehead, a sharp hooked nose and angular chin. Cajal often spoke with some disdain of this genetic freak and its "regular monotony" in the family.

One feature he did obtain from his mother was the name "Cajal" which was his mother's maiden name. Craigie (1949) believes it was probably vanity which caused him to use the name "Cajal" in place of the more common "Ramón".

During the first few years of Cajal's life the family lived in several small towns of northern Spain, finally moving to Valpalmas in 1856. At four years of age Cajal was "a restless little devil, wilful and unbearable." His schooling began at this period and he learned a great deal from his father who was a natural teacher. He was able to speak French well at six and the following year corresponded regularly with his father who was in Madrid. The elder Ramón took a year's study at Madrid at this time to qualify as physician and surgeon.

Even as a child, two features gave Cajal a characteristic personality. These were his "love of investigation and contemplation of natural phenomena" and "an antipathy for social intercourse". He was by nature shy, secretive and unsociable. Garrison (1929) states that to Cajal "solitude (was) preferable to society for engendering ideas and permitting their

[1] Given before the Osler Society, London, Nov. 9, 1949. Awarded the first prize of $25 for the 1949-1950 Session—The Rowntree Prizes in Medical History.

serene development." Further, most conversation caused "the weakening of will power and sterilization of effort."

Looking back over his life while writing his memoirs some fifty years later, Cajal distinctly remembered three events which had a profound effect upon him. The first of these occurred at the age of seven when a surge of nationalistic pride swept over him when he heard of the Spanish victories in Africa. The second event took place in school. One day, while the class was praying, "Lord, deliver us from all evil," lightning struck the tower, killed the priest ringing the bell, knocked the school mistress insensible and destroyed a picture of the Saviour which was hanging on the wall. Cajal feels this had the effect of confirming "his natural bent to irony and pessimism" and displayed the helplessness of man before nature. The third event he recalled was the eclipse of the sun in 1880 which his father explained to him. He marvelled at the science which could predict this occurrence millions of miles away.

When Cajal was eight years old, the family moved to Ayerbe and the native children fought with Cajal, resenting his strange clothes and dialect. But seeing that he was one of them at heart, he was finally accepted into the "gang" which busied itself pillaging and marauding the neighbouring farms. He was a ringleader in pranks and made a science of arrow-making; he cut up his boots to make slings and was constantly being whipped for shooting birds and hens, cats and dogs.

About this same period, Cajal began to show his talent for art and decorated books and walls with his sketches. His father, a strict utilitarian and pure intellectualist, did not appreciate art in any form and did all that he could to discourage his young son. In order to prove that the drawings had no merit, his father called in a local "house-painter" who said that the drawings were crude and that "the boy will never be an artist".

Like the young Osler, Cajal was also something of a naturalist. He collected birds, nests, eggs and made notes and sketches of the wild-life he encountered. Because of these outside interests, his studies progressed poorly and regulai paternal floggings made things worse. One day, caught making caricatures of the teacher and passing them around the class for inspection, Cajal was locked up in the cellar for punishment. He rather welcomed this enforced leisure since it gave him an opportunity to carefully plan his escapades for the following day. Like many others, Cajal "rediscovered" in this cell the principles of the *camera obscura*, described centuries before by Leonardo da Vinci.

Determined to make his son a doctor and feeling that he required a sterner discipline, Cajal's father sent him to a school at Jaca where the boy lived with his mother's brother, Uncle Juan, a weaver of the town.

Cajal's dislike of Latin grammar was unreasonably intense. He considered the didactic style of teaching "dry and harsh, like a dusty road in summer". His textbooks were monuments to his imagination and artistic

ability and he regretted that the Latin text was "not all margins". Father Jacinto, the ferocious Latin master, believed in pure memorization and for a sluggish memory used such stimulants as the strap, whip or solitary confinement. This noble educator once knocked a student seven feet who bowled over a blackboard and two other pupils in his flight.

Throughout his life, Cajal avowed that he was interested only in learning principles. His father, possessing a photographic memory, could reel off pages and pages of pathology by rote and could never understand the lack of this character in his son. Cajal was a "visual" learner and seldom forgot anything once he had seen it; never forgot anything once he had learned and understood the mechanism. For his lack of interest and misbehaviour, he was flogged repeatedly, which only served to make him the more defiant. When locked up and starved for a day he reacted by escaping to the country to paint the beautiful valleys and distant mountains.

During one of his periods of "freedom" he arranged spikes in the wall so that he could escape from his prison and for some time he enjoyed being put away. But fellow students being caught using the same manner of escape revealed to the head master that it was Cajal's handiwork and he was threatened with expulsion. He passed his examinations only because the examiner felt himself indebted to Cajal's father for a surgical operation he had once performed on him.

Returning to Ayerbe for the summer he looked like a "living skeleton" and built up his lost vitality by abstaining from study, eating heartily and keeping fit by skirmishes and battles with his old gang. One of his most notable projects at this time was the construction of a wooden cannon. He bored a hole through the length of a post, wrapped the outside with wire and rope for strength and constructed a priming hole from an old oil can. He and his companions mounted this weapon on a garden wall, charged it with gunpowder, tacks and stones and aimed it at a farmer's gate. The result was a huge success and blew the gate off its hinges. For this mischief, Cajal was put in the local gaol, at the insistence of his father, and spent three days among the fleas and bed-bugs in the filthy place. Worst of all, the townspeople laughed and jeered at him through the bars and he suffered much loss of pride. This did little in the way of correction and he over-compensated by later constructing another wooden cannon and also one from a bronze pipe. Both exploded, causing minor injuries to several of his playmates.

The following year, at the age of twelve, Cajal was sent to the Institute of Huesca, his father more determined than ever that his son should learn Latin. He proved the saying of Goethe that "every father desires for his children that which he himself has not been privileged to attain."

The new Latin master, Don Aquiline, was the exact opposite of the terrible Father Jacinto. The lecturer had to shout to be heard above the uproar caused by pupils talking, smoking, playing cards or shooting pel-

lets at the old man's bald head. Cajal admits to being "the boldest and most insolent" of the lot.

Other masters were not so easy and once again Cajal found himself flogged and given detention for his anti-social behaviour. During this period Cajal wore an extremely long overcoat which delightfully amused everyone except one eighteen year old rustic, a known bully, who called Cajal a "Dago" and beat him cruelly. Although he could have controlled the bully with flattery, he decided to surpass him in vigour and cunning. To accomplish this, Cajal spent months outdoors in violent exercise, practising all the while the use of cudgel and sling. Eventually, he informed the bully that if he were ever again insolent to him, he would "embed a stone in his skull" proving forthwith that he would be able to do it. This incident typifies a trait which Cajal displayed throughout his life—that is, the response to a challenge. No matter what form the challenge took, physical or to the point of questioning his work, Cajal always responded at once and vigourously vindicated himself.

Cajal continued with his painting, developing the ability to shade colours and capture the various "greens" of nature. The class scholars shunned him as being unbalanced and silly but Cajal's response was "I greatly regretted (this attitude), for I have always rendered to talent and appreciation the homage of cordial sympathy."

Home again for the summer in Ayerbe, Cajal's father desired him to review the previous year's work and to give up his foolish painting. Cajal did neither. He fixed up an old pigeon-house on the roof as a "study" and continued to paint unmolested. Although the elder Ramón allowed no member of his family to read fiction, his wife had a trunkful of illicit treasure which she secretly handed out to the children.

From his pigeon-house on the roof, Cajal discovered a wealth of books in one of the rooms of the house next door. One at a time he "borrowed" these and was able to read Dumas, Hugo, Cervantes, Defoe and other celebrated authors.

To cut down the boy's leisure time, the elder Ramón apprenticed his son to a barber in Huesca. He wanted Cajal to exchange the paint brush for a shaving brush and to learn a trade for the future. But Cajal still had much spare time and became so adept with the sling that he could pierce a hat thrown in the air at twenty paces. He wrote a pamphlet on "Lapidary Strategy" outlining rules and hints in the use of the sling. On one occasion he and his brother had a pitched battle with the police and managed to injure two of the officers and break the sabre of another with their slings.

His studies were so poor during this year that he did not dare present himself for examinations. His father was furious and apprenticed him to a shoe-maker and Cajal became skilled in making delicate footgear. After a year of this his father relented and allowed him to return to school to take a course in science and drawing. He did well enough in this to win

a prize from the Art Academy and his teacher wanted him to study art. Cajal's father refused and arranged for him to take a course in rhetoric and philosophy the following year. The boy was not happy over this arrangement, failed his exams, considered running away from home (for a day or so) and returned to Ayerbe.

Cajal was sixteen at this time and his father decided to educate his son himself and began to teach him osteology. Father and son made a few nightly excursions to a deserted cemetery and obtained bones for study. His father spent all his leisure time teaching Cajal the most minute details of anatomy and he learned rapidly, assimilating this knowledge by reflection. Cajal made excellent coloured drawings of anatomy and his father would have published an atlas of anatomy a few years later had not the printing facilities been so backward in Spain at that time.

Finally obtaining his bachelor's degree, mainly extramurally, Cajal was accepted as a medical student at Zaragoza. His studies progressed fairly well because his interest was maintained by splendid teachers and he gave up most of his reckless ways. While still a student, he was made a demonstrator in anatomy and also did some private tutoring. But spending most of his time in anatomy and physiology, he barely scraped through some of the other courses. At this time he often displayed a violent temper and obstinate nature. He argued with professors, annoying them greatly by quoting foreign authorities. The professor of pathology told Cajal's father that if his son thought he were right he would not keep quiet even though his parents' lives depended upon his silence.

One day, Professor Ferrer, head of the Department of Obstetrics, annoyed because Cajal was not attending lectures, attempted to humiliate him before the class by asking him about the origin of the foetal membranes. Whereupon Cajal went to the blackboard and gave a thirty minute discourse on the subject complete with perfect illustrations. This brought applause from the class and professor, who said that he would give him a grade of "excellent" even if he did not attend another lecture. Cajal writes of this ". . . only from time to time did I appear at the class, as if I were conferring a favour". But he adds that if he had ever been asked about the foetal presentation he would have been "floored as an ignoramus".

From 1871-1873, Cajal was assailed by three new manias: literature, gymnastics and philosophy.

During the revolution an epidemic of lyricism swept across Spain and Cajal, along with many other university students, became infected. He wrote "silly verse" and stories *au Jules Verne.* One of his stories concerned an explorer from earth on Jupiter who discovered animals ten thousand times his own size. This intrepid adventurer, being relatively microscopic in size, was able to enter a cutaneous gland and finally climb aboard a red blood cell. Cruising around in this fashion he observed first-hand the struggle of leucocytes and parasites, watched the neuro-

muscular mechanism in action and saw the cells of the cortex functioning. To illustrate this book he used illustrations adapted from the histology texts of Kolliker, Henle and Ranvier.[2]

At eighteen, Cajal considered himself the strongest fellow in the university, an opinion he soon changed after being thrashed for his boasting by an engineering student. To answer this blow to his ego Cajal took up weight-lifting and gymnastics, developing by this means a forty-five inch chest and powerful biceps. Instead of carrying a walking stick he swaggered around town with an iron weighing sixteen pounds. He won many contests of a muscular nature but gave it up because it diminished his aptitude for intellectual work.

Following the fad to develop brawn Cajal swung over to a superficial study of philosophy. He "craved radical and categorical theses" and adopted "absolute idealism". He made out that he was impressed by Berkely[3] and bored fellow students with his discourses on the ego.

In 1873, at the age of twenty-one, Cajal graduated as a Licentiate in Medicine, *sine laude*, and was drafted for military service. He wrote examinations and obtained the rank of Assistant Physician and was sent to Cataluña. His regiment pursued the Carlists[4] for eight months without sighting the enemy and the only medical care required by the soldiers was the treatment of "Venus" and indigestion. Cajal was eventually promoted to Captain and sent to Cuba in the spring of 1874. Here he was stationed in an isolated and devastated district of Puerto Príncipe and soon fell ill with malaria and dysentery. During his enforced rest he began to learn English.

He was shocked at the corruption of government employees and the high army officials. To have "cleaned up" the colonial corruption would have meant the discharge of seventy-five percent of the personnel. After convalescence, Cajal was stationed at San Isidro, an infirmary of three hundred patients suffering from smallpox, dysentery and malaria. He did not get along with the Commandant and fellow officers because he would take no part in the grafting and deprivation of the patients' rations, and life was unbearable. He was never well while in Cuba and finally obtained a medical discharge on the grounds of having "malarial cachexia". Improved by the sea voyage home and a convalescence in northern Spain, he returned to Zaragoza and was given an assistantship in anatomy in 1875. Cajal began graduate studies in histology, preparing himself for examinations at Madrid in order to gain a medical degree.

In 1878 he suffered a severe bout of haemoptysis and had all the classical signs of the dreaded tuberculosis. His father had him confined to bed for two months and then sent him to the mountains to convalesce, with one of his sisters as a nurse. During this period Cajal began to doubt the value of mineral water and cast aside all therapy except sun, air, silence and art. He did much walking and drawing and became interested in photography. He improved the emulsion formula for gelatin-bromide

plates and was soon manufacturing this preparation for local photographers. He could probably have made a fortune with this process had he gone into business but gave it up to return to his anatomical studies.

Upon resuming his work at Zaragoza he was made Director of the Anatomical Museum at Zaragoza. Shortly after this he married Senorita Fañanas, a girl who reminded him of Faust's "Marguerite". He did this on a monthly salary of only thirty-five dollars with grave prognostications for the future from friends and relatives. He took delight in proving them wrong, when, a few years later with two of his children already born, he had published his first scientific papers and had gained the chair of anatomy at Valencia by competitive examination. His wife was a perfect mate—simple in tastes and with no other aspirations than to be a good wife and mother and maintain the happiness of the home. She was Cajal's second wife; his first wife was science. Craigie (1949) states that "his family life . . . was entirely subordinated to his scientific enthusiasm (and) his wife was a martyr."

In 1880 Cajal published the first of a long list of monographs. His first paper was on the histology of experimental inflammation and the second was on observations of the nerve endings in skeletal muscle which were "re-discovered" by Dogiel[5] some ten years later.

