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Some Unusual Conditions Which May Produce Acute Abdominal Symptoms

There are so many conditions which must be considered in the differential diagnosis of cases with acute abdominal symptoms that any additions to the list will not be looked upon with much favour. However, unless one is aware of them they are unlikely to be considered at all. Hence the following brief outline of four conditions, (three of which have been noted for the first time within the past few years), which may present on occasion with acute abdominal symptoms, may be helpful.

The fourth condition, porphyria, has been recognized as a clinical entity for some considerable time now, but one still sees cases of this condition which have been subjected to an unnecessary laparotomy on account of the quite severe abdominal symptoms of thich they complain. In these cases, however, the objective findings on abdominal examination do not conform with the severity of the symptomatology.

The Carcinoid Syndrome

E. G. Vaughan, M.D.

The discovery of the very fascinating carcinoid syndrome by Thorson et al in 1954 has stimulated much interest. To date, some 50 cases have been reported and investigations have solved some of the mysteries of the previously ill-understood carcinoid tumour.

Known facts about the syndrome extracted from the growing literature are herein described under four headings.

A. THE TUMOUR

Kulchitsky cells are normally present in the crypts of Lieberkohn of the gastro-intestinal tract. They are also called chromaffin or argentaffin cells because of their affinity for silver stains. These cells give rise to small, round, firm, yellowish-white tumours called carcinoids. These tumours are frequently multiple in origin and are found at various sites in the gastro-intestinal tract.

Two-thirds of all carcinoids occur in the appendix.

Two-thirds of the remainder occur in the small bowel of middle-aged persons.

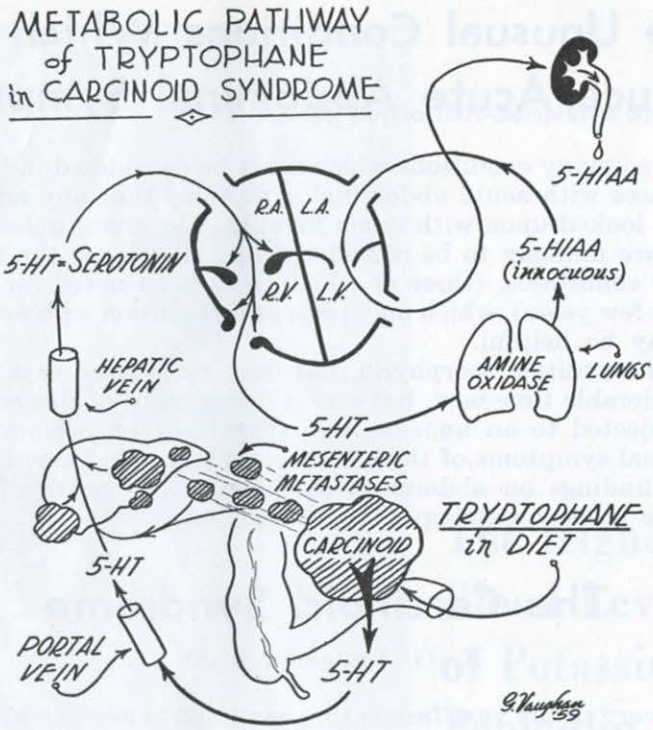
One per cent of appendiceal carcinoids metastasize.

Three-quarters of small bowel carcinoids metastasize.

The fact that in the first group the tumour obstructs the appendix and thereby produces symptoms leading to its early removal may well account for this low rate of metastases.

Microscopically the tumour consists of strands and irregular masses of spheroidal cells with dark nuclei. These cell masses are supported by a scant amount of collagen stroma.

K-cells, both naturally occurring and in carcinoid tumours, secrete 5-hydroxytryptamine (5-HT) which is also called SEROTONIN. This is derived from the metabolism of tryptophane, an amino acid whose metabolic pathway in the carcinoid syndrome is depicted in the accompanying diagram.



The reaction within the K-cells whereby tryptophane becomes 5-HT is as follows:

TRYPTOPHANE

↓ (hydroxylase)

5 - HYDROXYTRYPTOPHANE

↓ (decarboxylase)

5 - HYDROXYTRYPTAMINE = SEROTONIN

Normally only 1% of ingested tryptophane is used in the production of serotonin; the rest going to form protein and Vit B_5 or Niacin. In the carcinoid syndrome 60% of tryptophane becomes serotonin. Therefore one might expect deficiencies of protein and Niacin in patients with the syndrome.

Pharmacologically, serotonin causes smooth muscle contraction. In the carcinoid syndrome this effect reaches pathologic proportions because serotonin is present in the blood in greatly increased amounts. It is carried in the blood wholly within platelets and on passing through lung tissue undergoes the last stage of its metabolism. In lung tissue there exists an enzyme called amine oxidase which renders most of the 5-HT innocuous by converting it to 5-hydroxyindoleacetic acid (5-HIAA). This is excreted in the urine and is recoverable by a simple quantitative bio-chemical test which makes it a useful diagnostic aid.

B. THE SYNDROME:

The symptoms and signs of the syndrome are confined mainly to the abdomen, skin, lungs and heart.

Abdominal pain is at first mild, crampy and intermittent. With increasing severity it eventually presents a clinical picture of subacute intestinal obstruction and is accompanied by watery diarrhoea. The liver may be palpable and nodular due to metastatic growths. In advanced cases, ascites may become manifest.

Patchy crimson flushing of the skin, beginning in the face and neck, brought on by physical exertion or emotional stress is an outstanding phenomenon. It occurs in many patients and is confined to this area in some while in others it spreads to involve a greater surrounding area. Accompanied by a feeling of warmth and tingling, the flush is usually followed by a peculiar cyanosis. In advanced cases, brownish scaly thickening of the skin resembling pellagra and localized to the dorsum of the forearms has been described.

Dyspnoea and bronchospastic stridor resembling asthma occur in about one-half of the cases. Some patients have been treated for asthma for prolonged periods prior to correct diagnosis. As ascites develops in late cases, so pleural effusion may occur.

Heart murmurs due to pulmonary stenosis and tricuspid regurgitation occur in the later stages of the disease. E. K. G. evidence of right heart strain then appears.

C. Relation of Symptoms to Lesions:

Laparotomy reveals a small bowel tumour usually in the terminal ileum. Depending on the stage of the disease there will be metastatic nodules in the mesentery, liver, and other organs, e.g., pancreas and ovaries, etc. Invasion of the tumour in the wall and narrowing of the lumen of the gut is responsible for the subacute obstruction.

Autopsy performed on advanced cases has revealed fusion and thickening of the cusps of the pulmonary and tricuspid valves accompanied by right sided myocardial hypertrophy. Dilatation of the right heart and tricuspid valve ring have been noted. These findings explain the cardiac murmurs and E.K.G. abnormality. Serotonin has been recovered in much greater concentration from blood entering the right heart than from blood returning to the left heart. This is due to the conversion of 5-HT to 5-HIAA in the lungs. The causes of valvular lesions and the reasons for localization of these changes to the right side of the heart are held to be, (a) the direct action of prolonged high concentrations of serotonin in the right heart chambers, and (b) the increased right ventricular pressure resulting from pulmonary vasoconstriction.

The cutaneous vascular phenomena, the asthmatic symptoms and abdominal cramps and diarrhoea are explained on the basis of the potent spastic effect of 5-HT on smooth muscle of cutaneous arterioles, bronchi, and gut.

The pellagra-like skin changes noted in some cases are presumed to be due to niacin deficiency referred to earlier.

Tissue wasting and weight loss are prominent features of advanced cases. Electrophoretic studies in these individuals show hypoalbuminemia. This is conceivably due to diversion of tryptophane away from protein synthesis.

Arthritic symptoms which have been observed in several patients suggest the changes noted in the heart valves might actually be part of a more generalized connective tissue disorder.

D. **Practical Application of Known Facts:**

The presence of some or all of the described phenomena might suggest the presence of a carcinoid tumour. Urinary estimations of 5-HIAA might aid in diagnosis or serve as a follow-up check on patients who have had an appendiceal carcinoid removed but in whom other such tumours were not looked for, or were not found.

Removal of the primary tumour will afford relief of obstructive symptoms and may result in improvement of prognosis.

Increased amounts of tryptophane in the diet have given relief of pellagra-like skin changes.

Carcinoid tumours are notoriously multiple; if one is found, others should be sought.

Summary:

The Carcinoid Syndrome has been described. The patho-physiology and clinical manifestations have been correlated. The practical importance of the syndrome to the practitioner has been presented.

Ulcerogenic Tumour of Pancreas

(Zollinger-Ellison Syndrome)

R. O'Driscoll, M.D.

This recently described syndrome consists of a triad of findings. The first is a fulminating peptic ulcer disposition, especially when the upper jejunum is primarily involved or when secondary gastrojejunal ulceration follows surgical treatment. Despite adequate medical, surgical and even radiation therapy of the remaining gastric mucosa, the tendency to recurrent ulceration persists. The second is gastric hypersecretion and hyperacidity. This is shown by the twelve hour nocturnal gastric secretion and persists as long as any secreting gastric mucosa is retained. Bon-Beta islet cell tumour of the pancreas completes the triad.

Males seem to have a slight predominance in numbers and age can vary from the second to the eighth decade, onset of symptoms being commonest in the fourth and fifth decades. Twelve hour nocturnal gastric secretion volumes exceed 1,000 mls. in about 85% of cases and may approach 3,000 mls. as opposed to a normal upper limit of 800 mls. The total free hydrochloric acid secretion of 18 mEq. for the same period is usually greatly exceeded with most figures over 100 and some as high as 300 mEq. These levels may be found following all surgical procedures except total gastrectomy. The patient may present with only one ulcer or they may be multiple; they can be found anywhere from the oesphagus to the jejunum, and reeurrence following surgery may involve all the previously mentioned areas. The tumour may be single or multiple and is usually situated in the body or tail of the pancreas. Alpha, gamma, and delta cells have been identified in various tumours, the name non-beta cells being used to distinguish it from the functioning islet cell tumour causing hypoglycemia. About two-thirds of them are considered malignant and metastasize to liver, peripancreatic lymph nodes, duodenum and general

peritoneal cavity. Function in these metastases depends probably on the degree of differentiation. Diffuse hyperplasia of islet cells tissue seems also to cause the syndrome.

A high percentage of cases have associated endocrine tumours such as adenomata of the pituitary and parathyroid, adrenal cortical tumours and medullary hyperplasia. Symptoms and signs of these latter lesions may overlie the syndrome itself.

The clinical course of early cases is usually stormy, ending in death. They present with peptic ulceration accompanied by hypersecretion and hyperacidity. Multiple procedures for recurrences usually leave some residual gastric fundus which continues to secrete. A total gastrectomy has saved some cases but most die of haemorrhage, perforations and debility.

The etiology is still not definitely proven. Surgery may remove both gastric and cephalic phases of secretion without improvement, while the experimental evidence tends to exclude the functoning beta-cell tumours with hypoglycemia as a cause. Present thinking implicates glucagon, a protein, and insulin antagonist, which is present in commercial insulin, and is also secreted from the pancreatic islets. Its specific site of production within the islets is not known.

The suggested principles of diagnosis and treatment include:

(1) Hypersecretion and hyperacidity in ulcer patients, especially if ulcers are multiple or in bizarre locations, should raise the possibility of pancreatic tumour or hyperplasia.

(2) Recurrent ulcers, especially if multiple or in bizarre locations, should make one alert.

(3) Originally it was felt that a definitely identified tumour should be resected and a conservative gastric resection done. The frequency of multiple tumours and the possibility of metastases have tended to produce recurrent difficulty.

(4) Total gastrectomy therefore should probably be done following the surgical verification of such a tumour of the pancreas as well as removing the tail possibly together with the body.

(5) If ulceration follows previous surgery, carefully examine the pancreas for a tumour and if necessary do a hemi-pancreatectomy for verification. Opinion is divided as to whether a total gastrectomy should follow positive pancreatic findings or whether the remaining pancreatic tissue should be allowed to prove itself free of tumour or diffuse hyperplasia.

Peutz - Jeghers Syndrome

J. H. MacLeod, M.D.

This syndrome consists of a familial association of multiple adenomata of the gastro-intestinal tract and a melanin pigmentation of the oral mucosa, lips and face, hands and feet.

The disease has a definite familial tendency due to transmission of a dominant gene which is carried by both males and females and it has an equal incidence in males and females.

The pigmentation is present at birth and is due to deposits of melanin. It consists of dark brown discrete spots of pin head size particularly around the

mouth and in a butterfly pattern below the eyes and over the bridge of the nose. Pigmentation of the oral mucosa is consistent and is essential to diagnosis. It has also been noted on the fingers and toes.

The polypi may be scattered throughout the whole length of the gastrointestinal tract in contrast with familial polyposis which involves the large bowel only. The term polyp is a poor one since a great number of the lesions are sessile. Microscopically they are adenomas. The small bowel is involved in all cases, colon and rectum in over half the cases and the stomach less frequently. Symptoms of polyposis are:

(1) Symptoms of obstruction due to recurrent and frequent intussusception. This is the most frequent manifestation.
(2) Bleeding which may be minimal and occult leading to anaemia, or overt with profuse haemorrhage.
(3) Symptoms produced by local irritability.

Onset of symptoms is usually between 10 and 30 years of age. X-ray diagnosis is often difficult particularly in regard to the small bowel so that pigmentation is important in diagnosis. A negative X-ray does not exclude polyposis especially of the small intestine.

Prognosis is generally good although in cases characterized by recurrent episodes of intussusception, there is not infrequently early death or invalidism. Malignant degeneration has occurred in twenty-four of the cases quoted in the literature, most in the small intestine, the rest in the colon or rectum.

Treatment:

Most authors feel that no treatment is indicated until the need is determined by symptoms, except in the case of polyps of the sigmoid which are accessible to sigmoidoscopic removal. In other words there should be continuous supervision with periodic X-ray examination of the colon since polyps can grow here for a long time before symptoms occur. Laparotomy is reserved for the acute complications of small bowel polyps, the larger polyps being removed by enterotomy or resection. However, Bailey in 1957 advised more aggressive prophylactic surgery in order to avoid the later malignant degeneration and compares this with familial polyposis of the colon in which this treatment is indicated. If the colon is involved, he advises segmental resection; if, however, there is diffuse involvement of the small bowel, no prophylactic surgery can of course be undertaken.

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Acute Porphyria

J. H. MacLeod, M.D.

This condition is one of a group of diseases, in which, because of an inborn error of porphyrin metabolism, there is increased urinary excretion of uroporphyrin. It is the most common of the group although not a common

condition, but it is frequently overlooked. It is twice as common in the male as in the female and the usual age of onset is between 30 and 50 years. It has a familial incidence, being transmitted by a dominant gene.

It is characterized by intermittent attacks. The signs and symptoms are either nervous or abdominal or both. The nervous symptoms are varied and may be central, peripheral or autonomic. There may be neuroses or psychoses convulsions or involvement of cranial nerves with optic atrophy, dysphagia or hoarseness. There may be severe pain and weakness of one or a group of muscles leading to paralysis which may be patchy or may consist of a quadriplegia. The **abdominal symptoms** consist usually of pain which may be severe and may be generalized or localized; there is however, no rigidity or rebound pain. The pain may persist for several days and is considered to be due to segmental spasm of various parts of the small intestine. Distension may be present and marked constipation is a characteristic feature.

This condition is often undiagnosed and many patients have undergone laparotomy because of an error in diagnosis. This condition should be considered in the presence of any obscure nervous disturbance such as a peripheral neuritis or flaccid paralysis or any unexplained abdominal pain. The diagnosis is established by urinalysis. The urine is usually dark during the acute attack but if not, it will become dark on standing for a few hours in approximately 70% of cases. This is due to oxidization of the uroporphyrin. Most of the remainder show a positive test for porphobilinogen. This test is quite simple, being performed by the addition of equal parts of Ehrlich's Reagent, chloroform and urine.

The prognosis is poor, the mortality rate in the acute attack being variously reported as 50 - 90%. It is particularly poor if there are neurological symptoms, but if abdominal symptoms alone are present prognosis is much better; neurological symptoms, however, may begin at any time. It should be remembered that, since most mild cases are missed, the prognosis is probably better than is realized.

There is no treatment of any proven value. All authors advocate general supportive treatment with the avoidance of alcohol and barbiturates which may precipitate or intensify an acute attack. It is stated that sulfonamides and opiates may also do so. Beyond this opinions are divided. Spontaneous remissions render evaluation of treatment difficult. Numerous treatments have been reported beneficial by some and of no value by others. These include vitamins, liver, intravenous protein, A.C.T.H., intravenous calcium and most recently chlorpromazine.

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Prevention of Tetanus

E. A. Nugent, F.R.C.S.(C)

With the advent of summer, the number of patients presenting with apparently trivial wounds increases rapidly, and one is confronted daily with the practical aspects of the prevention of tetanus. Unfortunately, this frequently encountered and apparently simple matter has become quite complex in the past few years, and it is hoped that a brief review will be of value to the busy general practitioner.