During the next few years Cajal worked with mounting enthusiasm, displaying a patience bordering upon the obstinate. He once spent twenty hours at the microscope watching "a sluggish leucocyte in its laborious efforts to escape from a blood capillary". At this time he had little money for journals but managed to subscribe to a few French, German and English periodicals which were publishing histological reviews. During these early years of his scientific career, Cajal descibed the mechanism of phagocytosis, some time before Metchnikoff.[6]

In 1883 Cajal became professor of anatomy at Valencia and is said to have avowed that within ten years he would have gained international recognition. (Gibson, 1936). He remained faithful to his belief that "things are more interesting than people" and in order to spend more time studying these "things" he set up a laboratory at home as well as in the university. He supplemented his meagre income by tutoring in anatomy and pathological histology.

In 1885 the devastating cholera epidemic swept Europe and the medical schools began to study the disease. The cause of the disease, the comma bacillus, had recently been isolated by Robert Koch,[7] in India. Cajal was directed by the Central Committee to render a report on the value of a vaccine which had been produced by Dr. Ferron, a physician from Tortosa. This was found to offer no immunity in humans and could not be tested on animals since there were no known animals susceptible to cholera. Cajal showed, independently of Pfeiffer,[8] that the comma bacillus, though harmless in subcutaneous injections and *"per os"*, was hghly toxic to the peritoneum of the guinea pig. He also made some

studies on the degenerative processes in the protoplasm of the vibrio comma. All in all, he made a modest beginning in the study of bacteriology but gave it up because he could not afford the expense of animals and equipment and returned to his more economical first-love, histology.

During the years 1885-1888 Cajal busied himself with histological studies, writing and illustrating a text on histology and including methods of microscopical technique. He also wrote at this time a column in a local medical weekly of a philosophic-scientific nature which he signed with a pseudonym. Other forms of "recreation" were photography and hypnotism. Cajal and several colleagues founded a group for the study of hypnotism in hysterics and neuraesthenics. They found out nothing new but supported the views of Bernheim[9] of Nancy. Word spread through the city of their "cures" and people flocked from far away, only to be "turned away by the shy and modest Cajal".

In 1887 he had the choice of accepting the chair of anatomy at either Zaragoza or Barcelona and chose the latter because of the more peaceful surroundings and the fact that there seemed to be less rivalry between faculty members. Here, at the age of thirty-five, Cajal began the life-long study which was to prove so fruitful — the histology of the nervous system. Cajal had learned of the capricious and tricky silver chromate stain of Golgi[10] from Dr. Luis Simarra, a neurologist of Madrid, and had greatly improved it by certain modifications such as the use of double impregnation, ammoniated alcohol and other changes.

The following year was one of his most important. He was able to trace out the terminal endings and collaterals of the axis cylinders in the grey matter of the spinal cord. He followed the terminations of these fibres to the cell bodies and dendrites of other neurones and observed the basket endings and end-bulbs. He thus disproved the reticular theory of Golgi and Gerlach[11] which suggested that the axons of cells entering the spinal cord ended by a reticulum composed of the intermingling of processes with those of other cells. Cajal believed that the incoming fibres were conducting impulses which were relayed on by nerve cells in a sort of conduction chain. This theory had been suggested by His and Forel[12] many years previously and in 1891, Waldeyer,[13] on the basis of Cajal's work, formulated the Neurone Doctrine, coining the term "neurone" for "nerve cell". In brief, the Neurone Doctrine states that the neurone is the genetic, structural and functional unit of the nervous system and that the axone is in contiguity, but not continuity, with the next cell in the conduction chain. All neural circuits are composed of such chains of neurones.

The manner in which Cajal had approached this problem is worthy of note. Instead of attempting the hopeless task of tracing cell processes in the dense forest of the grey matter, he went back to the beginning of things and studied the embryo of the mouse through progressive stages to the adult. Golgi had also done this but lacked the finer technique of the silver stain. It is almost the acme of irony that Cajal should have used

Golgi's stain to disprove the latter's reticular theory which had been based on the picture revealed by that stain.

Annoyed at the slowness of the press, Cajal published his own journal in May, 1888, and wrote the six contained articles himself. He printed sixty copies, sending them to foreign workers, especially those in Germany. During that year Cajal discovered the climbing and mossy fibres, the peri-cellular baskets, the axones of the granule cells and other structures of the cerebellum. The schematic drawings he made of these structures are in every modern text of neuroanatomy. He also published papers on the structure and function of the retina, (a subject he returned to repeatedly during his life), and the histology of muscle spindles, heart muscle and nerve fibres. The following year he described the bile capillaries of the liver, independently of Kupffer,[14] observed the sympathetic nerve endings on the gland cells and laid the foundation for the theory of dynamic polarization.

Disappointed at the lack of enthusiasm given to his efforts by foreign workers, Cajal translated his papers into French and published them in German periodicals. He joined the German Anatomical Society and in the fall of 1889 he travelled to Berlin armed with his best slides for demonstration at the annual meeting of the society. Here he met the famous names in scientific investigation: Edinger, Ehrlich, Kolliker, Retzius, Schwalbe, Waldeyer and Weigert[15]. Cajal received sincere felicitations from all and Kolliker, patriarch of German histology, was greatly impressed, so much so that he spent several years confirming and publicizing Cajal's discoveries.

Pleased by their consideration, encouraged by their interest, Cajal threw himself into a frenzy of labour upon his return to Spain. During the following year he published fourteen monographs and rocked the industrious German investigators with the vigour of his efforts. He followed the development of embryonic nerve cells, observing the growth of axones and dendrites from the parent cell body, thus upsetting the cell-chain method of development as postulated by Hensen.[16] He discussed a chemotactic mechanism in an effort to explain the factors determining the direction of growth of nerve fibres. In this he preceded, or at least anticipated, the neurobiotaxic theory of Ariëns Kappers.[17] This same year a polemical strife began between Golgi and Cajal with Golgi claiming priority in the discovery of the collaterals of the spinal cord. He had mentioned this in a paper published in an obscure Italian periodical in 1880. Cajal wrote an article conceding Golgi the priority but at the same time could not forego adding a severe criticism of the reticular theory and briefly summarizing his own findings and conclusions.

By 1894 Cajal had written a manual of pathological histology, had published the theory of dynamic polarization (i.e. that the neurone could only transmit the impulse in one direction) and had published a great many more papers on the structure of the cerebellum and retina. Cajal

was at this time forty-two, with a family of five children (one having died from meningitis) and with an international reputation as a scientist. He obtained the chair of Normal Histology and Pathological Anatomy at Madrid by competitive examination in 1894.

During these years of his life Cajal met frequently at the café with friends for noon-day discussions, but he did not dally at these meetings. He writes, "It is a good thing to digress a little every day, but it would be dangerous to prolong the *diastole* of the mind at the expense of the *systole* of work."

Besides the appointment to Madrid in 1894, Cajal was invited to give the Croonian lecture before the Royal Society of London. During his sojourn in England he was entertained by Sherrington[18] and met such notables of science as Horsely, Lord Kelvin, Langley, Mott[19] and many others. Cajal was greatly impressed by the magnitude of the British scientific institutions. Before leaving England he was given an honorary D.Sc. by Cambridge.

Back in Spain Cajal began the systematic study of the basal ganglia, thalamus, pituitary gland and pineal body. He found time somehow to write a treatise on malignant tumours, on the phagocytic properties of the blood platelets of lower vertebrates and a text of histology. By 1897 he was publishing the microscopical work being done in Madrid in a journal which he had founded and was editing. Besides much of his own work, the journal contained that of his brother and of his pupils. During these closing years of the last century Cajal was acclaimed on all sides for his outstanding work. He was awarded prizes and society memberships by Madrid, Paris, Würzburg, Berlin, Vienna, Lisbon and many other scientific centres.

In 1898 Cajal was saddened by the "lamentable and insane war with the United States; a war brought on by the greed of . . . (Spanish) exporters".[20] Spain was poverty-stricken, "drained by four desolating civil wars".

During the next two years Cajal disproved the claim of Michel, who stated that the fibres of the optic tract crossed completely. He did a tremendous amount of work on this feature in lower animals and showed the phylogenetic development of binocular vision. He also began at this time to study the structure of the cerebral cortex. It was law in Spain that bodies must rest in state for twenty-four hours before being released to anatomists or morticians. But since in this length of time the delicate structures of the neurones are so altered that they lose their affinity for the silver stains, Cajal looked around for fresh human material. He found a source at the Foundling Home and Maternity Hospital which were out of reach of the law and obtained the bodies of hundreds of foetuses and children of all ages. Cajal was absorbed in this study for the next few years and summed up his results in a treatise of three volumes in 1904. This momentous work consisted of 1800 pages with 887 original illustrations.

In 1899 Cajal was invited to give a series of three lectures on his work at the decennial celebration of Clark University. Although he was not in the best of health at this time, suffering from insomnia and having cardiac irregularities, he was urged by friends and government to accept the invitation and he embarked for the United States accompanied by his wife. Garrison (1929) states that "Cajal was a handsome figure, with the abstracted mien of a laboratory worker" and that "he was agreeably impressed" by the American people. He was somewhat awed by the fast pace of life and considered a Spanish bull-fight tame compared to the frenzy of the American populace during the Independence Day celebrations.

In 1900 Cajal was awarded the Moscow Medal by the International Medical Congress in Paris for the most outstanding medical work of the previous three years. By this time he had also been awarded the Rubio, Fauvelle and Martinez Molina Prizes. He received thousands of letters and signals conveying congratulations and it required a month to answer them all. In this same year he was made Director of the National Institute of Hygiene which he put on a scientific basis and a strict economy. He later passed this duty over to his star pupil, Tello.

During the year 1903 Cajal published fourteen monographs, some as large as books. He was president of the International Medical Congress which was held in Madrid in this year in Cajal's honour. He received the Helmholtz Prize the following year for the "most important discoveries in any field of human knowledge".

In order to study the neurofibrillar structure of the neurones, Cajal devised his famous reduced silver nitrate method of block-staining and once again began the tremendous task of working up through the various embryonic stages. For this work he used the mouse, (Addison, 1930), which, because of its small size, meant that there were relatively fewer sections to study and he was thus able to follow the processes of the neurones to their destination. He also made an intensive study of the regeneration of experimentally-cut peripheral nerves.

In 1906 Cajal reached the pinnacle of international honour by being summoned to Stockholm to receive the Nobel Prize conjointly with Camillo Golgi. In his address he made cordial praise of Golgi and paid that notable savant worthy tribute. But instead of replying in like vein, Golgi pointed out the valuable facts that he himself had discovered and "attempted to refloat the almost forgotten theory of interstitial nerve nets" and made a very poor impression upon the entire scientific audience. Cajal said later that Golgi was the "vainest, most self-worshipful character" that he had ever met. But one gets a little different opinion of Golgi from Chorobski (1935). The scope of Golgi's activity was tremendous and he openly admired the work of Ramón y Cajal, although disagreeing with him in regard to the theories of nerve impulse transmission. Cajal frequently spoke admiringly of Golgi and greatly respected his brilliant work in histology.

Congratulations, banquets and other honours flowed to Cajal in such quantities that it required several months to acknowledge them all.

During the next few years Cajal's work touched on almost the entire nervous system. He continued to work with great vigour and intensity, not content to rest on his laurels. His manner of working was such that after receiving a reward, he worked with redoubled effort in order to deserve it; and after an error he worked harder that it might the sooner be forgotten. These were the drives which forced him on and on. In 1907-8 he had a round of polemics with Held who tried to revive the ancient neurogenetic theory of Hensen; and with Apàthy who once again claimed a neurofibrillar continuity at the synapse.

In 1913 Cajal produced the gold sublimate stain and obtained beautiful preparations of the astroglia, especially the protoplasmic type. He also published at this time his great work on the degeneration and regeneration of the nervous system, printed at the expense of Spanish physicians in Argentina, and a book on colour photography besides numerous scientific monographs.

During the first World War Spain remained "neutral" and was the seat of radicalism, riots and military revolutions. Cajal was depressed by the stupidity of the nations at war and the utter futility of war. He observed that wars were becoming more horrifying and grimly prophesied future bacterial warfare. Saddened by the deaths of colleagues (which he blamed in many cases to the stress of war), saddened because two-thirds of Spanish scientific work was unknown to the world, Cajal's investigative work lacked its customary vigour.

In 1918 Cajal wrote a paper on stereoscopic photomicrography, as applied to the neurofibrils. Although Cajal speaks glowingly of the discovery of the oligodendroglia and microglia by Río-Hortega[21] in 1919 by a new silver carbonate stain, Prados and Gibson (1946) give us a little different picture. When Río-Hortega discovered these neuroglial elements, Cajal showed some coolness and indifference towards his work, hinting that the discovery of the microglia rightly belonged to Robertson, which was not true. There was a split between Cajal and Río-Hortega with the result that the latter left and took with him several of Cajal's pupils. The group's main regret over this was that they no longer had access to the enormous library that Cajal had built up over the years.

In 1923, at the age of 71, Cajal published the third edition of *"Recollections of my Life"*.[22] Looking back over the years Cajal had enjoyed the battle, had the pleasant memories of his accomplishments and was proud of his pupils carrying on such splendid work in the Spanish school of neurohistology which he had founded.

Ramón y Cajal never retired. He continued to go daily to the Institute Cajal — a beautiful building for biological research built in Madrid by the Spanish Government. He directed the work of his pupils and rounded out some of his own earlier researches. Among his illustrious

pupils may be mentioned Tello, Achúcarro, Sânchez, del Río-Hortega and Lorente de Nó. Besides these Spanish students were foreigners from many other countries eager for graduate study under the famous Cajal.

Spain also recognized her famous son by erecting in the Retiro (a beautiful park in Madrid where Cajal was wont to stroll) a statue of Cajal. But the shy and retiring savant never again walked in the park after the monument had been placed there.

In 1925 Penfield[23] spent six months in Madrid and found "Don Santiago" very much disturbed over the fact that he was reading almost daily in foreign journals of "discoveries", which he himself had made years ago, because foreign scientists had never read of his work. Penfield saw Cajal again in 1932 and found him becoming a little deaf and feeble, annoyed and impatient at the way the inexorable years had finally overtaken him. But his eyes still blazed fiercely — his heart was still willing.