The danger of tetanus is greatest when wounds are contaminated with highly fertilized soil which is the most frequent source of the organism. Deep puncture wounds, and wounds with much necrotic tissue offer anaerobic conditions suitable for growth. However, the possibility of tetanus exists with every wound; and with this in mind, a decision regarding the advisability of prophylactic measures should be made in every case.

PROPHYLAXIS:

A. Local Treatment of the Injury:

It has been noted that tetanus is often associated with suppuration resulting from injuries which have been neglected. The general surgical principles with respect to wound care apply equally well to the prevention of pyogenic infection and tetanus. Thorough cleansing minimizes contamination; debridement of devitalized tissue and ample drainage prevent the establishment of an anaerobic environment.

B. Immunity:

(1) If absolutely certain that complete toxoid immunization has been given, with a booster dose within five years, then tetanus toxoid should be administered.

If very massive contamination is present, the incubation period may be as short as two days. Toxoid alone will not have time to revive antitoxin production, so antitoxin should be given as well to cover this initial period. (Antitoxin will be neutralized and ineffective if given in the same syringe with the toxoid).

(2) If — the patient has had no toxoid
— or an inadequate course
— or more than five years have elapsed since the last booster dose
then antitoxin should be given.

This leads to the

PROBLEMS OF PROPHYLAXIS:

The foreign protein in the antitoxin causes allergic reactions; of every two hundred patients so treated five may be expected to have local reactions of varying degrees of severity, and five to develop the delayed reaction of serum sickness. Sporadic deaths have been reported. Attempts to avoid these untoward sequelae of antitoxin have been based on efforts to detect probable reactors, by —

— enquiry concerning allergy, reactions to previous injections of horse serum, etc.,

— a skin test with 0.1 c.c. of undiluted antitoxin injected intracutaneously. Unfortunately, such a test dose has itself caused fatal anaphylactic shock, and the test has not been of value in determining which cases will have the delayed serum sickness reaction. Despite these objections, it is thought that these measures should always be taken prior to the administration of antitoxin. If an allergic reaction is anticipated, the need for prophylaxis should be carefully reviewed, and if it is truly necessary, antitoxin given in one of the following ways —

— in divided doses
— in divided doses with an antihistamine.
— as antitoxin made from hyperimmune human serum rather than horse serum.

There has been a tendency of late to elect to run the risk of tetanus and not use antitoxin at all under these circumstances. If prophylaxis is indicated by the nature of the injury, this approach has rather obvious medico-legal implications.

The only other means of avoiding antitoxin presently available is based on widespread immunization with toxoid. Allergic reactions to toxoid are extremely rare, and a recall dose at the time of injury curtails the need for antitoxin administration. There is ample evidence of the efficacy of this approach in the experience of the Armed Forces, and civilian groups such as police and fire departments. Responsibility in this regard has been assumed by public health departments for school children, but large segments of the present adult population are not immunized.

By immunizing selected patients in this group and by giving recall doses of toxoid to the children, one can virtually eliminate the problems concerned with tetanus antitoxin in one's practice.

However, if this is done, it is essential that accurate records be kept, and the patients be informed and given cards with the relevant data, so that at time of risk no doubt exists as to their immune status.

The Frozen Section, The Surgeon and The Pathologist

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To the surgeon, a frozen section can be a source of comfort, providing an escape from a therapeutic dilemma; or a source of irritation, compounding his difficultues and occasioning bitter regret. Which of these antitheses prevails, depends upon the accuracy of the pathologist's diagnosis, and the reliance the surgeon places upon it, to the exclusion of his clinical judgment. The exact ratio between correct and incorrect diagnoses, made in the operating suite, is difficult to establish in the absence of statistical data, because of the overtones of recrimination which follow in the wake of misdiagnoses and their consequent mistreatments. One mistaken diagnosis is more apt to sway a surgeon's evaluation of all frozen sections than are ten correct diagnoses so made.

One of the purposes of this paper is to review the literature on frozen sections in an attempt to evaluate what the surgeon can reasonably expect from the pathologist in reply to the question, "Quickly, what is it?" The other purpose is to present a statistical analysis of one hundred consecutive frozen sections performed in the Victoria General Hospital between July 1958 and January 1959. From this review, it is hoped that the surgeon will gain a statistical impression of the effectiveness of frozen section diagnosis as performed in the Victoria General Hospital at the present time, will be able to appreciate the difficulties under which his colleague, the pathologist, is laboring, and will be able to forgive the pathologists' rare mistakes.

The technique of preparing a diagnostic frozen section is admirably described by Dockerty,[2] a name of some note at Dalhousie. A careful reading of this article is rewarding, for it gives one an insight into the intricacies of this technique and underlines the pathologists' pleas for adequate technical facilities. It also shows that familiarity with the procedure makes for greater reproductibility of results and that diagnostic brilliance can only be expected from exact methodology. The technical difficulties of preparing adequate microscopic tissue sections and of interpreting the appearances of vitally stained tissues are pointed out. It would appear that, ideally, the procedure should be carried out by one technician, especially trained in the preparation of frozen sections; and interpreted by one pathologist, who has had sufficient experience to familiarize himself with the unfamiliar appearances of vitally stained frozen tissues as compared with ordinary formalin fixed, paraffin blocked, haematoxylin and eosin stained slides. A very adequate bibliography of staining techniques, together with a description of a new stain for frozen section work, is contained in an article by Esekelund[3].

A review of the only other papers found, shows the high degree of accuracy which can be obtained by this technique, providing one pathologist or group of pathologists, works with good technical assistants and facilities, and the full co-operation of their surgical colleagues on a sufficient volume of material. H. H .Pitts et al[5],[6] and Sjolin[7] show that an accuracy of 96-98% is possible, but

that an error of up to 10% is acceptable. The series quoted are not representative of the work of a large general hospital. Pitts' project was a large one, undertaken by a research team intent upon reviewing a large group of tissues. They did frozen sections of a large volume of surgical material upon which the surgeon does not usually request a decision. For this reason, the statistics they present are not strictly applicable to the situation here, in which the only tissues presented for analysis are from cases on which the surgeon feels he cannot make a therapeutic decision without the pathologist's opinion. Sjolin's series is predominantly of one type of tissue (lung and bronchus), since he was reporting from a Pulmonary Resection centre in Denmark. The only reported series reviewed which is applicable to a general surgical service is the one by Ackerman and Ramirez,[1] reporting on 1269 consecutive frozen sections. Their article is highly recommended reading for anyone interested in the subject, not only because of their extensive esperience, but also because they review their material by breaking it down into organ groups, pointing out the pit-falls of diagnosis in each group and illustrating their points by reference to case records. The micro photographs show remarkable tissue and cellular detail. If their routine frozen sections approach the clarity of their illustrations, it is not surprising that they report an overall accuracy of 98%. The article concludes with an extensive bibliography.

Pitts et al point out that an accurate gross diagnosis is made in approximately seventy five per cent of all cases and only in approximately sixty per cent of all malignancies. These figures compare with the minimum acceptable rate of at least ninety per cent accuracy provided by frozen section. If the exact accuracy of the frozen section techniques of his hospital's pathology section is known to the surgeon, the figures quoted above provide a useful yardstick with which to judge his own clinical accuracy, as well as that of his pathologist.

Two hypotheses appear tenable from an analysis of the publications reviewed:

(1) Some tissues are impossible to diagnose, with certainty, from frozen sections, and a pathologist, if he is honest with himself, will occasionally refuse to make a definitive diagnosis, before he has examined a formalin fixed, paraffin blocked, H & E stained section. The number of delayed diagnoses is small, (it approximates one per cent) but, if the surgeon realizes, in advance, that a definitive diagnosis is not always possible, he will accept the delay with better grace.

(2) Errors in diagnosis are due to:

(a) **Misinterpretations:** These errors consist chiefly of calling inflammatory reactions malignant changes or vice versa and in distinguishing between benign and malignant neoplasms where the boundaries are ill-defined. The groups of tissues chiefly responsible for these errors are:

(i) the salivary tissues including the parotid gland.
(ii) the thyroid gland.
(iii) the bile, ducts gall bladder and head of the pancreas.
(iv) lymph nodes.
(v) bone neoplasms.

(b) **Faulty Block Selections:** This error derives from two sources:

(i) The pathologist who selects a non-representative part of a biopsy specimen to block for frozen section, only to find the diagnostic appearances in the remainder of the biopsy specimen blocked for H & E sections and examined twenty-four hours later.