Craigie (1949), writing of his personal impression of Cajal states that he was the most remarkable, impressive and overwhelming personality he had ever known. In any conversation Cajal dominated the minds of all about him. His pupils only reflected his views, aims and thoughts. "Like all men, he had weaknesses, but they were completely overshadowed by his tremendous strength".

Until a few hours before his death on October 17, 1934, Cajal preserved the vigour and clarity of his intellect and with his passing "science lost one of her greatest and most striking personalities".

Following his death the Spanish Government issued a special mourning stamp, erected several monuments to his memory and undertook the republication of all his scientific works.

Cajal's contributions to science were so widespread and of such great compass that it would be difficult for a bystander to point to any one feature of his work as being the "most important".

Gibson (1936) states Cajal's greatest contribution was "the law of the polarization of the nerve cell".

Sprong (1935) considers the stains which Cajal developed as being his important contributions: in 1888, the improved silver chromate stain of Golgi; 1903, the discovery of the reduced silver nitrate method; 1913, the gold sublimate stain.

Garrison (1929) feels that Cajal's crowning achievement was the study of the degeneration and regeneration of the nervous system. (Published 1913-14).

It is an idle pastime to try and find the "greatest" contribution of a scientist. The Dedication of his life to the ideals of science places a man in a common group and the "greatest contribution", so far as society should be concerned, has already been made — namely, the dedication. Individuals concerned with the "contributions" of a scientist are usually the so-called practical men. But most scientific work, such as Cajal's, is

of a fundamental or basic nature and is actually "pure science". To speak to such men of the "practical" value of their work is considered utter heresy by most of them.

Ramón y Cajal was to the science of neurohistology what Rudolph Virchow[24] was to the science of pathology. For over fifty years he contributed to the knowledge of the microscopic anatomy of the nervous system and during his life published some 22 books and 266 monographs. The awards and honours he received are in the hundreds.

Besides being a scientist of great renown, Cajal was something of a philosopher and in a new edition of "Café Chat", published just before his death, he has left us many clever aphorisms. For example, "... every investigator works with confidence because he knows that if individuals are capable of ungratefulness, communities very seldom are..." and again, "It is idle to dispute with old men. Their opinions, like their cranial sutures, are ossified".

"As long as our brain is a mystery, the universe, the reflection of the structure of the brain, will also be a mystery".

Cajal also wrote "Suggestions for the Scientific Investigator", Hilton (1933). Considering the lazy worker who says "all the substance of each scientific theme has been exhausted" Cajal replies "... problems are not exhausted, but men are exhausted in a problem. Fresh talent arriving without a reputation will always find a new aspect". Cajal urges the young scientist to read the most recent papers in his subject first and "above all, the most difficult, because they are the least exhausted".

The novice in investigation must accept that it is "his destiny by a cruel but inexorable law to grow a little at the cost of the reputation of the great authorities... But it is not necessary to destroy; it is necessary to build". Aspiration toward scientific work is "the most dignified and laudable that man can follow, because... it is impregnated with the perfume of love and universal charity". But "men of science are moved by... two dominating forces... 'the cult of truth and the passion for glory'."

"The ideal of science is to elucidate the dark mysteries and unknown forces which invest us, for the benefit of our descendants, and to make the world more agreeable and intelligible, while we ourselves are forgotten like the seed in the furrow."

FOOT NOTES

[2] Kolliker, R. A. von; Swiss histologist, 1817-1905.
Henle, F. G. J.; German histologist, 1809-1885.
Ranvier, L. A.; French Pathologist, 1835-1922.

[3] Berkely, G.; Irish philosopher, 1685-1753.

[4] The Carlists were a Spanish political faction which upheld the claims of Carlos of Bourbon (1545-1568) and his descendants to the Spanish throne.

[5] Dogiel, J. von; Russian physiologist, 1830-1905.

[6] Metchnikoff, E.; Russian zoologist of Paris, 1845-1916.

[7] Koch, R.; German bacteriologist, 1843-1910.

[8] Pfeiffer, R. F. J.; German bacteriologist, 1858- ?

[9] Bernheim, H. M.; French psychiatrist, 1840-1919.

[10] Golgi, Camillo; Italian histologist, 1843-1926.

[11] Gerlach, J. von; German anatomist, 1820-1896.

[12] His, W.; German anatomist and embryologist, 1831-1904.
Forel, A.; Swiss neurologist, 1848-1931.

[13] Waldeyer, W. von; German anatomist, 1836-1921.

[14] Kupffer, K. W.; German anatomist, 1829-1902.

[15] Edinger, L.; German neurologist, 1855-1918.
Ehrlich, P.; German scientist, 1954-1915.
Retzius, M. G.; Swedish histologist, 1842-1919.
Schwalbe, G. S.; German anatomist, 1844-1916.

[16] Hensen, V.; German anatomist, 1835-1924.

[17] Ariëns Kappers, C. U.; Dutch neurohistogolist, 1877-1946.

[18] Sherrington, Sir C. S.; British physiologist. Contemporary.

[19] Horsely, Sir V.; British surgeon, 1857-1916.
Lord Kelvin, (Wm. Thompson); British physicist, 1824-1907.
Langley, J. N.; British physiologist,, 1852-1925.
Mott, Sir F. W.; British neurologist, 1853-1926.

[20] The Spanish-American War was officially declared on April 25, 1898 against Spain to liberate Cuba from Spanish domination and to protect American economic interests in the Caribbean. The conflict lasted less than four months and deprived Spain of her last possession in the Western hemisphere. The American casualties were 285 killed.

[21] del Río-Hortega, Pío; Spanish neurohistologist, 1882-1945.

[22] *Recuerdos de mi vida*—Madrid, 1923. Translated by E. Horne Craigie, Professor of Zoology, U. of Toronto, 1937; with the assistance of Juan Cano, Associate Professor of Spanish, U. of Toronto.

[23] Penfield, W.; Canadian neurosurgeon, 1891 - —.

[24] Virchow, R.; German pathologist, 1821-1902.

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POLYNEURITIS *

ALAN S. DOUGLAS, M.D., M. Sc., F.R.C.P. (C).

Multiple peripheral neuritis, a term sanctioned by long usage, represents a striking and uniform reaction of the nervous system to several pathogenic processes. More often than not it is a symmetrical affection, the maximal effects of which are manifested in the finer branches of the peripheral nerves of the extremities. However, cranial nerves may also be involved and the mental changes that accompany certain cases show that the central nervous system is not immune. It is also important to remember that a reaction of the myocardium is sometimes associated and that in cases of polyneuritis there is a recognized liability to sudden and fatal heart failure.

Epidemics of palsy, presumably due to exposure to lead, had long been known in the lead-mining districts of Poitou and of Derbyshire, where it was known as 'dry belly-ache palsy', and cases of peripheral neuritis were described and attributed to alcoholic excess by Lettsom in 1789. But our present concept of an affection of multitudinous peripheral nerves, beginning in the finer terminals of the periphery and advancing towards the spinal cord arose in the mind of a brilliant young Irishman whose name is familiar to you all in another connection. In the year 1828 Dr. Robert Graves chanced to be in Paris during an epidemic which ravaged the town from March until August. The onset was abrupt, the course often relapsing, the deaths were many as were the slow recoveries. Health was often regained without complete recovery from the palsy and sensation was sometimes affected equally with movement. Graves spent two months investigating the epidemic both clinically and pathologically. The striking thing about the fatal cases was the complete absence of any observable change in the central nervous system. At the conclusion of his study he wrote: "This was one of the most remarkable examples of disease of the nervous system, commencing in the extremities and having no connection with lesions of the brain or spinal cord. Here was an instance of paralysis creeping from the extremities to the centre. Here was a paralysis affecting all parts of the extremities as completely as if it had its origin in the central parts of the nervous system; can anyone with such palpable evidence before him hesitate to believe that paralysis without any disease of the brain or cord may arise from disease commencing and originating in the nervous extremities alone? May not the decay and the withering of the nervous tree commence occasionally in its extreme branches and may not a blighting influence affect the latter when the main trunk remains sound and unharmed?" There is little doubt that Graves' epidemic was one of acute polyneuritis. In 1834, Richard Bentley Todd, who is best known for the first delineation of tabes dorsalis, supported this concept. In a lecture on lead palsy he remarked: "I believe that the muscles and nerves are early affected and that at a later period the nerve centres may

* Delivered in conjunction with the 10th Dr. F. R. Eccles Memorial Medical Alumni Lectureship, University of Western Ontario, October 25th, 1950.

become implicated. The nervous system is thus first affected at its periphery and in the nerve terminals and the poisonous influence, continuing its contamination, gradually ascends towards the centre." The next important episode in our story comes in 1859 when Landry described his "Ten Cases of Acute Ascending Paralysis". This communication emphasized the fact that complete and often fatal paralysis could occur in the absence of structural change in nervous tissues. Although our improved methods for the histological investigation of the nervous system have shown us that there are changes in most of the cases of the Landry type, the principle that some chemical or metabolic change that we cannot see precedes any structurally demonstrable degeneration must remain. The completeness and rapidity of recovery in some of Landry's cases made it unlikely that there was any structural change and certain that there could be no process akin to Wallerian degeneration. The first demonstration of anatomical alteration confined to the nerves in polyneuritis came from Dumenil of Rouen, who in 1864 showed degeneration in the small nerves of the hands and feet in a case of four months' duration. Thus the term "general spinal paralysis", by which name the syndrome was known in France, was banished forever. Finally, in 1884, Sir Thomas Grainger Stewart, Professor of Medicine at Edinburgh, named the affection Multiple Symmetrical Peripheral Neuritis; so it has been known ever since. Time does not permit the further elaboration of the history of this condition as our knowledge of bacteriology, vitamin deficiencies and the more intimate pathology of many of the so-called metabolic diseases has developed. But the principles laid down by Graves and Todd have only been confirmed by subsequent developments.

Generally speaking, then, the term neuritis is applied to inflammation of nerves and also to certain degenerations affecting nerve fibers in which there is usually little or no evidence of inflammation. Thus active inflammatory lesions of nerve sheaths (perineuritis) and of the endoneurium (endoneuritis) are included generally under the heading of *interstitial neuritis*. The degenerative forms, on the other hand, affect the axis cylinders and the myelin sheaths of the nerves, and in some cases the nerve cells as well; to these the designation *parenchymatous* is applied, and of late there has been a tendency to call this group the neuropathies. Clinically, the two forms can usually be distinguished. The interstitial type tends to be localized, affecting one nerve or the contiguous nerves of a plexus, whereas the degenerative type affects especially the peripheral parts of the nerves, the lesions being as a rule both multiple and symmetrical. In practice the two types of lesion are sometimes associated, as may be the case in polyarteritis nodosa. And when the noxa causing the degeneration acts purely locally, as in cutaneous diphtheria for example, the resulting parenchymatous neuritis may likewise be localized and not bilaterally symmetrical. It is with the parenchymatous form that we are concerned when we speak of multiple peripheral neuritis.

From the standpoint of aetiology, despite the diversity of responsible poisons, the clinical and pathological result is remarkably uniform, whether one is dealing with a simple element like arsenic, a more complicated organic compound like ethyl alcohol or a complex protein molecule like the diphtheria toxin. Whether such different agents act directly on the nerves or indirectly by producing a single toxic metabolite which is in itself a direct neural and myocardial poison is problematical. For example, beri-beri is probably induced by a toxic product formed in the course of disordered carbohydrate metabolism which results when carbohydrate is taken in large quantities without the vitamin normally found with it in nature. In the absence of sufficient thiamin, the process of carbohydrate metabolism is arrested at the pyruvate stage of breakdown, and this substance may accumulate in the cell. Whether or not it is toxic is not known. In spite of this, however, the essential disturbance of function and the site of the most obvious visible change in most cases of polyneuritis is in the peripheral nerve and not in the cell. Hence there are important gaps in the chain of evidence linking B-avitaminosis with the development of polyneuritis. It is certain that the diphtheria toxin and arsenic can produce severe degeneration of peripheral nerves in the presence of an abundance of thiamin and nicotinic acid, and such states as acute infective polyneuritis and that form occurring in people who are adequately nourished and free from all discoverable infection and toxic exposure are difficult to fit into such an hypothesis. In the final analysis it is difficult to assign a cause to many of our cases.

The most important causes of the syndrome may be conveniently grouped into the following categories: (modified from Brain).

1. External poisons:
   (a) Metallic—arsenic, mercury, bismuth.
   (b) Organic — carbon bisulphide, triorthocresyl phosphate, sulphonamides, immune sera.
2. Deficiency and metabolic:
   Beri-beri, chronic alcoholism, pregnancy, combined systemic disease associated with macrocytic anaemias, sprue, other chronic diseases of the gastro-intestinal tract and short-circuiting operations performed thereon.
3. Vascular:
   Diabetes, hematoporphyrinuria, polyarteritis nodosa.
4. Infective:
   (a) Infections in which polyneuritis is an integral part of the clinical picture: acute infective polyneuritis; polyneuritis with iridocyclitis and parotitis (sarcoid); erythroedema (pink disease)—? deficiency.
   (b) Polyneuritis complicating acute and chronic infections.
   (c) Organisms whose toxins have an affinity for peripheral nerves—Diphtheria and Tetanus.
5. Local infection of nerves—Leprosy.

6. Familial—Progressive hypertrophic polyneuritis of Dejerne and Sottas.
7. Many of the cases we see in this part of the world—no ascertainable cause.

In the short time at our disposal, it is impossible to say more than a few words about some of the more common or interesting types of peripheral neuritis. But first, I would review certain aspects of the clinical picture which are, generally speaking, common to all. Of the motor phenomena, a variable loss of motor power is nearly always present. It usually makes its first appearance and is most severe distally in the extremities. The legs are usually more affected than the arms, and the extensor groups more than the flexors, giving rise to the characteristic foot—and/or wrist-drop. Cranial motor nerve involvement is seen, most characteristically in the facial diplegia of acute infective polyneuritis and the ocular and palatal pareses of the diphtheritic form. Muscular atrophy of a moderate degree is often seen and contractures of flexor groups may develop. Diminution to absence of the tendon jerks is one of the cardinal signs, although they may be exaggerated for a very short time at the onset of the affection. Often the knee and ankle jerks disappear before there is any other evidence of neuritis, and frequently they remain absent for years after complete recovery from the other manifestations of the disease. The organic reflexes having to do with the sphincters are practically never lost. Signs of irritability or hyperexcitability of the lower motor neuron are occasionally observed in the form of cramps and spasms which are most prone to occur in the calves. Tremors due to weakness may complete the motor picture.

Sensory findings are more variable. Distal numbness, burning, tingling and crawling feelings are often seen very early in the alsoholic form whereas in diphtheretic palsy such phenomena are very uncommon. In the early stages of acute infective polyneuritis which often seems a purely motor affection, subjective sensory changes may be marked for a short time. Pain is often a prominent feature; spontaneous pains of a "tearing" nature are almost invariably a troublesome complaint in the alcoholic, arsenical and diabetic types. These pains are most frequently complained of in the calves and are often worse at night. Hyperaesthesia may precede, or paradoxically, accompany, objective sensory loss. In an area for example which is relatively insensitive to a pin-stroke of light or moderate intensity, a stimulus of greater intensity elicits a sensation which is very different from that which results when the same stimulus is applied to normal skin. The sensation is intensely unpleasant, the pain is of a burning quality, and instead of being restricted to the site stimulated, it seems to irradiate over an area the limits of which are several centimetres distant. This is usually best demonstrated on the sole of the foot. Objective sensory loss is usually distributed in the classical "stocking and glove" fashion, rarely extending above elbows or knees. The widest loss is usually for touch, the least for temperature. Deep

tenderness of muscles, particularly those of the calf, is characteristic. Ataxia of a sensory type is often conspicuous, especially in the lower limbs, in the diphtheritic, alcoholic and diabetic groups, giving rise to the designation 'pseudotabes'.

Trophic changes are common. The skin may become thin and glossy or thick and rough. The nails may become furrowed and thick, and pain and limitation of motion may develop at the joints. Oedema, redness, increased sweating and congestion on dependency all attest to the autonomic disturbances which accompany the syndrome as a result of similar degeneration of autonomic nerves. The diarrhoea that sometimes accompanies severe diabetic polyneuritis has likewise been attributed to this cause.

Alcoholic polyneuritis is very probably related to nutritional deficiency, and many consider this condition, as well as polyneuritides developing during gestation, and those following gastrointestinal short-circuiting procedures and such causes of chronic intestinal malabsorption as sprue, as closely related to if not indentical with beri-beri. Soon after the synthesis of thiamin by Williams in 1936, isolated, and later, groups of patients with unclassified and alcoholic polyneuritis who had improved rapidly under treatment with this agent began to appear in the literature. As soon as larger series began to appear, however, it became obvious that the reported results from one series to another were anything but uniform. In 1941, Brown studied the case records of all patients with alcoholic polyneuritis admitted to the Boston City Hospital during the years 1920-38. From 1920 to 1929 patients were given the ordinary hospital diet without additional vitamins. From 1930-38, vitamins were adequately supplied in the form of egg-noggs, fruit juice, salads, cod-liver oil and yeast or yeast extracts. Some patients had injections of vitamin B1 or liver extracts. When the two groups were compared, it was found that the average time spent in hospital by patients who were discharged as "well, relieved or improved" was the same regardless of treatment. Walshe in 1945 commented as follows: "Though I have sought it for over twenty years I have yet to see the case of polyneuritis, acute or chronic, that gave a clear or striking response to the administration of the vitamin B complex or to thiamin, in whatever dosage or by whatever channel". When one stops to consider the question, one realizes that the administration of vitamins has reached fantastic proportions in North America, where they have perhaps taken the place of many of the patent medicines, just a shade short of quackery. As the devil is said to be able to quote scripture to further his own nefarious purposes, so also is it possible to find papers in today's welter of medical literature to justify the use of accessory food factors of all descriptions for all manner of human ills, organic and functional. In the pellagra belt of the United States there can be no question that the B vitamins effect seemingly magical relief of the leg pains and burning associated with that disease, but as Aring has said, in the paralysing

types of polyneuritis they may as well be poured down the drain as down the patient. If general experience during the past ten years had established the specificity of the vitamin in the treatment of this condition there would be no need to debate the question at this time.

So-called "lead neuritis" is becoming increasingly uncommon, but I have decided to mention it only to point out one thing in particular. It has long been known that the muscles paralysed by lead are those most used in the patient's occupation. Aub and his co-workers experimentally produced selective muscular paralysis in experimental animals with lead poisoning by fatiguing certain muscles. The lactic acid liberated in the muscles by their contractions leads to the focal formation of lead acetate from the lead phosphate in the blood. From the lead acetate, insoluble lead phosphate is precipitated in the muscle cells .Thus it is suggested that lead has no direct action on the peripheral nerve, and what has long been considered neuritis is really a myopathy, a local poisoning of muscles which are used most. This view, you will remember, was put forward by Todd over a century ago. Of course there are well recognized direct effects of lead on the nervous system; these are acute and chronic lead encephalopathy and lead-induced progressive muscular atrophy.

Acute infective polyneuritis is often known on this continent under its eponymous designation, the Guillain-Barré syndrome. Its virus nature has never been proven, but there are strong grounds for suspecting such a cause. It was probably first adequately described by Osler in 1893, and the main contribution of Guillain and Barré was the mention of the fact that the cerebrospinal fluid protein is often considerably elevated in the absence of any increase in cells. It must be remarked, however, that in any severe case of polyneuritis due to whatever cause, such a cell-protein dissociation may be found. It is true that the protein levels seldom reach the heights sometimes seen in the acute infective form, but I have also seen undoubted cases of the latter in which the protein was below 35 mgms./100 cc. throughout the period of observation, and others in which the cell count reached as high as twenty-five. The disease, especially in its ascending or Landry form, is a dangerous and often fatal one. The fatalities can usually be attributed to bulbar involvement. However, unlike the cases of cervical polio which go into a respirator and rarely come out alive, these patients carefully maintained, frequently recover completely after as long as two weeks or more in the machine.

The group which I have mentioned as vascular in origin all have as their basis disease of the vasa nervorum. In diabetic neuropathy, atheroma of the intimate vessels is found, and although many of the patients showing this complication of diabetes mellitus give histories of poor control, it is generally felt that hyperglycaemia alone has little to do with its development. In acute porphyria the cause of the neuro-

pathy is probably the same as that of the abdominal pain so common in this condition — prolonged vascular spasm related to the presence of porphyrins in the circulation. The peripheral neuritis of polyarteritis nodosa may take one of three clinical forms. In the first there is a successive assymetrical neuritis of individual nerve trunks sometimes designated by the ugly term 'mononeuritis multiplex', and simulated only by leprosy. In 1923, Wohlwill demonstrated its origin in obliterative endarteritis of the vasa nervorum. In the second form, a neuritis of this type is associated with the more usual type of symmetrical polyneuritis, maximal in the lower limbs. In the third and commonest type, the familiar syndrome of symmetrical polyneuritis occurs alone. This type has often been called 'toxic', but careful pathological examination leaves no doubt that endarteritis is the cause as with the others, and it is probable that the nature of the lesion is probably determined by the localization and calibre of the vessels chiefly involved by the disease.

When one comes to a consideration of the treatment of polyneuritis, one must first make it clear that at present there is no specific remedy available. If an identifiable cause is found to be operating, it should, of course, be removed. Rest in bed is essential until recovery is well established. Protection of the weakened limbs by cradle and footboard should be ensured. Passive motion should be carried out at least three times daily to the point of moderate pain. If pain is not relieved by acetylsalicylic acid and codeine, hot packs may be applied every four hours as in the acute stage of poliomyelitis. When the pulse rate does not become unduly elevated by mild exercise, one can justifiably assume that any myocardial lesion has subsided and activity should be encouraged with the help of braces, walkers and crutches where necessary. Vitamin therapy has already been dealt with. Liver extract will relieve the neuritic manifestations which accompany subacute combined degeneration, and in any other type of peripheral neuritis in which nutrition is faulty it is as good and as cheap a means of ensuring adequate absorption of supplementary food factors as any.

Finally, in severe peripheral neuritis of any type a trial of British Anti-Lewisite might be considered. This substance removes heavy metals and possibly other substances from enzyme systems regulating carbohydrate and fat metabolism which may be disordered in polyneuritis. Two to three mgms./kilo body weight per day is given intra-muscularly in divided doses every four hours for two weeks. A few successes have been reported in the heavy metal and acute infective varieties, and recently a report has come from Cleveland stating that the pain of diabetic neuropathy has been relieved by this substance.

WHAT'S DOING AT WESTERN?

ALLAN LANSING, (Ed.), '53

EVERY Department of the University of Western Ontario Medical School is actively participating in research, either of the applied or of the purely academic type. A group of over sixty graduate students, aided and guided by an experienced permanent staff are tackling problems in all fields of medical research. This report is intended merely as a summary of some of these projects. Unfortunately it is impossible to include all the departments or even completely to cover any one. It is hoped that those departments not covered in this review will be mentioned in future issues.

The assistance of Drs. R. L. Noble, M. L. Barr, R. J. Rossiter, G. W. Stavraky, R. A. Waud, and R. G. E. Murray is gratefully acknowledged. Their unstinting co-operation has made this report possible.

A. *The Collip Medical Research Laboratory*

The Collip Medical Research Laboratory is situated on the University campus and was established when Dr. Collip came to the University of Western Ontario as Dean of Medicine. The Department of Medical Research is essentially a graduate department interested in the developing of research work in many aspects of Medicine. At the same time, however, the Department is concerned with the undergraduate teaching of endocrinology and physiology and some of the members of the staff also serve in undergraduate departments.

Some of the research problems may be briefly summarized:

(1) *Cancer Research*: The cancer research program is concerned with several aspects of the experimental approach to cancer, one of which is the question of the relationship of the tumour to the host. By this is meant the changes which take place in those tissues of the host which have not been invaded by malignant cells. For example, an animal bearing a tumour has a depression of liver catalase activity although there are no cancer cells in the liver.

The investigations are concerned with defining what types of systemic effects occur in the host and the mechanism by which they are produced. Several approaches to the problem are being made.

The reaction of the endocrine system to the presence of a tumour is being studied both to determine the effects on endocrine organs and to study the changes in metabolism as a result of endocrine dysfunction. The metabolism of haemoproteins is abnormal in an animal bearing a tumour and this is also a subject of study. In the field of intermediate metabolism a particular interest at the moment is that of the lipid metabolism of the host. And finally ,at the cellular level, an attempt is being made to study the distribution of enzymes within the cells of organs exhibiting the systemic effects of tumours.

Extensive studies are being made on a transplantable mammary tumour of the rat. Oestrogens and pregnancy are found to stimulate the growth rate of this tumour, although it may be inhibited by large doses of the former. The effects of various hormones on changes in the malignancy of this tumour are also being studied.

From time to time there are reports of diagnostic tests for cancer. A number of these have been investigated to test their authenticity. At present problems concerning changes in the protein and lipid of cancer blood are being investigated.

(2) *Studies on Extracts of Plants*: From the time of the earliest medicine men and witch doctors, plant extracts have been used in attempting to cure the ills of man. More and more these empirical treatments are being found to have some basis in fact as compounds with therapeutic activity are isolated from plants. This laboratory has been particularly interested in plant constituents which effect the endocrine glands.

For instance, it has been known for some time that feeding excessive amounts of cabbage or turnip to animals may produce goitre. The pure compound responsible for this effect has been isolated in this laboratory from turnip seed and from the closely related rape seed. This compound has been shown by a group in Boston to have a structure and mode of action similar to antithyroid compounds such as thiouracil. Its natural occurence in foods is of interest, in the problem of aetiology of goitre in humans.

A separate factor in these seeds which has not yet been isolated causes a four fold increase in the cholesterol content of the adrenal glands of rats. Since cholesterol has been suggested as the precursor of the adrenal cortical hormones and in view of the present interest in cortisone, tests are in progress to determine whether this treatment causes an increased or decreased production of these hormones.

According to Nevada Indian medicine men, *Lithospermum ruderale,* a plant of the Boraginaceae family was capable of contraceptive powers when ingested in the form of a tea.

Work in this laboratory has shown that subcutaneous injections of water extracts of the plant prevent sexual maturation in immature male and female rats alike. In addition, the activity of the thyroid gland was depressed as determined by histological studies. Similar inhibitory effects on thyroid and gonads were noted in adult animals.

The actions of separately injected gonadotrophins or thyrotrophin were markedly inhibited by simultaneous injections of the plant extract, while mixing extract and hormone prior to injection resulted in almost complete inactivation. Preliminary work indicated that prolactin was similarly affected, while posterior pituitary extracts and insulin remain unaffected.

Efforts have been made to extract the active principle in sufficiently pure form to allow further studies on the mode of action and, eventually, on clinical investigation.

(3) *Posterior Pituitary*: By suitable chemical methods it has been possible to extract from the urine of patients a substance which apparently is the antidiuretic hormone of the posterior pituitary. This substance is increased after dehydration, electro-convulsive therapy and after syncope. The possible relationship of posterior lobe function to other clinical states and to the adrenal gland is under investigation.

(4) *ACTH and Cortisone*: Experimental work on animals with these substances has included a comparison of activity of various commercial preparations. Attempts have been made to augment or depress the activity of these hormones and to study the actions in animals which have altered metabolic patterns. Collaboration with clinical research has included various biochemical determinations and special tests associated with the study of these hormones.

(5) *Cardio-vascular Research*: Studies are being carried out on the aetiology and pathogenesis of experimental arteriosclerosis in rabbits, and of so-called spontaneous arteriosclerosis in chickens, and on the influence of certain hormones and dietary ingredients on the progression and regression of the disease in these species.

A series of investigations on venous thrombosis and pulmonary embolism in man is also underway in collaboration with the Department of Veterans' Affairs.

B. *The Department of Anatomy*

The main field of research in the Department of Anatomy is normal and experimental cytology. The various projects are supported by the National Research Council, the National Cancer Institute, the Defence Research Board (Department of National Defence) and the Federal Department of Health (Mental Health Division).

(1) *Nuclear Morphology*: It is known that the difference in chromosome content, according to sex, leaves its mark on the morphology of the resting nucleus. This interesting observation was made first on the nerve cells of mature cats. This matter is being extended to (a) other somatic cells in the cat (b) other mammalian species, including man and (c) animals of various ages from birth to maturity.