(ii) the surgeon who chooses a non-representative part of the questioned tissue to biopsy. This latter error can only be discovered if the surgeon decides to disregard the benign frozen section diagnosis and remove the lesion on clinical grounds, or when the subsequent clinical course of the patient demonstrates the original mistake in diagnosis. A critical judgment of this error is nearly impossible, since there are too many variables, but it is certainly not insignificant.

Proper co-operation between the surgeon and the pathologist, including pre-operative consultation and attendance in the operating theatre by the pathologist, can do much to forestall these errors, since, in this way, the pathologist can help the surgeon select a diagnostic sample. Furthermore, the pathologist can more intelligently evaluate the microscopic appearance of the biopsied tissue in the light of his detailed knowledge of the clinical course of the patient to date and the gross appearance of the lesion in situ.

Table I is a breakdown of one hundred consecutive frozen sections requested by the Department of Surgery of the Victoria General Hospital between 1 July 1958 and 15 January 1959. It is a representative sample of the requests ordinarily received from this busy surgical service. It shows the heavy preponderance of requests from the surgeons dealing with lesions of the breast. The miscellaneous group contains two tumours of the abdominal wall, one of which was "secondary adeno-carcinoma", the other "adult adipose tissue"; one tumour of the thigh reported as "leiomyoma"; one biopsy of tissue from the neck reported as "carcinoma in neck tissue, probably metastatic transitional cell carcinoma"; and one biopsy of an inguinal mass reported as "reticulum cell sarcoma." It will be seen that ten disagreements are recorded between the frozen section diagnoses and the diagnoses arrived at from a study of the H. and E. stained slides. These disagreements have been classified as "errors of frozen section diagnosis." Although this supposition is by no means certain, it seems more likely to be correct, since difficult H. and E. slides were seen by several different pathologists who had ample opportunity to study them at leisure, whereas frozen sections were usually seen by only one pathologist. No attempt has been made to record the errors as percentages, since gross distortion would result in so small a series as this. Only one decision was "deferred." An analysis of these eleven controversial slides is presented in Table 2.

In each "error," the surgical procedure carried out on the strength of the frozen section diagnosis is recorded. Since the "acceptable" procedure which would have been performed, had the correct pathological diagnosis been made, carries one into the realm of "surgical judgment" and is so controversial, in most cases, that no one procedure would be considered "correct" by all surgeons, this aspect of the analysis will be left to the reader to decide how serious a "mistreatment" resulted from the pathologist's "misdiagnosis." It will be seen that, at least in one case, the surgeon preferred to exercise his clinical

judgment and carry out a procedure which is usually contraindicated in the light of the findings reported by the pathologist. Subsequent analysis of the total tissue removed proved the surgeon's judgment to be sound. This case illustrates the balance that must be struck between slavish reliance upon the pathologist's report and belief in one's own infallibility. In the case of the mistaken frozen section diagnosis of the bone tumor, this patient was later presented at a clinical conference. During the subsequent discussion, the pathologist expressed the opinion that, had he seen the X-rays of the lesion before operation, he would have asked for a biopsy of tissue presenting the "sun ray" appearance, since this tissue was more likely to be diagnostic than the necrotic central area which was actually presented to him. This experience has led the writer to recommend fuller pre-operative consultation between surgeon and pathologist, whenever possible, in the hope of reducing the number of misdiagnoses.

Finally, the writer wishes he possessed the wit of a Janigan[4] to describe the technical facilities available to the pathologists called upon to perform "frozen sections" in the Operating Suite of the V.G.H. The vicissitudes of "waiting for a V.G. elevator" fade into insignificance when compared with those facing the pathologist trying to cut, stain and read a frozen section in the cubicle provided for his use. It would seem that, if a procedure, requiring as high a degree of technical skill as does a frozen section, enjoys a sufficiently high reputation that it is called upon two hundred times in the course of a year, the technical facilities provided should be of reasonably high calibre, especially since grave mis-treatments can and do result from misdiagnoses.

The errors here recorded fall within the acceptable range, but it is the opinion of the writer that they could be much lower were better technical facilities available and greater consultation between surgeon and pathologist carried out.

SUMMARY:

A review of the available literature on frozen sections is presented.

An attempt to acquaint the surgeon with the type and amount of information he can expect from the pathologist, reading frozen sections in the operating suite, is made.

An analysis of 100 consecutive frozen sections, prepared and read between 1st July 1958 and the 10th January 1959 at the Victoria General Hospital, is presented.

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TABLE I

Analysis of 100 Consecutive Frozen Sections

Tissue Biopsied	Frozen Section and H & E Diagnosis Agreed	Frozen Section and H & E Diagnosis Did Not Agree	Deferred Diagnosis	Benign By H & E Section	Malignant By H & E Section	Totals
Breast	45	3	0	35	13	48
G. I. Tract	8	0	0	6	2	8
Lymph Glands	6	2	0	3	5	8
Thyroid	6	1	0	7	0	7
Lip & Skin	6	1	0	3	4	7
Female Genitalia	6	0	0	5	1	6
Neurological	4	0	1	2	3	5
Gall Bladder	1	2	0	0	3	3
Bone Tumours	2	1	0	1	2	3
Miscellaneous	5	0	0	2	3	5
Totals	89	10	1	64	36	100

TABLE II

ERRORS OF FROZEN SECTION DIAGNOSIS

Slide Number	FROZEN SECTION DIAGNOSIS	H & E STAINED SECTION DIAGNOSIS	OPERATION PERFORMED
58-8017	a) Lumph node from area of gall bladder bed reported as "Benign." b) Tissue from gall bladder bed reported as "Fibrous Tissue and Glands. Questionably Malignant."	Paraffin block of remainder of same lymph node reported as "Metastatic Adenocarcinoma." "Adenocarcinoma of Gall Bladder." Paraffin block of same tissue.	Cholecystectomy
58-9747	Section of cystic duct biopsied; reported as "Inflammatory."	Same tissue on paraffin section reported "Adenocarcinoma of Gall Bladder."	Exploration of Common Duct and Cholecystectomy.
58-8796	Breast nodule biopsy reported "Scirrhous Carcinoma of Breast."	Same tissue, "Intraduct Papilloma of Breast, with Fat Necrosis.	Radical Mastectomy.
58-8798	Breast nodule biopsy reported as "Benign."	Same tissue block "Intraduct and Lobular Carcinoma of Breast, Low Grade." Very small focus.	Simple Mastectomy.
58-12006	Breast nodule biopsy reported as "Equivocal (a) Sclerosing Adenosis (b) Non-Invasive Intraduct Ca."	Same tissue block reported as, "(a) Intraduct Ca. of Breast with Invasion (b) Sclerosing Adenosis."	Simple Mastectomy.
58-9101	Lymph node from iliac vessels reported "Metastatic Carcinoma."	"Inflammatory Change, No Carcinoma Seen," reported for the rest of the same lymph node. (There was Ca of cervix.)	Wertheim.
58-13570	Lymph node removed from drainage area of large stomach ulcer reported "Negative for Ca."	Same lymph node showed, "Microscopic Focus of Metastatic Carcinoma." Stomach ulcer was also "Carcinoma."	Sub-total Resection.
58-12460	Thyroid nodule biopsy reported "Solidly Cellular Tumor, Suspicious."	Same tissue reported as "Fetal Adenoma of Thyroid."	Excision of Right Lobe of Thyroid.
58-8257	Biopsy of recurrent skin lesion of nose reported as "No Carcinoma Seen."	Same tissue reported as "Basal Cell Carcinoma."	Local Excision.
58-13172	Biopsy from large tumour at upper end of humerus reported as "Necrotic Tumour, Probably Not Sarcoma."	Same tissue "Osteogenic Sarcoma of Unusual Type." Tumour, Probably Not	Curretage and Packing with bone chips.
58-13311	Needle biopsy of brain reported as "Not Diagnostic."	Edematous brain tissue showing swelling of astrocytes.	Needle Biopsy Brain.