(2) *Function of the "Resting" Nucleus*: There is evidence that nuclear structures participate in the synthesis of certain cytoplasmic components, especially those containing nucleic acids. This point is being investigated in the nerve cell, in which the cytoplasm is particularly rich in nucleic acid-containing Nissl substance. Changes within the nucleus are followed, by cytochemical methods, as Nissl material is being restored following its experimental depletion.

Further, the influence of various hormones on the function of the "resting" nucleus is being followed by removal of various endocrine glands and by the administration of hormones, followed by cytological examination of tissues.

(3) *The Effect of Anoxia on the Central Nervous System*: This subject is of interest in general medicine, anaesthesia and aviation medicine. The histopathology of the brain, following exposure of animals to low oxygen concentrations in the inspired air, is being followed.

(4) *Synapse Morphology*: Details of synapse structure is essential to the interpretation of many problems in neurophysiology. The synapse is being studied in a detailed manner, therefore, using quantitative methods.

(5) *Effect of Partial Isolation on Neurones*: Dr. George Stavraky, of the Department of Physiology, has shown that partially isolated nerve cells develop markedly altered physiological properties. This matter must be taken into consideration in numerous neurological conditions. The cause of the acquisition of altered properties, after partial isolation, is not known. The cytology of such neurones is being investigated, therefore, in the hope that some clues may come to light.

These projects are being carried out by a small group of research assistants, working either full time or during the summer months. Their conscientious work is much appreciated by those responsible for guiding the work in the Department.

C. *The Department of Biochemistry*

Much of the research at present being carried out in the Department of Biochemistry is of a fundamental rather than an applied nature. Fundamental research more properly falls within the province of a University Department whereas applied or developmental research frequently demands the greater resources of an industrial laboratory. Within the Department of Biochemistry, research is in progress on a number of aspects of carbohydrate metabolism, on some aspects of absorption from the gastro-intestinal tract, on the enzymes of the cerebrospinal fluid and the relation of these enzymes to the number and type of white blood cell in the cerebrospinal fluid, on the chemistry of white blood cells, and on the lipids, nucleic acids and enzymes of degenerating nerve.

(1) *Nerve Degeneration Studies*: One of the major problems that has been claiming the attention of the Department for the past few years has been that of nerve degeneration. A number of diseases are characterized by a degeneration of nerve fibres. It is hoped that a knowledge of the chemical events that occur when a nerve degenerates will lead to an understanding of why a nerve degenerates in diseased conditions. Until this is known, any attempt at therapy in the degenerative diseases of the nervous system will be, for the most part, empirical. It is highly desirable that such an attempt should be scientific and based on the results of exact

knowledge. So far, some observations have been made on the changes that occur in the concentration of certain lipid substances when a nerve is cut. Most of the lipid substances are present in the white myelin sheath that surrounds each nerve fibre. This sheath degenerates when the nerve is cut. At the present time further observations are being made on the changes in the concentration of nucleic acids and in the activity of a number of enzymes. Some of these changes take place earlier than those in the concentration of the lipids of the myelin sheath and so may be of more importance in the degeneration. This project is receiving financial support from the Dominion Department of Health through the National

(2) *Studies of White Blood Cells*: The work on the chemistry of white blood cells is being undertaken in the hope that a knowledge of the chemical nature, including the enzyme constitution, of each type of white cell will eventually lead to a better understanding of the precise function of each of the different types of white cell that is found in the blood. The function of each type of white cell has been the subject of much speculation among medical scientists. This work is receiving financial support from the National Research Council and the National Cancer Institute.

(3) *Bacteriophage and Arteriosclerosis*: In collaboration with the Department of Bacteriology investigations have been carried out on the infection of micro-organisms with bacteriophage and, in collaboration with the Laboratory Service of Westminster Hospital, observations have also been made on the chemistry of atherosclerosis.

(4) *Radioactive Isotope Laboratory*: Another activity of the Department has been the establishment of an Isotope Laboratory for the handling of radioactive isotopes. In conjunction with the Department of Radiology, this laboratory will be used for the dispensing of radioactive isotopes for the treatment and diagnosis of disease at Victoria Hospital. This part of the isotope programme is being financed by the Ontario Cancer Foundation. In addition, a research programme financed by the National Research Council is about to be undertaken on the incorporation of radioactive phosphorus into different phosphorus compounds of the various organs of experimental animals and the effect of certain hormones on this incorporation. It is also planned to use radioactive tracers in the work on nerve degeneration and white cell chemistry.

D. *The Department of Physiology*

In the Department of Physiology, research, under the supervision of Dr. G. W. Stavraky, is being conducted along three general lines. The main interest of the group working under Dr. Stavraky lies in the field of neurophysiology and the work is concerned with the study of the sensitivity of various levels of the central nervous system to chemical and reflex stimulation following partial isolation of the neurones.

(1) *Deafferentation of Spinal Neurones*: It was previously assumed that unilateral excision of the motor cortex leaves the corresponding side

of the neural axis less excitable than the intact side. On reinvestigation of this concept, it was found by Dr. G. W. Stavraky, aided by Drs. S. M. Fisher and C. G. Drake that the spinal neurones deprived of their cortical connections become more sensitive to chemical stimulating agents such as acetylcholine, metrazol ,camphor, picrotoxin, strychnine and others. It was further noted by C. G. Drake and G. W. Stavraky that deafferentation increases the excitability of spinal neurones in a similar way. In a systematic study of this latter observation, Drs. R. D. Teasdall and G. W. Stavraky found that deafferentation increases the excitability of spinal neurones not only to chemical stimulating agents but also renders spinal neurones more susceptible to excitation by physiological nerve impulses reaching them via the pyramidal tracts as well as to other forms of intersegmental reflex stimulation. It was found during the progress of this latter study that a sensitization and in some instances a reversal of the postural reflexes takes place after deafferentation. Furthermore, Dr. R. D. Teasdall found that section of the corpus callosum renders animals more susceptible to convulsions. In addition to this, Dr. R. A. Hughes, in collaboration with Drs. R. D. Teasdall and G. W. Stavraky found that strong afferent stimulation causes a reversal of reflexes in previously decentralized segments of the spinal cord while intact spinal centers respond in a normal way to an identical stimulation.

As a result of these studies, Dr. C. G. Drake and Dr. R. A. Hughes were awarded Master of Science degrees and Dr. R. D. Teasdall was awarded the degree of Doctor of Philosophy. The work along these lines is continuing and at present the effect of cortisone and of barbiturates as well as other sedatives on sensitized neurones in the central nervous system is under study, this being carried out by Mr. P. R. Pase and Mr. J. J. Seguin, while Dr. William H. Cook is making an extensive investigation on the part played by the cerebellum in convulsive manifestations. The general aim of this research (which is financed by the National Research Council of Canada and by the Federal Department of Health) is to acquire more detailed information about the mechanism of epileptiform convulsions than is available at the present time and, where possible, to gain insight into the basic mechanisms which govern the functions of the nervous system. As one side-result of this study, the exact nature of sensory ataxia was revealed and an understanding gained of many of the hitherto perplexing features of this clinical entity.

(2) *Studies of the Physiology of the Gastro-intestinal Tract*: Another line of research in which Dr. G. W. Stavraky has been interested for many years deals with the physiology of the gastro-intestinal canal. In collaboration with Dr. G. M. Morton, a study of the effects of intra-arterial injections of acetylcholine on gastric secretion was carried out. By this method of injection, an overstimulation of the gastric mucosa was achieved and knowledge was acquired of the functional pathological conditions which may lead to gastric ulcer formation and other disorders of the stomach. This work proved to be quite fundamental in nature and

at present is being extended upon by Dr. Andrew Ivy's laboratories in Chicago. Dr. G. M. Morton was awarded a degree of Master of Science for his part in this research which is continuing at the present time. Mr. A. R. Graham and Dr. G. W. Stavraky are conducting a similar investigation on the mechanism of salivary secretion in conditions of overstimulation by means of intra-arterial injections of acetylcholine and adrenaline. It is hoped that this research will lead to a more basic understanding of the hypersensitive states and of the conditions ensuing during super-maximal stimulation.

(3) *Other Fields of Study*: Finally, a study of anoxia and asphyxia and the effect of reflex stimulation of the pituitary hypothalamic complex on the action of adrenaline is being carried out by Mr. R. J. Oliver and Dr. G. W. Stavraky. This investigation is an extension of the research done by Dr. Stavraky during the war. It is a type of research which has practical application to flying at high altitudes, and is being financially assisted by the Department of National Defence.

E. *The Department of Pharmacology*

Research in the department of Pharmacology is confined mostly to the study of the action of drugs on the cardiovascular system. At the present time, there are five main problems under way;

(1) *Heartless-Lungless Animal Studies*: A study of the effects of digitalis and other drugs is being carried out using a heartless-lungless preparation, that is an animal in which the heart and lungs have been replaced by a mechanical heart and lung. This preparation excludes any action the drug might have on these organs. The mechanical heart-lung was devised in the department and the heart involves two new features. The actual pumps consist of two large glass syringes from which the cardiac output may be read off at any moment; the pistons of the syringes are operated by an especially designed cam which produces changes in the volume of the syringes corresponding to the volume changes in the mammalian ventricle. Previous mechanical hearts have been operated by a simple crank, which produced volume changes which followed the sine wave and are far from physiological.

(2) *Work With Plant Extracts*: In a systematic investigation of the effects of extracts made from various plants growing in Western Ontario work in the department has shown that a bulb *Ornithogalum umbellatum* (common Star of Bethlehem), contains a glucoside which has an effect on the heart much like that of Digitalis. It causes slowing of the beat and conduction, increased force of contraction and finally in large doses systolic standstill. It is hoped that it may prove to have some advantages over digitalis. The bulb is a distant relative of Squill which has long been used for its Digitalis-like effects.

In addition to the above, the study of plants growing in Western Ontario have shown that the perennial *Herculeum lanatum* (Cow Parsnip)

has a direct stimulating effect on the heart. Extractions of the stems and leaves of this plant have been made and experiments are being carried out on the isolated heart of the frog to determine the optimum dosage for postive inotropic action. Side effects of the drug are also being studied.

(3) *Effect of Osage Orange Extracts*: Since 1939 the department has been interested in the stimulating effects of extracts made from the Osage Orange on the heart. It was shown that part, at least, of this action was due to the presence of a steroid, Phytosterol, in this orange; this lead to an investigation into the cardiac action of all steroids. About thirty of these compounds have been obtained and studied. The results of this work are to be published in the near future.

(4) *Studies of the Action of Blood Substitutes*: In the department a study is also being made on dogs, of the effects of the injection of large amounts of blood and blood substitutes including gum acacia, on arterial blood pressure, right and left auricular pressures, right ventricular pressure, heart rate, oxygen consumption, cardiac output (by the Fick method), muscle and skin blood flows, and haematocrit. In other experiments the stroke volume and diastolic size have been measured. The effects of digitalis glucosides are also being studied under the above conditions. It has been found that as the infusion of plasma substitute continued the haematocrit fell, while the cardiac output, diastolic volume, and skin flow increased. The auricular pressure does not rise markedly until long after the cardiac output has increased. The experiments suggest that Starling's law is inadequate to explain changes in cardiac output. Increased venous return without increase in venous pressure and oxygen carrying capacity of the blood are the important factors in the intact animal.

(5) *Studies of Acetylsalicylic Acid*: A comparative study is being made of acetylsalicylic acid (A.S.A.) and a combination of acetylsalicylic acid with calcium carbonate. When this combination is placed in water the calcium salt is formed. It is claimed that the salt is less irritating to the stomach and is absorbed more rapidly. Absorption and excretion are being studied by estimation of plasma and urine levels and penetration into tissues. Efects on coagulation including bleeding time and inhibitory effects on vitamin K, analgaesic and antipyretic efficiency, and the degree of irritation of the gastro-intestinal tract are also under investigation.

"The man of science appears to be the only man who has something to say just now and the only man who does not know how to say it."—Sir James Barrie.

INTESTINAL OBSTRUCTION AND THE DANGER OF PERFORATION

G. BENDING, '52.

Intestinal obstruction is a dangerous condition in which the most dangerous sequel has not been sufficiently stressed. Perforation follows a high proportion of cases of acute intestinal obstruction, and it carries a very high mortality rate.

Aetiology: Intestional obstruction is caused by mechanical factors such as strictures, presence of a foreign body, adhesions, pressure from without, herniae, volvulus, intussusception, and congenital abnormalities. Paralytic ileus can result in intestinal obstruction also, but often this can be treated medically. Embolism, or thrombosis of blood vessels supplying the involved portion of intestine, will cause a gangrenous section through which intestinal contents will not normally pass.

Strictures may be congenital or acquired, inflammatory or neoplastic. Segmental atresia of small intestine, or imperforation of the anus, are the congenital varieties. Benign and malignant tumours may occur anywhere in the large and small intestine, and may cause a progressive obstruction, but tumours involving the ascending portion of the colon, rarely, if ever, cause obstructive. Obstruction by external compression is common only where the tract is adherent to the other structures. Adhesions and herniae are the most common causes of obstructions; the two main divisions of these are simple and strangulating in the latter of which there is interference of the blood supply of the involved intestine.

Symptoms and Physical Findings: Pain, nausea, vomiting, and later distention in well established cases, are the cardinal signs of intestinal obstruction. The pain is of short duration but rises in intensity to a peak which persists for a few minutes and then abruptly ceases. The pain may be colicky, and may recur frequently or at long intervals. When the intestine is considerably dilated, the pain is less severe. In obstruction of the small intestine, there is frequent and copious vomitus as well as distention, due to the accumulation of gas and fluid above the site of the obstruction. In obstruction of the colon, there is usually marked abdominal distention without vomiting since the ileocolic valve and sphincter remain competent.

The patient does not appear acutely ill early in cases of obstruction. Later, largely due to dehydration, the patient appears more acutely ill. If strangulation exists, the pulse may be hurried and there may be blood loss and shock. The abdominal wall remains soft since there is no peritonitis, unless there is perforation. If the distention is great, there will be marked tympany, and borborygmi may be heard during the peak of the pains.

Diagnosis: Roentgen examination enables the distended bowel, together with gas on the proximal side of the obstruction, to be visualized.

Delay in diagnosis is usually due to a lack of appreciation that there is no, or little, abdominal tenderness, or rigidity. Always suspect intestinal obstruction when abdominal pain, nausea, and vomiting are present.