Eye Injuries

(From A Week In Surgery April 13-17, 1959)
Dalhousie University

J. H. Quigley, M.D.

Since many eye injuries are seen first by the general practitioner, it is important that he know:

(1) what to look for
(2) what to do
(3) what to refer

ETIOLOGY: **TRAUMA**

(Various Forms Which May Affect The Eye)

A. **PHYSICAL**

Infra-red rays
Ultraviolet rays
Roentgen rays
Radium
Thermal

B. **CHEMICAL**

Acids
Alkalis
Other (Arsenicals
Quinine
Methyl alcohol
Naphthalene
Ergot)

C. **MECHANICAL**

Non-perforating
Abrasion
Contusion
Compression
Rupture (or fracture)
Perforating
No Foreign Body retained
— laceration
— puncture
— surgical incisions
Foreign Body retained
— non-toxic (gold, silver, platinum, glass, plexiglass, etc.)
— non toxic (lead, zinc)
— markedly toxic (iron, copper, limestone)

RESULTS:

The physical group by our classification comprises much of the electromagnetic spectrum outside of visible light. **Infra-red** rays are often responsible for cataract (glass blowers). Extremely long waves such as radio, etc. produce thermal effects only. **Ultraviolet** rays produce photophthalmia (snow blindness, electric ophthalmia) but no permanent damage. **Radium and roentgen** rays have immediate effects similar to ultraviolet rays, or if massive radiations, produce ulceration and necrosis and corneal opacity. Disastrous late effects are sudden and extensive sloughing of tissue and development of panophthalmitis. Thermal effects are by coagulation necrosis of cells.

The chemical group produce necrosis of the tissues to a depth determined by the nature and concentration of the agent and the extent and duration of contact. The necrotic tissue is sloughed off, and healing is accompanied by very dense scar formation. **Acid** burns tend to be limited by the buffering reaction of the tissues and the lesions are sharply demarcated. **Alkali** burns are particularly severe and give the clinical impression that they are progressive, since tissues damaged by alkali may initially preserve a grossly normal appearance. The alkali penetrates deeply into the tissues and cannot be easily removed. Various gases (war) vary in their toxicity to ocular tissues. Many chemical agents are conveyed to the eye via the blood stream or penetrating wounds. These can be divided into (1) bacterial toxins, (2) poisons, (3) organic alkaloids, (4) drugs which cause optic atrophy.

The mechanical injuries are essentially divided into perforating or non-perforating. Either may cause loss of the eye, but obviously the perforating variety is more dangerous. **Contusions** may be direct or indirect and may lead to contre-coup lesions (commotio retinae or displacement of ocular tissues (iris, lens, retina). Hyphema is the usual result and the blood may or may not absorb. **Perforating** sounds vary in severity in direct proportion to site and extent, but the complication of a retained foreign body alters prognosis for the worse. Iron, particularly soft iron, and copper oxidize rapidly with resultant siderosis and chalcosis. Limestone elicits a marked reaction. In short, the most important complications taking place at the time of perforating wounds are haemorrhage and prolapse of intraocular tissue; infection, with resultant endophthalmitis is the most important complication to occur in the first few days following the injury. Secondary changes may be intermediate (a few weeks to several months following injury) being characterized by healing with more or less damage, or by continued inflammation and irritation; late changes are chiefly degenerative and may continue to progress years after the original injury.

TREATMENT:

A. **PHYSICAL INJURIES**

(1) local anaesthesia (sparingly): ophthaine, or pontocaine
(2) mydriatic 1% cyclogyl, or homatropine
(3) tight patch for 24 hours
(4) refer if severe

B. **CHEMICAL INJURIES**

(1) immediate massive lavage—plain water
(2) remove particles
(3) refer if severe

C. **MECHANICAL**

(1) Non-perforating—rest—local (patch) and general (bed)—if you can't see the fundus, refer
(2) Perforating—refer
(3) Foreign bodies under lid and in cornea
— remember upper conjunctival sulcus
— remove corneal F.B. with spud or needle and patch
(4) Lid lacerations
— repair with 6-0 black silk (atraumatic needle)
— be sure to approximate edges accurately
— if laceration is full thickness or involves tear canaliculi—refer

Personal Interest Notes

Doctor William A. Cochrane, Associate Professor of Paediatrics, Dalhousie University Faculty of Medicine, has been accepted into membership of The American Society for Paediatric Research, one of the highest and most select research societies in that field. He was one of the thirteen members from the United States and Canada to be accepted out of 86 candidates.

The marriage took place recently in Bedford of Doctor Margaret Edna MacMurdo, daughter of Mr. and Mrs. Robert Erle MacMurdo of Wilmot Valley, Prince Edward Island, and Doctor Alan McMillan, son of Mr. and Mrs. Frank McMillan, Burlington, Ontario. Doctor MacMurdo graduated from Dalhousie Medical School in 1957, and Doctor McMillan is a naval research chemist.

Enteroviruses, Adenoviruses and the Encephalitis Problem In Eastern Canada*

by

R. L. Ozere, M.D. and C. E. van Rooyen, M.D.

Shortly after tissue culture methods were applied to enable growth of poliomyelitis virus in vitro, by Enders et al[1] of Boston, it became manifest that several other groups of viruses were capable of invading the human enteric tract. These agents were first noted by Enders and his group using human tissue culture. Subsequently, monkey kidney cultures were substituted for the isolation of these hitherto unknown viruses. During the years 1954-1955, many other investigators recovered similar viruses from healthy normal children, as well as from patients with the aseptic meningitis syndrome. These viruses did not produce disease in laboratory animals, including infant mice.

In May 1955, the National Foundation for Infantile Paralysis called a conference on these "orphan viruses" as they were then named, and a committee was to decide upon their nomenclature and classification. They proposed the name of "Enteric Cytopathogenic Human Orphan" to designate these viruses of which there were 13 known prototypes at that time. They are presently referred to under the abbreviated title of "ECHO" virus and comprise 24 well recognized strains today, most of which have been proven pathogenic to man.

Echo viruses have been associated with epidemic aseptic meningitis and types 5, 6, 9 and 14 have been isolated from cerebrospinal fluid by the laboratories of the Hospital for Sick Children of Toronto, Ont., by P. DeSomer in Louvain, Belgium and D. T. Karzon at the University of Buffalo, Buffalo, N.Y. In 1955 and 1956 a study of 221 cases of aseptic meningitis was made in Connecticut. From these 221 cases the following different viruses were recovered: —Poliovirus-32; Echo 6-32; Coxsackie B2, B3, B4-19; unidentified virus-6; giving a total of 103 isolations from the 221 cases.[2] Thus it became evident that Echo virus was at least as prevalent as poliovirus in causing aseptic meningitis or non-paralytic polio-like illness concurrently with the polio season. The success of the polio vaccine has contributed in a large measure to the recognition of other agents, notably the Echo and Coxsackie group, as aetiological factors in the disease syndromes associated with these two names.

In 1957, a type virus isolated by D. M. McLean, and by D. A. T. Tyrrell in England, from an epidemic in Bourne, proved to be due to Echo prototype 9.[3] Likewise P. DeSomer isolated the same virus from spinal fluids of 7 patients and from 26 fecal specimens. The Bourne strain of Echo 9 virus, after 6 passages on monkey kidney tissue culture produced paralysis and myositis in infant mice, exhibiting properties similar to that produced by injection of Coxsackie group A viruses into suckling mice, raising the question of a relationship between Echo 9 and the latter named group of organisms.

Crawford, Macrae and O'Reilly[4] in 1954, described an outbreak of an epidemic disease characterized by fever, macular rash and aseptic meningitis

*Being work conducted under Public Health Research Grant No. 602-7-24 of the National Health Grants. For study of Neurotropic Virus infections in the Atlantic Provinces of Canada.

in infants, also noted by Tyrrell and Snell, in England, both of which proved to be due to Echo 9 virus. During the summer of 1956, in Toronto, an epidemic of aseptic meningitis occurred, characterized by fever, severe headache, muscle pain, drowsiness and a macular rash which appeared on the face, limbs, palms and soles. In some cases, the cerebrospinal fluid cell count was so high (see Table 3), that purulent meningitis was suspected and antibiotic therapy started.[5]

In 1957, in Nova Scotia, Faulkner, MacLeod and van Rooyen[6] described an outbreak of virus meningitis affecting all 7 members of one family, from whom Echo 9 virus was isolated from stools and CSF. Two patients from the group developed a rubelliform rash during the course of illness.

During the period of March to September, 1957, a widespread epidemic occurred in Nova Scotia and Newfoundland, with cases also reported in New Brunswick and Prince Edward Island. These cases, investigated by MacLeod et al[7], revealed 40 strains of Echo 9 from a group of 141 cases, clinically designated as aseptic meningitis. A range of cytopathogenic agents was recovered on monkey kidney and human amnion tissues, including Coxsackie A9, and B4, and poliovirus Type II and III. Headache, nausea and vomiting with neck stiffness, muscle pain and normal reflexes were cardinal signs and symptoms. About 25% of the patients exhibited a maculopapular rash, and the paper included speculation as to the relationship of this illness to German measles. In many of the cases virus was isolated from the cerebrospinal fluid. Three cases of Echo 9 infection affecting pregnant women were reported without damage to the foetus. It is also of interest that in 36 patients, unidentified agents were obtained.

An epidemic of diarrhea in premature and older infants caused by Echo virus type 18, has been recently described by Eichenwald et al.[8] The disease was not severe in the 12 out of 21 infants affected in the hospital nursery. This virus has not as yet been identified as a pathogen in Canada.

Ultrafiltration experiments carried out by A. D. Macrae et al, and Ramos-Alvarez and Sabin, show that the Echo viruses are of the same size as Coxsackie and Polioviruses, having an average diameter of 30 mu. Echo 10 is larger, having a diameter of 75 mu.

The committee on the Echo viruses[9] has added the following characteristics as being diagnostic of this group of agents:—

(1) They are cytopathogenic for human and monkey cells in culture—they favour monkey kidney cells.
(2) They are not neutralized by pooled polio antisera.
(3) They are not neutralized by Coxsackie antisera.
(4) Non-pathogenic for infant mice—(exception Echo 9).
(5) Not related to Herpes, influenza, mumps, measles, varicella, EKC, PCF viruses.
(6) Neutralized by gamma globulin and human sera.
(7) A number have shown a complement fixing antigen.
(8) Size is 11-90 mu.
(9) Plaque formation is distinctive in bottle cell cultures.

In summary, the Echo viruses, not all of which are proven human pathogens, have been implicated in epidemics of aseptic meningitis, occasionally associated with rash, and also with epidemic diarrhea associated with upper respiratory infection, during the winter months.

A summary of the known aseptic meningitis syndromes produced by certain of the Echo viruses are herewith reproduced for those who may have not seen the excellent summary in the October 1958 issue of Modern Medicine of Canada. (By Dr. Albert B. Sabin).

TABLE I CLINICAL CHARACTERISTICS OF ECHO 4 VIRUS DISEASE

Age	50% under 14 years.
Incubation period	Probably three to five days, occasionally longer.
Fever	99 to 102° F., lasts two to three days in those without meningeal signs, three to five days in those with meningeal signs.
Alimentary tract	Sore throat in about 40%. Nausea, vomiting, or diarrhea in about 70%.
Exanthema	None seen in United States epidemics; reported in Sweden.
Enanthema	None reported.
Central Nervous System	
Aseptic meningitis syndrome	Seen in 55% of surveyed population. Nuchal and spinal rigidity but no Kernig or Brudzinski signs.
Paralysis or other signs	None observed during epidemics; 2 sporadic cases reported by Hammon et al.
Fatalities	None reported.
Laboratory findings	Cerebrospinal fluid: Leukocytes of 16 to 900 (average 200). Peripheral blood: leukocytes within normal limits.
Site of virus recovery	Throat, stools, cerebrospinal fluid.
Inapparent infection	Uncommon.

TABLE 2. CLINICAL CHARACTERISTICS OF ECHO 6 VIRUS DISEASE

Age	Children and adults.
Incubation period	Probably three to five days, occasionally longer.
Fever	100 to 103° F., rarely up to 106° F. Lasts three to six days, biphasic in about 25%.
Alimentary tract	Sore throat in 25 to 40%. Vomiting, common; abdominal pain, occasional; diarrhea, rare except in young infants.
Exanthema	Extensive maculopapular eruption over entire body reported thus far in only 1 patient.
Enanthema	Reported only in sibling of patient with exanthema.
Central Nervous System	
Aseptic meningitis syndrome	Majority of patients.
Paralysis	Transitory muscle weakness observed with varying frequency in different outbreaks. No cases with frank residual flaccid paralysis.

Other signs	Convulsions occasionally at onset.
Fatalities	None reported.
Laboratory findings	Cerebrospinal fluid: leukocytes 18 to 855 (most under 500) Peripheral blood: leukocytes usually within normal limits.
Site of virus recovery	Throat, stools, cerebrospinal fluid.
Inapparent infection	Rare.

TABLE 3. CLINICAL CHARACTERISTICS OF ECHO 9 VIRUS DISEASE

Age	Children and adults.
Incubation period	Probably three to five days, occasionally longer.
Fever	Usually under 103° F., rarely higher. Frequently biphasic and rarely triphasic. Lasts two to fifteen days with a median of six days.
Alimentary	Sore throat in about 50%. Nausea, vomiting, generalized abdominal pain more frequent in young children. Diarrhea usually absent; rarely seen at onset.
Exanthema	Present in all but 2 outbreaks. Macular or maculopapular, only rarely petechial. Discrete, only occasionally confluent. Usually on face, neck and chest but also on trunk and extremities in 56%. Onset during fever. Persists for one to nine days with median of four to five days. Does not itch or desquamate. Occurs in about 75% under 5 years. 45% between 5 and 15 years, 7% over 15 years.
Enanthema	Occasional yellowish or grayish-white 1-to 3-mm. spots on tonsillar fauces or buccal mucosa.
Central Nervous System	
Aseptic meningitis syndrome	Minority of ill persons exhibits distinct nuchal spinal rigidity, but many without distinct signs have pleocytosis.
Paralysis	Transitory paralysis seen in only 1 patient in Milwaukee epidemic, 1 in Minnesota, and few in Switzerland.
Other signs	Transitory choreiform movements, loss of balance, severe vertigo, ataxic gait, and nystagmus seen in only few patients in Milwaukee epidemic.
Fatalities	Only 1 confirmed case in 8-month-old baby in Holland.
Laboratory findings	Cerebrospinal fluid: leukocytes less than 1,000 in majority; occasionally 6000 to 8000. Peripheral blood: leukocytes diminished or normal, rarely increased.

Site of virus recovery	Throat, stools, and frequently cerebrospinal fluid; rarely blood, rarely minute amount in mouth.
Inapparent infection.	Only 15% of infected persons in Milwaukee epidemic.

TABLE 4. CLINICAL CHARACTERISTICS OF ECHO 14 VIRUS DISEASE

Age	Children and adults.
Incubation period	Four to five days.
Fever	100 to 104° F., lasting only one to two days in patients without aseptic meningitis.
Alimentary tract	Sore throat mild but frequent. Abdominal pain frequent; rarely diarrhea at onset. Vomiting only in patients with aseptic meningitis.
Exanthema	Common in children, less in adults. Usually appears after defervescence and disappearance of symptoms. Macular or maculopapular, pink or salmon-colored. Usually discrete, from 1 mm. to 1 cm. Mostly on face, chest and back, occasionally more extensive. Lasts two to four days. Does not itch.
Enanthema	Single or multiple, raised red or yellowish-white lesions on soft palate, fauces, or uvula. See in 50% of Pittsburgh patients.
Central Nervous System	
Aseptic Meningitis syndrome	Uncommon; only 10 patients on record.
Paralysis and other signs	Only in 1 sporadic case.
Fatalities	None.
Laboratory Findings	Cerebrospinal fluid: leukocytes usually less than 50 and not more than 100. Peripheral blood: leukocytes within normal limits.
Site of virus recovery	Stools, throat; once from blood.
Inapparent infection	None known.

TABLE 5. CLINICAL CHARACTERISTICS OF ECHO 18 VIRUS DISEASE

Age	Only infants under 1 year of age.
Incubation period	Probably three days.
Fever	Neither fever nor hypothermia in 17 infants in New York outbreak.
Alimentary tract	Diarrhea consisting of 5 to 6 large, watery, greenish stools a day, lasting one to five days with a mean of three days. No mucus or pus cells; rarely flecks of bright blood. Moderate abdominal distension in few.
Exanthema	None.
Enanthema	None.

Central Nervous System	None observed during epidemic.
Fatalities	None during N. Y. epidemic, but virus recovered from stools of 5-month-old baby who died in Milwaukee (1957) after illness of six days; fever, repeated vomiting of bloody or coffee-ground material, slight hepatomegaly, and coma. No pleocytosis. No necropsy.
Laboratory findings	None available.
Site of virus recovery	Stools only.
Inapparent infection	In adults and older children. None in infants.

Whilst most of the Echo viruses cause Aseptic Meningitis syndromes, it should be noted that these same viruses are the cause of epidemic diarrhea in the summer and diarrhea associated with upper respiratory infection in the cold months of the year, e.g., Echo types 8, 10 and 20.

Factors Indicating a Suspected Echo Epidemic. These are summarized as follows:

1. High incidence of aseptic meningitis with few or no paralytic cases.
2. Febrile illness in children and adults with high incidence of rash, especially in very young children, with or without concomitant aseptic meningitis.
3. Diarrheal disease, especially in very young infants, not associated with enteropathogenic bacteria.

ADVICE ON COLLECTION OF SPECIMENS

Throat swabs or preferably physiological saline garglings or throat secretions aspirated in infants, which travel better and do not dry up like throat swabs. These should be transported to the Laboratory, frozen in dry ice.