The greatest danger following obstruction is perforation. Intestinal obstruction is an emergency and it should be diagnosed as quickly as possible in order that surgical or medical intervention will remove the ever present danger of perforation. In the past, in cases of acute intestinal obstruction, the mortality has been 40 to 60 per cent. This almost unbelievably high rate is largely due to a failure to diagnose the obstruction in time to prevent perforation and resultant generalized peritonitis. The lack of many acute signs and symptoms and the similarity between those symptoms of simple intestinal colic and associated conditions with those of obstruction, lead to delay in diagnosis. The seriousness of obstruction and the frequency of succeeding perforation should be stressed.

FOUR CASES OF ACUTE INTESTINAL OBSTRUCTION WITH RESULTANT PERFORATION

The first case to be considered occurred in an 84 year old white male, who entered the hospital with a history of abdominal pain and vomiting which extended over a period of seven days. Nausea, persistent vomiting, abdominal pain, distention and tenderness in the left lower quadrant were the cardinal signs. A flat x-ray plate showed large and small bowel distention. The patient lost twenty pounds in one week.

The patient was given enemas and a motor tube was inserted. Under this treatment, the patient's condition seemed to improve.

A barium enema and x-ray examination showed a diverticulitis of the sigmoid colon. A malignancy was suspected, but a sigmoidoscope examination was negative.

At this time, the patient complained of abdominal pain in the epigastrium but there was no rigidity or rebound tenderness.

The patient died. At post mortem, a ruptured caecum was discovered. An annular constricting carcinoma at the hepatic flexure was the cause of the obstruction and perforation.

The second case is a female of 62 years who arrived at the hospital in an acutely ill and badly shocked condition. She had an acute abdomen with acute peritonitis. Her pulse was 120 per minute and was weak and thready. The patient was very cyanosed. Black fluid was vomited by the patient and continuous suction was instituted. Oxygen and 500 cc. of intravenous blood were given but in spite of supportive therapy the patient died 36 hours after admission to hospital.

At post mortem, a perforated stenosing fibrocarcinoma (grade 3), of the sigmoid colon with metastases to the regional, mesenteric and paraortic lymph nodes, was discovered. A generalized fibrino-purulent peritonitis was present. The perforation was secondary to the acute obstruction due to the malignancy.

The third case of perforation following acute obstruction, occurred in a male child, two years of age.

The child swallowed a copper coin on Friday, August 25th, up to which time he was perfectly well. The same afternoon the mother noted frequent loose stools. The child was feverish on the 26th of August. On the following Monday the child complained of acute abdominal pain. The next day copious projectile vomiting was frequent. The child became cyanosed and oxygen did not relieve this. To relieve the dehydration, intravenous fluids were given since the child was unable to take food or fluids orally.

X-ray revealed the copper coin at the iliocaecal valve. A Levine tube and Wangensteen suction were applied. The patient was now semi-comatose, with a fever of 104.3° F., and with a rapid, weak pulse. The abdomen was distended and firm, with no palpable masses or intestinal sounds whatever. The temperature rose to 107 degrees; cyanosis became gradually more marked on August 31st; in the evening the patient stopped breathing. Up until the last, there was no abdominal tenderness, rigidity or bowel sounds. Tremendous collapse made laparotomy prohibitive.

At post mortem, three salient facts were shown: (1) Coin in Meckel's Diverticulum,

(2) Perforation of Meckel's diverticulum and (3) Generalized peritonitis.

The fourth case: This example of perforation following obstruction occurred in a 68 year old Indian male, who had a history of a previous abdominal perineal resection for adenocarcinoma of the rectum (Grade 2), one year previous to the final hospital admission.

On admission, the patient complained that his colostomy had not been functioning for five days and that he had had projectile vomiting for five days. Continuous Wangensteen suction was applied. The patient was given intravenous glucose but ran a progressively down hill course until his death twenty days after admission.

At post mortem, no residual malignancy was found. Fibrous small bowel obstruction, fibrous peritoneal adhesions and perforation of the small bowel with localized peritonitis were discovered.

Summary:

1. Intestinal obstruction is due to many different factors, of which malignant tumours, strictures, foreign bodies, adhesions, herniae, volvuli, intussusceptions, paralytic ileus and congenital abnormalities, are the most important. Adhesions and herniae are the commonest causes of obstruction.

2. The most important symptoms of intestinal obstruction are pain, nausea, vomiting (usually projectile) and distention.

3. X-rays following a barium meal or enema, are valuable in confirming the diagnosis.

4. Perforation of the intestine following obstruction, is an ever present danger which must be carefully considered in all suspected cases of obstruction.

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ABSTRACT: FOLLOW-UP STUDY OF ONE HUNDRED PRIVATE HYPERTENSIVE PATIENTS WITH CARDIO-VASCULAR COMPLICATIONS

P. D. WHITE, E. G. DIMOND, A. WILLIAMS

J.A.M.A. 143: 1311 Aug. 12, '50

This study is an analysis of a series of 50 hypertensives with serious cardiovascular complications, who had thoracolumbar sympathectomies done by Dr. R. Smithwick between 1941 and 1946. These cases are compared with 50 control patients of similar sex, age and cardiovascular complications, who were treated medically.

After a three-year follow-up of the 50 sympathectomized patients, the results were excellent or good in 11, fair in 11, little or no change in 5, worse in 11 and 12 were dead. In contrast, the control group showed 1 patient in good condition, 4 in fair condition, 4 unchanged and 41 worse or dead.

The large number of failures even among the sympathectomized group points out a need for better methods of selection of patients with cardiovascular complications of hypertension. To meet this challenge, Dr. Smithwick has drawn up a new system of selection of patients for whom sympathectomy is indicated and this system is outlined in the original article. An application of his new grading to the original sample of 50 patients operated on would have been helpful in excluding a considerable portion (26%) of the original group in which unfavourable results were obtained, by operating only on those fulfilling his present criteria. Sympathectomy then, would appear to be of use in hypertension with mild to moderate cardiovascular complications.

H. M. BROWN, '52.

EDUCATION: ITS POTENTIAL INFLUENCE FOR UNITY *

ALBERT W. TRUEMAN, M.A., D.LITT. **

Mr. Chairman, President Hall, Dean Collip, Members of the Alumni of the University of Western Ontario and of the Hippocratic Society, Ladies and Gentlemen:

One of the disadvantages of giving an address before a strange audience and in a strange place is that you don't know whether they are familiar or not with your favourite stories that you hope you may be able to work off on them, and the most highly complimentary introduction of my good friend President Hall reminds me of one suitable for the occasion. I don't know whether it is common up here or not, but I want to tell it because the feelings expressed are in a general way my own at the present time.

There was a farmer in Cape Breton who was driving a calf along the road and he had occasion to get it across a stream over which there was a small bridge guarded by a rather weak handrail. A motorist came along at this time and saw the farmer was having difficulties, and with a sincere desire to be of help came up behind and suddenly gave a prolonged blast on his horn. The calf struggled out of the grip of the farmer and broke through the handrail of the bridge and dropped into the creek and was drowned. The motorist offered his apologies as he realized the loss of the small animal probably meant considerable to the farmer. He gave probably the mildest rebuke that was ever offered by anyone at such an injury. The farmer, who was a Highland Scot, remonstrated, "After all, it was the hell of a big toot for such a small calf." (applause). I am sure you will see the propriety of this anecdote at the beginning of my address.

May I express the great pleasure it gives me to be here at the University of Western Ontario and to have an opportunity of speaking to the Medical Alumni and to graduates during their homecoming week. At the University of New Brunswick we greatly admire the work of the University of Western Ontario and observe with a congratulatory interest the progress this great institution is making. One cannot refer to that fact without having in the forefront of one's mind your Medical School. It is an additional pleasure to meet old friends among whom I am glad to mention President Hall and Dean Collip.

I must confess that although the circumstances to which I have referred are most delightful, I experience now, as I have on other occasions, a certain trepidation when I begin to speak before a medical audience. A layman always feels at a disadvantage before a professional gathering because he cannot hope to meet them on their own ground and finds it perplexing to fix a criterion for determining the generalities he

* Delivered at the Annual Hippocratic Banquet of the Faculty of Medicine, University of Western Ontario, October 13th, 1950.

** President of the University of New Brunswick.

has to offer, for they are experts or budding experts who confront him. These being the conditions, I rely on what experience I have and draw on those other little addresses I have given to other groups of the medical fraternity.

May I begin what I have to say by congratulating you on this homecoming week. This seems to me a most excellent thing. There are always these conventions, conferences and assemblies of one kind or another and sometimes those of us whose austere lot it is to attend a good many of them are inclined to grow weary and wonder about their value. Sometimes we try to cheer ourselves up by saying, "After all it doesn't matter what goes on at these meetings, it is the contacts we make." This is an over-worked word, but it is a most fortunate word in describing the activities at a conference.

And I am convinced, the more I think about it, that we do need this conference business in Canada. We are so sprawled out, we are so big, there are so many factors which operate against us for the achievement of unity that anything which serves to bring people together so that they can have some kind of common bond can serve an important purpose over and above the specific professional business in which we are engaged.

Sometime ago I was much struck by a passage in a delightful book by Logan Pearsall Smith called *REPERUSALS AND RECOLLECTIONS.* One chapter in the book is about the great English novelist, Jane Austen. May I venture to give you an extract which I have copied out in which the writer deals with Jane Austen's particular power of dealing effectively with a small group of people in a confined locality. Here is the passage:

"But this effect of richer colour and chiaroscuro is still more due to one subtle and exquisite power which Jane Austen developed in the maturity of her genius; the power of rendering what I shall call, for want of a better term, the moral atmosphere of places; the tones, that is, of collective feeling; the moral climates which are produced by, and surround, different groups of people, and fill, as with a body of dense and saturated air, the places where they live. We are all sensitive to these local atmospheres; we have all experienced what happens when we change them; how values and interests which flourish in one climate wither away at once in another; how anecdotes which are welcomed and laughed at among one set of acquaintances become unspeakable in a different group. The part that these all-pervading atmospheres play in social life is enormous, but how inadequate are almost all the renderings of them which we find, even in the greatest fiction."

Then he goes on to say:

"Jane Austen indeed explicitly notes herself in this novel how 'every little social commonwealth dictates its own matter of discourse,' and how 'a removal from one set of people to another, though at a distance of

only three miles, will often include a total change of conversation, opinion and idea.'"

Now Jane Austen lived between 1775 and 1817. Thus in the paragraphs I have just read, she refers to the England of 130 or 135 years ago. But the passing of time has taken away nothing essential from the truth of her observation. And I suggest to you that if her observation was true of the "tight little island" in which she lived, then the same observations may truthfully be made of this great sprawling country of Canada in which we live. Are we not familiar with the differences in conversation, opinion and idea as they exist between, say, Halifax and London, between Winnipeg and Vancouver, between Quebec and Montreal, two French cities though they are, between Regina and Calgary, between Toronto and anywhere else? One should apologize to Toronto. These little references to Toronto have become almost part of the national folklore and possibly Toronto will never get rid of them.

It is perfectly true that these differences exist. And their existence is one more reason why a home-coming is valuable, quite apart from the natural pleasure you all take in the renewal of close, personal association with your beautiful University. I take it that no small part of the value of your celebration here this week lies precisely in the opportunity thus made yours to observe, to interpret and to accept finally, with common sympathy and understanding, at least some of these differences in conversation, opinion, and idea.

You will note, I trust, that I have not described your opportunity as that of doing away with these differences. The differences to which I refer are not the divergent views of fundamental issues, not the disagreements among scientists about new hypotheses, which if carried to great length, might prevent forward movement in the profession along a solid front. Not at all. The differences to which I refer are simply those which are created by difference of locality, those which give rise, as Smith puts it, to the characteristic atmosphere and tones of collective feeling which we recognise as we move from one populated place to another. These differences cannot be destroyed. They should not be destroyed. But they should be expected and they should be understood, for otherwise they can be a serious disadvantage to this country. We are in many ways an inconsistent people. We wish to found our society on the economic basis of free enterprise, but we are inclined to resent and to take no trouble to understand the differences which must exist among people who enjoy this fundamental freedom.

It would seem to me that one aspect of the great Art of Living is the joyful recognition of these differences; that one great hope for Humanity is that we need not, if we will not, sacrifice the powerful inspiration of Unity to the ineffective dullness of Uniformity. These considerations are worth while in a country in which we have to work hard to complete our unity and avoid perilous misunderstanding.

To illustrate this matter of understanding, I again draw on fruitful

Cape Breton. This story is an old favourite of mine, and I hope it hasn't got up here yet. It tells about Father Cody and big Angus MacDonald, both Highland Scots, who, though they were accustomed to driving about the Island, lost their way and had to ask how to get on the road to Margaree. They stopped beside a little cottage and Angus knocked at the door. An old white-haired crone came out. He asked her how to get to the road to Margaree, and she replied in Gaelic, so that the conversation wasn't productive of results. So Father Cody took over and went up the same path and knocked on the door and the same old lady came out. He asked, "Could you put us on the road to bring us into Margaree?" When she replied he answered her in kind and her face lit up that he could talk in the great tongue. She descended to the vulgar tongue and spoke English and Father Cody got his information. Just as he was turning to leave she asked him what was the matter with the young man. Father Cody answered, "The difficulty is he hasn't got the Gaelic." Her face broke and she said, "What a hell of a way to live!" (applause) I think that is a lovely story. And although it is exaggerated, these are the materials out of which unity in this country will have to be made; these problems arise and have to be solved.

It is because I believe that these matters are important that I want to speak about an aspect of education which has a relation to them.

It seems evident to me that our education has something to do with the possibility of our achieving unity — not uniformity — in this country. In fact, I think the possibility of achieving unity in this country will become greater as individuals achieve a kind of unity or wholeness within themselves.

There is a great deal of inevitable nonsense talked by people like myself about education. There are those who advocate Science, who advocate professional education or technical education almost to the exclusion of everything else, so that they lose sight of the humanities. They want more of this and less of that. One gets out of patience with it. Of course the services of the great professional schools must go on, must be maintained and enriched and extended.