Rectal swabs. Collected as usual and placed in a sterile screw-capped test tube and transported frozen in dry ice to the Virus Laboratory.

Stools. About 50 grams should be picked up on a wooden tongue depressor and placed in a **STERILE** glass screw-capped phial. It must be forwarded to the laboratory frozen in dry ice.

Cerebrospinal Fluid. First exclude meningococcal or other pyogenic bacterial infection of the brain and meninges by appropriate bacteriological examination. In all other cases of suspected meningeal involvement—a specimen of CSF should be sent to the Virus Laboratory for attempted isolation of virus. Up to date, the following types of ECHO virus have been recovered from CSF, in the acute phases of illness; namely, ECHO viruses types 1, 2, 4, 5, 6, 9, 14 and 16.

During the past year, it has been the experience in the Atlantic Provinces that specimens of CSF showing pleocytosis 40 to 400 lymphocytes per cu /mm have frequently yielded virus on monkey kidney or human amnion tissue culture. This strongly suggests that clinicians would be well advised to request virus culture of all specimens of CSF where lymphocytic pleocytosis is present. Ocassionally CSF yielding virus has shown a preponderance of polymorphs, but this could be a phase in the cellular reaction as we have noted in the case of ECHO 9 infection We would like to stress that whereas in several ECHO and Coxsackie A and B types of infection, virus is recoverable from the CSF,

this is **NOT SO** in poliomyelitis, where the virus is usually **NOT** found in CSF at any stage of the disease. The virus of poliomyelitis is however found in over 90 per cent of stools in acute cases of poliomyelitis and in carriers in poliomyelitis infected areas. CSF should be sent to the Virus Laboratory in a sterile screw-capped phial, frozen in dry ice.

Blood-Serum. In all suspected viral conditions, it is necessary to obtain two phase sera collected in the EARLY FEBRILE ACUTE (preferably first 24 hrs. of illness, and CONVALESCENT STAGES of illness. It is most important to have these two specimens of serum.

If a virus can be identified from the throat secretion, stools of CSF of the patient in the acute stage and be readily identified serologically, diagnosis is made and there is no problem.

But unfortunately as so frequently happens and particularly in encephalitis, a positive culture may not be obtained. In this case, the identification of the patient's illness rests on attempting to demonstrate a rise in antibody level on 2 phase sera by neutralization tests against known strains of virus.

Conversely, a virus may be grown from the patient but which cannot be typed by known specific antisera. In this case the aetiological relationship of the suspected virus to the patient's illness can only be adduced by demonstrating a rise in antibody titre in the patient's own serum against his own virus.

Transmission of Serum. Serum should be separated with sterile aseptic technique packed in dry ice and sent to the laboratory promptly.

Air Shipment. It would facilitate the operation of the labs if a telegraphic message were sent in advance, intimating the flight by which the specimen was due to arrive in Halifax.

COXSACKIE GROUP OF ENTEROVIRUSES

In recent years large epidemics of Coxsackie infection have occurred. Today there have been described at least 24 immunotypes of Coxsackie A virus and 5 serologic types of B virus.

The coxsackie or C viruses represent a group of filterable agents which have in common certain biologic properties, including an unusual pathogenicity for suckling mice and hamsters. The viruses are widely distributed throughout the world and their recognition as causative agents in various disease syndromes or conditions, is increasing yearly.

In 1948, in association with an epidemic of a polio-like illness, in the town of Coxsackie, N. Y., Dalldorf and Sickles isolated in suckling mice, strains of a filterable agent from faeces of 2 children with paralysis. The agent differed from poliovirus in that it induced fatal disease and paralysis with destructive lesions of striated muscles in suckling mice, but not in adult mice, monkey or adult hamsters. It was subsequently shown that this agent was one of a group of related viruses, so-called Coxsackie group A, all producing myositis in suckling mice, and in humans, producing illness simulating poliomyelitis. Today, there are over 24 immunotypes of this group recognized.

Another distinct group of Coxsackie viruses, so-called group B, isolated in 1947, cause little or no change in muscle tissue but produce inflammatory changes in the pancreas, brain and dorsal fat of suckling mice. Schwartzman, however, has noted, that poliomyelitis virus causes similar effects in animals

that have been dosed with cortisone[10]. Tropism for pancreas is a property only of freshly isolated B virus, and is lost after repeated passage in brain suspensions.[11]

As agents in human disease, Group B viruses are receiving more current attention because of the better defined and possibly more serious illnesses that they produce. There are 5 immunologically distinct types, all of which are cytopathogenic on cultures of trypsinized monkey kidney cell, in contrast to only 5 of the 24 group A viruses.

The clinical syndrome of epidemic pleurodynia (Bornholm disease) was first described by Daae and Homann in Norway in 1872. Many eponyms have been applied to this disease over the years, including epidemic myalgia, devil's grippe, epidemic pleurisy, etc. The disease characteristically occurs in epidemic form and usually in the summer and fall. Various accounts of epidemics have been published, including that of Pickles[12] in 1933, and more recently (1956) by Gordon[13] in California.

The incubation period is from 2-4 days, with sudden onset heralded by severe thoracic pain at the level of the diaphragm. The pain is severe, throbbing and may be unilateral or bilateral. It may occasionally be confused with myocardial infarction, but the pain is aggravated by coughing, sneezing, or deep breathing. Occasionally, especially in children, the pain may be abdominal, epigastric, with local muscle guarding. Along with pain there is frontal headache, malaise, fever and tachycardia. Pain and fever may last 1-2 days and then subside after which the patient may remain asymptomatic for several days, followed by recrudescence of symptoms. Biphasic illness by history is a fairly common feature of this and other diseases due to B group Coxsackie viruses. The total duration of the illness, with relapses, may be 20 days[14]. Cough is unusual but nausea and vomiting are quite frequent, along with sore throat. (25% of cases).

Complications of pleurodynia are rare, but include pleurisy, meningitis and orchitis, the latter being the most common.[15]

An association between pleurodynia and aseptic meningitis has been noted by a number of investigators, with cases of both occurring separately or in the same patient during an outbreak[16], [17], [18], and aseptic meningitis per se has been associated with isolations from stools and CSF of Coxsackie B virus types 3, 4, and 5.[19]

McLean[20] in 1958, reports the cases of 4 children who developed pericarditis in an epidemic area of pleurodynia and aseptic meningitis in Southern Ontario. Coxsackie B_5 virus was isolated from the stools of the 4 patients, and from 9 patients with pleurodynia. Movitt et al[21] had isolated Coxsackie B_3 virus from a similar case in a young man with pericarditis. This group also isolated a Coxsackie A type I virus from an older patient with a similar illness.

In Halifax, Roberts, Lydon and McIntosh[22] reported a case of pericarditis in the fall of 1958, associated with orchitis, which on culture proved to be a Coxsackie B_5 virus.

In 1952, in Johannesburg, South Africa a number of babies became ill while in, or soon after, discharge from the maternity house in which they were born. Six of the ten affected infants died after an acute fulminating illness that ended in congestive heart failure and circulatory collapse. Tachycardia, enlargement of the liver and slight oedema of the feet were observed. At post-mortem, three of the fatal cases showed a severe, acute myocarditis. The brain tissue

of two of these cases yielded a group B_3 Coxsackie virus, as did the faeces.[23] Another outbreak yielded a group B type 4 virus. Kilbourne[24] had previously noted an association of myocarditis in infant mice with the same strain. Since these first reports there have been numerous reports of sporadic cases of fatal myocarditis in infants, usually presenting with acute congestive heart failure or sudden death often after a biphasic febrile illness.

Cases of severe persistent myalgia were studied by Lepine, Desse and Sautter, including that of a 61 year old female with sudden onset of violent pain of the right knee and muscles of the right leg. A portion of muscle biopsied from the point of greatest tenderness, showed severe degeneration of the muscle fibres.[25] The biopsy tissue proved infectious for mice.

A 1954 report[26] from South Africa relates an outbreak of febrile illness with fever of from 5 days to 4 weeks duration, splenomegaly and slight lymphadenopathy, to a group B Coxsackie virus infection, virus being recovered from 5 of 6 cases investigated

Herpangina, a febrile illness associated with superficial greyish ulcers on anterior tonsillar pillars, soft and hard palate, has been well described in association with Coxsackie A disease, occasionally linked with similar ulcers on the genitalia.[27]

Thus it may be seen that as laboratory aids to diagnosis become more generally available, it is possible that the protean disease manifestations associated with cultures of Coxsackie virus, may become more sharply defined. At any rate, for the present the relationship between Coxsackie viruses and herpangina, pleurodynia and aseptic meningitis, may be accepted as established. The association of Group B disease with occasional fatal illness in infants, is also indicated by recent reports, and should be borne in mind when faced with the problem of the sudden death of an infant after, or during, an apparently mild febrile illness. In general also, aseptic meningitis due to Coxsackie virus is more common in children, while pleurodynia is more common in the adult groups.