But the danger, as I see it, is a possible consequent fragmentation of education, and a possible fragmentation, so to speak of the individual. It isn't so much that he knows too much about one or two subjects, and too little about all the rest. That may be a danger, of course. But the sum of human knowledge being what it is to-day specialization in some degree is inevitable. The danger is that the individual may achieve the special knowledge and skill at too great a price. It may not be possible for him to be expert in more than one sphere of learning, but I believe it is possible for him to do enough in the way of general education to guarantee the stimulation of wider interests, the interest in and understanding of departments of life and learning not especially his own; in other words, enough general education to enable a man to avoid being a fragmented person, and to make a reasonable approach to wholeness or

unity within himself. I believe that whole men will understand and get along better with other whole men, than fragmentary men, so to speak, will understand and get along with other fragmentary men. Do you see the point that I make?

If our education is fragmentary we do not achieve any wholeness or unity within ourselves. We overlap each other, so to speak, in the business of life and in our associations we have such a small area in common that we don't understand each other in any deep sense.

One thinks of the ancient story of the two deaf Englishmen riding in a tram-car: "This is Wembley." "No, I think it is Thursday." "So am I, let's stop and have a quick one." There is no meeting of minds at all, however pleasant the entirely fortuitous result of the conversation may have been.

By the way, I never use that word "fortuitous" without thinking of a personal experience. You know how small things that happen to you as a child remain printed on the memory for life? When I was walking down the street in Truro, N.S., (I was around thirteen or fourteen) with my father who was an agriculturist and genetecist, we met a beautiful and eminently desirable young lady. As we passed her my father looked at her and said to me, "The very happy result of a no doubt wholly fortuitous combination of ancestral units," — a new way of describing a blonde. Can you see how that would stick? That sentiment was something that even at an early age I was able to grasp and from which I hope I have not departed.

What I am getting at is this: the study of the Humanities is important to all men — doctors, lawyers, engineers, fathers — not merely because it makes possible certain types of elegant amusement, not because it may possibly add to the grace of one's social appearance, not because this provides ammunition with which to kill a dull Sunday evening; these things are useful and important but the study of the Humanities, it seems to me, is important because that study does good things to the mind, because it helps a man to avoid what I have called fragmentation. These subjects: Literature, History, Philosophy, the Arts, cross the boundary lines of the more rigidly defined areas of learning and skill; they get men together on common ground; they make possible a type of judgment we must bring to bear on national and international affairs.

I sometimes teach a class of English at my University in third year engineering and we were using a textbook the other day in which this point was neatly made. In close juxtaposition in the book were two pages. One was an article on migratory labour. It was something people contribute to an economic journal or quarterly or something of that sort defining migratory labour and breaking it down into two or three different classes — 360,000 of this type in the United States and 250,000 the year before, and so on.

I thought it was very good that on the next page was part of John Steinbeck's *Grapes of Wrath*, which is also on the subject of migratory

labour — the chapter describing the arrival of that pathetic family, the Joads, at an encampment in California where they hoped to find work.

It seemed to me that this was a little metaphore or allegory suggesting that if the people in government and governmental agencies who have to do with the regulation of migratory labour, etc., etc., etc., could bring to their task of preparing legislation only the kind of knowledge and information represented by the article on migratory labour, they would not do a correct and fine job, but if they have that, plus the kind of understanding given by the man who can translate the article on migratory labour into human terms that make you see the perplexities and problems, they will do a better job. In this kind of thing we are talking about here you don't have fragmentary or partial men who have not achieved wholeness and unity in themselves. I say that these two articles, coming together as they do, illustrate that point rather well.

So these studies help a man to achieve a kind of wholeness which makes him better able to understand and get along not only with other whole men but with those who have remained fragmentary. The fragmentary man dealing with the fragmentary man is like the story of the deaf Englishmen; their minds and spirits don't meet, or if they meet, they meet only partially and provoke half understanding.

This brings me to the end of what I wanted to say. I have found one or two aphorisms which show the danger of being incomplete, and I would just like to throw them at you:

George Eliot once wrote "Ignorance is not so damnable as humbug, but when it prescribes pills it may happen to do more harm". And I suspect that one of the things that keep us all from humbug is this brief conception of wholeness, oneness, and unity. The fragmentary man will run into the humbug of uniformity or only partial knowledge.

Dr. Sidney Smith, not our worthy President of the University of Toronto but the witty English clergyman of the nineteenth century, contributes the following: "Errors, to be dangerous, must have a great deal of truth mingled with them." I suspect that many doctors will admit that much of humanity's tragic story could be accounted for by the acceptance of the half truth. I should think that ought to be true in medical terms. Again I say I think this matter of the acceptance of half truths is in being half a man, in being fragmentary. And particularly in your profession is it necessary for you to determine to be a whole person and not a fragmentary one.

The next aphorism is this by George Santayana: "To be brief is almost a condition of being inspired." So after that I must stop.

But I'll throw one more at you as a final contribution to the accomplishment during your home-coming week of the knowledge and understanding and liking of which I have been speaking. I suggest that you remember during the balance of your days here Samuel Johnson of the eighteenth century who said appropriately to this occasion: "Whoever thinks of going to bed before twelve o'clock is a scoundrel." (applause).

SOME ASPECTS OF POST-GRADUATE TRAINING IN BRITAIN

ERIC ROGERS, M.D., '44.

A medical student's awareness of the importance of wisely planning his post-graduate training steadily increases as graduation approaches. Most students realize that this part of their education should be planned so that their first appointment will give the best possible chance of obtaining a more senior position the following year. The medical student who wishes to specialize after graduation faces a complex problem in planning further training.

If you are hoping to do most of your training in one of the larger teaching centres, little or nothing is gained if you take first appointment in the Podunk General Hospital, for example, mainly because the climate is warm, the golf course is close, and the salary is two hundred dollars a month. One should always be mindful that, wherever one interns and whatever type of medicine one plans to practise, the excellence of a post-graduate training depends largely upon one's own efforts.

This brief outline is not intended to cover all phases of interning. The ideas are based on the impressions of one person and as such are subject to personal idiosyncrasies and opportunities. Present difficulties in locating suitable post-graduate training in Canada and the United States may bring to the potential intern's mind the question, "What are things like in England?" Having recently spent a year at St. Mary's Hospital in London, I thought the following might be of help in answering that question.

Great Britain's National Health Act, which began to function in July, 1948, has already made a profound change in the availability of post-graduate training opportunities. Almost all hospitals are subject to government regulation under the Act. No matter how long a man interns, or what qualifications he obtains, unless a doctor enters practice with a hospital appointment he must do general practise. In the majority of communities this deprives him of the right to supervise any aspect of the patient's hospitalization.

There is increasing reluctance to enter general practice. This is due to factors which are non-existent in Canada. However, to understand the interne situation one must be aware of certain aspects of the situation. With the inauguration of the Act, the general practitioner's role in many instances has been reduced to that of a form signer or glorified first aid man. Many of the men to whom I spoke who had returned to do further training after being in practice were bitter about the increasingly unreasonable demands made on them and the ever decreasing esteem in which the general practitioner is held. It is significant that at the present time the British Medical Association is waging a vigourous campaign to have fees increased. This follows the survey report at the July 1950 BMA

meeting which revealed that 36.4% of doctors in Great Britain had a net annual income below $2200.

Since he cannot admit patients under his care to a hospital unless he is a member of the staff, the result is that the recently trained surgeon, orthopod or paediatrician does only general practice. No one will deny that too many specialists are being trained, but how would you devise a scheme to say who trained as what? It thus follows that each interne or resident seeks other internships or retains his appointment as long as possible, while he endeavours to get a hospital staff appointment. An applicant is not even considered, even in smaller non-teaching hospitals, unless he possesses the FRCP or FRCS. This retardation of the normal flow of trained men into practice has had the result that extremely able and well trained men are filling even the most junior positions on the interne staff. The Act allows liberal interne salaries ranging from about $900 to $3100 yearly, depending on seniority and qualifications. This enables the interne to obtain his training with much less financial hardship than is the case in this country. This factor, combined with the lower cost of living (which is slowly rising), allows the interne to remain in hospitals, and in search of suitable positions, much longer than his Canadian counterpart.

From this, it is obvious that unless one goes to Great Britain with an assured appointment, or under a Canadian university sponsorship, or with "pull," the chance of finding a worthwhile hospital position is almost *nil*.

The situation is much brighter for the post-graduate student with financial support. Many centres, London particularly, abound with well organized, reasonably priced condensed courses in all fields of medicine. These courses are supervised by recognized authorities with long teaching experience. This, in addition to the wealth of varied clinical material available, gives opportunities for clinical study which are seldom equalled on this side of the Atlantic. Such courses, to mention only a few, are available at the Royal College of Surgeons, Guy's Hospital, Brompton Chest Hospital, Middlesex Hospital, the London Hospital, and the Royal Infirmary, Edinburgh. Particulars concerning these can be found in current issues of the *Lancet* or *British Medical Journal*. Do not be misled by the number of advertisements for positions vacant. Hospitals are required by law to advertise when staff vacancies are to be filled. At present there is some conjecture on both sides of the Atlantic as to the effect of the National Health Act on the quality and quantity of post-graduate teaching. Most believe that to date there has been little change from pre-war standards.

In addition to these courses there are always available many short term (two weeks to three months) *locums* in most of the larger teaching hospitals. Your way is made easier by the fact that Canadians are always welcome. One must go to Great Britain to learn that her people are anything but reserved when it comes to hospitality.

Teaching methods and aspects accentuated in training differ slightly from those in either Canada or the United States. In Great Britain more stress is laid on anatomy and the clinical aspects of surgery and medicine than on varied laboratory results. Unless one is a very brilliant student, or has had considerable training, one should not expect to obtain the Fellowship of the Royal College of Surgeons, England, with less than two years' study in England, i.e. nine months for the primary and fifteen months for the final examination. Since Edinburgh has recently introduced the primary examination for the fellowship in surgery, many feel that the degree is as difficult to obtain as the English fellowship.

One factor seldom mentioned as a stimulus to study is the association with institutions linked with the great names in medicine and surgery. Actually seeing the haunts or works of John Hunter, Addison, Gray, Sampson Handley, Bright, Miles, and Lister, to name but a few, adds a stimulus and interest to study which varies in degree from student to student but which is ever present.

One is often asked to compare the excellence of English and Canadian surgery. This involves so many factors, both personal and general, that it is difficult to judge the entire situation accurately, fairly and impartially. From my experience it appeared that although the pre-operative laboratory investigation and aseptic technique are not stressed to the same degree in Great Britain as on this side of the Atlantic, the actual surgery done and the results which I saw personally frequently excelled much of what I had seen in either Canada or the United States.

Please remember that the above is only a broad outline of personal beliefs which I hope may be of some assistance to students or recent graduates in shaping plans for the future. November, 1950.

ABSTRACT

THE EARLY DIAGNOSIS OF BRONCHIAL CARCINOMA

T. PARKINSON

The Clinical Journal, 79: 231 Nov. '50.

In his article the author emphasizes the necessity for the early diagnosis of this disease if there is to be any hope for curative treatment. Even today in the average case there is a lag of five to seven months between the onset of symptoms and the diagnosis. During the past 50 years there has been a real increase in the incidence of bronchial carcinoma so that now it is probably the commonest type of cancer in males.

The disease does not present a uniform clinical picture, but the author has tried to discuss the common symptoms — cough, chest pain, dyspnoea, haemoptysis, the symptom-complex of pneumonia and the loss of weight. The usual signs associated with the disease are also discussed.

The physical signs of bronchial carcinoma are so diverse that they can simulate those of almost any other disease but Dr. Parkinson points out that in the early stages when the tumour is localized to the bronchial wall or remains in a discret mass in the lung periphery there are usually no physical signs at all.

Finally the author discusses the value of special investigations — radiology, bronchoscopy, examination of sputum and exploratory thoracotomy together with their limitations.

D. R. THORNER, '52.

STUDENT INTERNESHIP AT THE ONTARIO HOSPITAL, WOODSTOCK

ELIZABETH Q. HARRISON, B.A., '52.

The medical student who has completed the second year has learned a good deal of basic medical science. Although he has begun his clinical studies he has learned little which can be applied to the understanding of a patient's medical problems.

There are not a great many ways in which clinical experience can be acquired at this stage of the student's learning, but Provincial Mental Hospitals do accept, as summer internes, students who have completed their second or third medical year.

The Ontario Hospital at Woodstock is one of these. It lies less than a mile north of the city in spacious grounds covering several acres. The property includes farm land, dairy farm, kitchen and flower gardens, and a well-kept lawn spotted by a tennis court, a bowling green and a beautiful little six-hole golf course.

The hospital consists of two parts, the Epileptic Unit and the Tuberculosis Unit, under the same superintendent but otherwise separately staffed. The T.B. Unit cares for all Ontario Hospital patients who contract tuberculosis or are suspected of having done so, and for all tuberculosis patients in sanatoria who develop psychotic symptons. The Epileptic Unit cares for all Ontario Hospital patients over sixteen years of age who are epileptic, and for any other adults who require institutional treatment for epilepsy. As my interneship was in the Epileptic Unit, most of my remarks will be about that half of the hospital.

Treatment of epilepsy consists of, first using drugs to depress the abnormal electrocortical activity which culminates in epileptic seizures, and secondly insuring a regular daily routine to which an adequate, well-balanced diet, sufficient sleep and a satisfactory balance of work and recreation all contribute. The duties of the medical staff, then, consist chiefly of determining the dosage of anticonvulsant drugs necessary to keep each patient as free as possible of seizures, of assisting the capabilities, mental and physical, of each patient, of seeing that his days are as busy and happy as possible and finally, of caring for any intercurrent illnesses or infections he may suffer.

Now, where does the inexperienced medical student fit into this picture? Well, it is true he has to learn to do most things for there are very few things he has ever done before. But he learns to conduct medical examinations and by the end of the summer he is doing all the admission physicals. He takes a few histories; he questions patients to determine their mental status; and he prepares the papers for presenting the patients at conference and may even present patients himself.

He makes morning rounds with the doctors and thereby learns a great deal about common minor ailments. He sees the doctor treat

paronychial abscesses, boils and burns, and he learns to recognize the toxic symptoms of the anticonvulsant drugs. He listens to complaints and learns how to deal with them; if he still has trouble discriminating between legitimate complaints and the laments of the hypochondriac, at least he begins to recognize that to the latter, his problems are as real as though they were of organic origin.

The doctors are generous with their time and instruction. They teach the interne to do such special procedures as gastric lavage and spinal punctures, aspiration of superficial abscesses and application of surgical dressings and plaster casts.

From time to time the student is called upon to deal with emergencies: a series of epileptic seizures, a sudden high fever, a fracture, an acute abdomen, and, most common of all in this hospital for sufferers from the "falling sickness," many minor lacerations requiring sutures. He deals with emergencies as well as he can but there is always a doctor on call in case a situation arises which is too serious for him to handle.

The duties in the Epileptic Unit keep the interne busy but he is encouraged to spend time also in the T.B. Unit where there is more active treatment going on. Here he sees some minor surgery, and such routine treatments as pneumothorax, electroconvulsive therapy, and electroencephalography.

In the main building of the T.B. Unit a room has been equipped for post-mortems and, in a high percentage of deaths, autopsies are performed. Internes and doctors from both units attend these post-mortem examinations. All internes receive instruction and practice in reading x-ray films (chiefly chest films, of course,) and are at liberty to attend the regular conferences and the special neurological conferences which are conducted at intervals. The fine medical library of the hospital is housed in the main building of the T.B. Unit and is open for use by all interested personnel.

All major surgery for both units is done at the Woodstock General Hospital, and the internes usually accompany their patients to hospital and observe or (occasionally) are permitted to scrub for the operation. The surgeons are as sympathetic and kindly towards the internes as are the Ontario Hospital doctors and take considerable trouble to permit the internes to see what is being done, and to teach and explain as they work.

Tuberculin positive internes are preferred in the T.B. Unit, but negativity to the test neither excludes students from visiting and observing, nor disqualifies them if they wish to work there. Naturally, careful precautions are taken by everyone against infection.

Internes may live in the hospital, and comfortable, roomy quarters are provided in the Epileptic Unit. Night duty is not arduous, and very late calls in the Epileptic Unit seldom occur. The patients in the T.B. Unit, since they are more acutely ill, more frequently require medical

attention at night but duty nights there are widely spaced because the number of staff doctors is larger.

Recreational facilities on the grounds include the tennis court and golf course mentioned before. A nearby swimming pool and picnic spots may be utilized, and downtown Woodstock is within fairly easy walking distance although a bus offers an easier means of transportation.

The valuable experience, combined with the pleasant surroundings, and the refreshing friendliness and co-operation of the entire staff make this hospital one which deserves high recommendation to those students who are considering student interneships.

ABSTRACT: ADRENAL NEUROBLASTOMA

R. WALLACE BOYD

Canad. M.A.J., 63:153-7, 1950.

This article deals with six cases of adrenal neuroblastoma, their symptomatology and clinical and X-ray findings, their treatment, and clinical course.

Neoplasms of the adrenal occur without a palpable tumour, in which there are widespread, confusing clinical and roentgen manifestations. Even though small, the tumour of an adrenal gland may be recognized by meticulous diagnostic methods and certain adrenal growths may be satisfactorily removed or favourably influenced by irradiation.

Dr. Boyd discusses a single type of adrenal tumour, neuroblastoma. While neuroblastoma is not a common tumour, it occurs more frequently than is generally believed. Less than 450 cases have been reported, although undoubtedly many more have occurred under other diagnosis. These six cases passed through the Vancouver General Hospital between 1945-1948, and ranged from fourteen months to five years in age.

The symptomatology is variable because the disease is so deep-seated and has such an obscure onset. Non-specific manifestations of early anaemia, fever and toxaemia are common in all cases. The earliest symptom in one child was a "black eye"; pain in the hip-joints, due to early metastases to the upper femora of another child, was first diagnosed as rheumatic fever. All patients presented a large, palpable, right or left upper abdominable mass, at or soon after admission to hospital. Radiological studies were a valuable aid to clinical examinations in determining the intra-abdominal relationship or origin of the tumours.

Roentgen therapy was used on five of the six cases. The tumours and skull metastases were irradiated. In three cases the abdominal masses disappeared completely four to six weeks following the onset of treatment. There was no effect on the metastases however, and the general condition of the patients was only temporarily improved. The highly malignant nature of the disease is illustrated by the fact that none of the cases lived longer than eight months from the onset of the first symptom.

Microscopically the tumour shows neurofibrils arranged in long bundles or little rounded masses, along which the cells are grouped into a rosette form. These rosettes are characteristic of neuroblastoma.

DONALD J. MUNN, '52.

Books in Review

DEMENTIA PRAECOX OR THE GROUP OF SCHIZOPHRENIAS

EUGEN BLEULER, (TRANSLATED BY JOSEPH ZINKIN),
INTERNATIONAL UNIVERSITIES PRESS, NEW YORK, 1950. 548 pp.

Eugen Bleuler has been described as one of the "Greats" of Twentieth Century psychiatry.

This volume is Joseph Zinkin's English translation from the original German of Bleuler's epoch-making monograph which appeared in 1911 as one volume of Aschaffenburg's *Handbuch der Psychiatrie.*

The disease is discussed in all of its many aspects. Case histories are used efficiently. The fundamental and accessory symptomatology is discussed. The multitude of sub-groups is classified. The course, diagnosis, prognosis and treatment are effectively considered. A discussion of the theory of the disease aids in understanding it.

A great work, unfortunately beyond the scope of the undergraduate, it would be of great value both to the psychiatrist and to the practitioner interested in psychiatry. —E. J. MORRIS, '52.

NEUROLOGICAL ANATOMY IN RELATION TO CLINICAL MEDICINE

A. BRODAL, OXFORD PRESS, NEW YORK, 1948.
496 pp., illus. 80, plates 14.

This book was written by the Prosector of Anatomy at the University of Oslo with the avowed purpose of correlating academic neuroanatomy with the clinical findings of neurology. Originally published in Norwegian in 1943, it has now been translated into English and brought up to date.

The scope of this study includes the whole human nervous system, both central and peripheral. The main emphasis is upon the clinical aspects of the subject, with many details included. The anatomical information is principally practical, with little space devoted either to cytoarchitecture or to relations. The data appears well authenticated since it is supported extensively by experimental evidence from pathological, physiological and anatomic studies.

The value of this book as a summary of, and a guide to literature in neurology and anatomy is indicated by the large thirty-page bibliography. Not only will anatomists use this text for the clinical aspects of neurology, but clinicians will find in it a review of pertinent neuro-anatomy.
—G. E. CARROLL, '53.

OPHTHALMIC MEDICINE

JAMES H. DOGGART, J. AND A. CHURCHILL LTD., LONDON, 1949.
329 pp., illus. 87, plates 28.

In the preface the author states that his main object is to emphasize how intimately the eye is linked not only with adjacent structures but with remote parts of the body. It is clear from the content that this purpose has been accomplished. The result is a volume covering fairly completely, if briefly, the field of ophthalmic medicine.

The approach to disease as reflected in the eyes, from the point of view of the ophthamologist, is a refreshing one. There are ample plates to clarify and illustrate the conditions presented.

It is recommended that this book be read along with a standard medicine text and used as a reference for enlargement of the ophthalmic detail. —T. MCLARTY, '52.

REGIONAL ILEITIS

BURRILL B. CROHN, GRUNE & STRATTON, NEW YORK, 1949.
229 pp., illus. 74.

Dr. Crohn, an eminent gastroenterologist at the Mount Sinai Hospital, has included in his book a comprehensive study of his experience with regional ileitis, the disease which he recognized and described as a distinct entity in 1932. This study is based on observations from about three hundred cases of segmental enteritis with which he has worked in the past eighteen years.

In the publication he includes a discussion of the condition from various approaches: aetiological theories, pathology, course of the disease with associated clinical features and recommendations for treatment. In many cases descriptions are given with innumerable X-ray plates and diagrams and a differential diagnosis of the condition (especially from appendicitis) all of which should be of very practical interest to the general practitioner. —L. M. BECKHAM, '52.

HARVEY CUSHING

ELIZABETH H. THOMSON, HENRY SCHUMAN, NEW YORK, 1950.
347 pp., illus. 13, plates 12.

A large and detailed volume on the life of Cushing, by John Fulton, was already in existence when Miss Thomson undertook this biography. She saw the need of a more concise account with wider appeal which would be especially attractive to students of medicine. This book very amply fulfills that need.

Harvey Cushing's life was rich and varied. These qualities could only have been captured by a writer of her calibre. In a skillfully woven, novel-like account, the story of Harvey Cushing, surgeon, author and artist, is sketched. The medical reader will find this record of Cushing's accomplishments a ready source of inspiration. —G. W. BRUNER, '53.

FREUD: DICTIONARY OF PSYCHOANALYSIS

EDITED BY NANDOR FODOR AND FRANK GAYNOR

THE PHILOSOPHICAL LIBRARY INC., NEW YORK, 1950. 208 pp.

This is a reference dictionary on psychoanalysis, edited by two workers who are well qualified for their task. The work is quite complete and presents concise and exact definitions of most of the basic terms used in psychoanalysis. Most of the book is comprised of direct quotations from the works of Dr. Freud and for this information the editors have drawn upon the Founder's books, papers and letters.

The dictionary should prove useful to the psychologist, psychiatrist, student and even to the interested layman. The editors have made a special effort to eliminate ambiguities and nebulous terms.

As Theodor Reik points out in the preface, the work undoubtedly contains the imperfections to be found in any scientific endeavour of this type. The book strives, however, to direct the psychoanalytic concepts back to their original forms and so to contradict the many distortions, misrepresentations and false interpretations which the years have inflicted upon them.

—F. N. LEWIS, '52.

THE MASK OF SANITY

HARVEY CLECKLEY, THE C. V. MOSBY CO., ST. LOUIS, 1950, 569 pp.

This is the second edition of Cleckly's well-known book written in 1941. The author has completely rewritten his earlier work on adult male psychopaths hospitalized in a closed institution to include psychopaths from all walks of life, male and female, young and old.

The main types of psychopaths are outlined and discussed with reference to actual case histories. The author impresses on the reader the large number of psychopaths found in every day life, people who cause untold misery to themselves and others, people whose successful treatment poses as yet an unsolved problem in the great majority of cases. The position of the psychopath on the borderline between psychoneurosis and the normal is stressed.

As the author states, his book is an attempt to clarify some issues about the so-called psychopathic personality and treatment is only referred to in its broadest principles.

This is a well-written book of value to both medical men and the thinking public, on a subject brought into prominence within the last decade.

—W. P. MCINNIS, '52.

ABSTRACT: THE RICE DIET IN THE TREATMENT OF HYPERTENSION

By a Committee Including
D. R. Cameron, D. M. Dunlop
et al. — *Lancet*, II:509, 1950.

In 1944 Kempner reported the result of a rice diet given to a series of patients suffering from renal and hypertensive vascular disease. In further papers he reported impressive improvement, not only in the blood pressure level, but also in the size, eye-ground changes and E.C.G. tracings. His results have been confirmed by some workers and refuted by others.

A committee was formed at the request of the Medical Research Council to make a clincial trial of the rice diet. Kempner's diet was followed closely, and consisted of rice, fruit, fruit juice and sugar or syrup, with added vitamins. The rice was boiled in water without salt, milk or fat.

The diet was continued for an average of 41 days. In the majority of patients the blood pressure fell, the average fall being 55/26 mm. Hg. Of 33 patients with hypertension 25 obtained relief. Headaches, present in 26, disappeared in all but 4, often within a few days of starting the diet.

The blood pressure remained low as long as the rice diet was continued and rose rapidly on changing to an ordinary low sodium diet. In 13 of the patients in whom blood pressure fell, radiographs suggested a reduction in heart size. Improvement in E.C.G. tracings and in the eyegrounds occured in only a few cases.

This short-term trial confirmed the claims of Kempner. Most workers believe the success of the diet due to the extremely low sodium intake. In several of the cases the addition of NaCl led to a rise in blood pressure. Impairment of renal function and uraemia are dangers of the diet.

It is believed that the Kempner rice diet can produce a considerable lowering of blood pressure in about 70% of patients but due to its unpalatability, it is extremely difficult for patients to continue it for more than two months. As soon as the NaCl intake is increased even slightly, the blood pressure is likely to rise again.—G. Garwood, '53.

ABSTRACT: MECKEL'S DIVERTICULUM AS THE SOURCE OF MASSIVE INTERNAL HAEMORRHAGE

Sanderson and Barrett
Post-Grad. M.J. 8:214, 1950.

The article deals briefly with the five pathological varieties of Meckel's diverticulum following Greenblatt's classification, viz: (i) the peptic group with gastric mucosa in which haemorrhage and perforation may occur; (ii) the inflammatory group of diverticula where acute inflammatory changes may cause perforation and/or gangrene; (iii) the obstructive group causing intestinal obstruction via adhesions, bands, intussusception or volvulus; (iv) the tumour group of benign, malignant or cystic tumours and (v) the umbilical group, including faecal fistula from a patent vitelline duct, or faecal cysts in the closed duct.

The authors have presented five cases of massive haemorrhage into the lower segment of the ileum which were diagnosed and surgically resected as Meckel's diverticulum of the peptic group. All the cases showed ulceration of the gastric mucosa especially at the junction of the ileum and the diverticulum. These ulcers closely resemble the ulcers at the margin of a gastroenterostomy.

It is stressed in the conclusion that frank haemorrhage from a diverticulum most often occurs prior to 20 years of age and especially in infancy, and has a predilection for males in the ratio of two to one. A rapidly falling haemoglobin, tarry stools, occasional haematemesis, and even syncope, in a child, form the basis of diagnosing a makes surgical intervention, preceded by adequate pre-operative build-up, an haemorrhaging diverticulum, and urgent necessity.

—John R. Augustine, '52.

"Clinical diagnosis is an art and the mastery of an art has no end; you can always be a better diagnostician."—Clendening.

"In medicine, sins of commission are mortal, sins of omission venial."—Tronchin.

"It is steadily forgotten that health is a diathesis, as much as is scrofula or syphilis and that each of these is a mode of growth."
—Allbutt.

"Brevity in writing is the best insurance for its perusal."
—Virchow.

"Disease is from of old and nothing about it has changed. It is we who change as we learn to recognize what was formerly imperceptible."—Charcot.

"True science teaches us to doubt and in ignorance to refrain."
—Claude Bernard.

"The duty of science is not to attack the objects of belief but to stake out the limits of the knowable and to centre consciousness within them."—Virchow.