The transmission of the Coxsackie viruses has been studied by several groups of investigators. A. J. Rhodes et al examined Toronto sewage between December 1948 and December 1949, searching for poliovirus. They recovered Coxsackie virus as well as polio during a period of very low poliomyelitis incidence.[28] Melnick et al reported similar findings from sewage in Connecticut and North Carolina[29] recovering the viruses from sewage in summer and fall.

Flies were rarely found contaminated with virus. These findings and those of others support the fecal-oral hypothesis of transmission of Coxsackie viruses with the alimentary tract as the portal of entry. Cockroaches have also been infected experimentally with Coxsackie virus and may be a possible vector of spread.[30]

Distribution of Coxsackie Viruses in Tissues.

Throat secretions, faeces, cerebrospinal fluid yield virus in the acute phase of illness. Virus may persist in stools for several weeks. Subclinical infections are frequent in contacts. Some 1 to 7 percent normal persons harbour Coxsackie Group A viruses in faeces. Excretion is commonest in Group A infections in summer and fall. In contrast, Group B viruses are rarely isolated from the throat or faeces of persons other than those ill with epidemic myalgia, aseptic meningitis, pericarditis, orchitis etc. throughout the year.

Collection of Specimens.

Virus is present in throat secretions, stools, anal swabs, CSF and blood, and the method of transmission to the Laboratory is similar to that used for Echo viruses.

POLIOMYELITIS

In the past, the Port City of Halifax has suffered repeated and severe epidemics of poliomyelitis. With the advent of the Salk vaccine, there has been a sharp decline and a virtual disappearance of poliomyelitis in this area. It should be remembered however, that inapparent cases of infection are still liable to enter this seaport from other areas where vaccination programs may not as yet have been thoroughly organized, e.g., Europe, the Mediterranean, the West Indies and the Far East. Constant vigilance should therefore be maintained for the introduction of cases into all seaport towns wherever these may be.

Collection of Specimens.

This is similar to those required for Coxsackie viruses as described above. Special note should be made of the fact that virus is present in stools in a very high percentage of poliomyelitis cases in the early febrile stages of illness. Thus in every suspected case of poliomyelitis, two or more specimens of stools should be collected on the first and second day of illness, placed in a sterile screw-capped jar, and shipped to the laboratory packed in dry ice or ordinary ice if dry ice is unavailable. The specimen should be accompanied by a requisition stating that the case is considered suspicious of poliomyelitis, and a speedy answer is required. Under optimum conditions it is sometimes possible to give an answer in 48 hours or less.

ADENOVIRUSES

Adenoviruses, so named in 1956[31] to cover a group of epidemic upper respiratory tract illnesses formerly called respiratory illness (R.I.) Adenopharyngeal-conjunctival fever (APC) and Acute Respiratory Disease (ARD), were first isolated in 1953 from human adenoid tissue[32] and later (1954) from acute respiratory disease (ARD)[33] and from pharyngo-conjunctival fever (PCF)[34] and epidemic kerato-conjunctivitis (EKC.)[35]

Over 18 immunologically distinct human agents have been reported from various parts of the world associated with upper respiratory and ocular illness, and it is estimated that this group of viruses is responsible for from 1%-8.5% of all respiratory illness due to virus.[36], [37], [38].

Their pathogenicity for man was proved in reproducing the clinical disease by infecting groups of volunteers, with the primary infection characterized by:—

(a) Non-fatal, frequently febrile state.
(b) Catarrhal inflammation of mucous membranes of respiratory and ocular systems.
(c) Follicular, sometimes persistent enlargement of submucous and regional lymphoid tissue and nodes.
(d) Prolonged carrier states with persistent (latent?) infection of adenoids and tonsils.

The adenoviruses attack the respiratory tract in man from the oropharynx to the lungs, (atypical pneumonia without cold agglutinins), the conjunctiva and the intestinal tract. Lesions produced, include cell damage with inflammation and hypertrophy of regional lymphoid tissue.

Most patients infected with adenovirus respiratory disease show a basic syndrome of fever (most marked in children and infants), with pharyngitis and cough. The cough may be severe and persistent for 2-3 weeks. This may be accompanied by conjunctivitis, coryza, exudate on tonsillar lymphoid tissue, local lymph node enlargement, tracheobronchitis and atypical pneumonia.[39] Constitutional symptoms of headache, malaise and myalgia are frequent.

A typical clinical picture of one form of adenovirus illness is shown by the history of a 2-year-old girl, who developed fever, vomiting, rhinorrhea, cough, anorexia and irritability. When admitted to hospital she had a fever of 104° F., bilateral palpebral and bulbar conjunctivitis, bilateral catarrhal otitis media, slight enlargement and marked inflammation of the tonsils and moderate cervical adenopathy. The tonsils showed a whitish-grey exudate. Fever lasted for a total of 6 days, and lymphadenopathy for 3 weeks. An adenovirus type 3 was isolated from a throat swab taken on the 5th day of illness. The child also showed a rise in serum complement-fixing antibody titre during the course of the illness.[40] The above is reproduced to show that adenovirus may produce a fairly severe and protracted, though non-fatal illness.

Adenoviruses have been recovered from humans throughout the world, and in epidemic form especially among military recruits favored by close contact. In the military recruit group, it is estimated that the attack rate may be as high as 25% during the winter months with a marked seasonal variation.[41] The attack rate among the civilian population is much less common, but summer epidemics have occurred among children, possibly related to exposure to contaminated water in swimming pools or lakes. The virus is probably spread not only by droplet-air infection, but also is excreted in stools where it may be carried in the gastro-intestinal tract for long periods of time.

Various types of adenovirus show a marked predilection for certain sections of the population. Among adult civilians, types 3, 4 and 7 are most frequent. Among infants, types 1, 2, 3, 5, 6 and 7 have been found. Among recruits in military camps in U.S.A. and England, types 4 and 7 have been most prevalent. Type 8 has been causally related to epidemic kerato-conjunctivitis. No explanation has been found so far to explain the peculiar distribution of these viruses among different age groups.

The presence of virus recovered from throat washings, stools, etc. is indicated by cytopathogenic changes in tissue culture, but the virus may grow very slowly, so that occasionally incubation is required for one month before tissue culture shows evidence of virus activity and presence.

At the present time, controlled studies are being continued on the evaluation of an adenovirus vaccine among the military population in the U.S.A.[42] It is probable that this vaccine will have less value to the civilian population, since, as previously stated, this virus does not represent a large segment of the total causes of respiratory illness during the winter months.

In Canada, adenovirus infections were first recognized in 1951 when an outbreak of epidemic kerato-conjunctivitis was noted at the Ford Motor Plant in Windsor, Ont. A virus was not isolated at that time, but convalescent

sera from patients were later found to contain neutralizing antibody to type 8 adenovirus. Similarly, during the year 1955-56, numerous cases of virus conjunctivitis in Toronto were reported from which four different types of adenovirus were isolated.[43]

Collection of Specimens.

Take naso-pharyngeal washings or garglings or aspirate conjunctival secretion in sterile capillary tube—seal in flame, pack in dry ice and ship to laboratory. Stools are also required, as well as 2 phase acute and convalescent sera, collected, separated and shipped as described under Echo viruses.

ENCEPHALITIS

In Canada, Western Equine Encephalitis is the only member of the arthropod borne virus group which has been isolated with frequency from human cases of encephalitis. In Toronto, recently, a possible new virus has been recovered by McLean[48] of Toronto, from a single case in Powassan, Ont.

In the U. S. Atlantic Seaboard, Eastern Equine Encephalitis has occurred in epidemic, endemic and sporadic form, extending as far north as Massachusetts, where epidemics occurred in the summers of 1938, 1955 and 1956, affecting both horses and humans. So far as the Atlantic Provinces are concerned, sporadic encephalitis is an annual occurrence throughout winter and summer, and has remained so for many years. This is confirmed from the case reports of general hospitals, polio clinics and mental institutions, and further substantiated from autopsy protocols and the reports of practicing physicians, stretching from Newfoundland to Yarmouth County, Nova Scotia. Inside this vast area no scientific information is available as to what the causal agents have been. Likewise nothing is known about the possibility of animal or insect vectors in Eastern Canada, if indeed arthropod-borne disease does occur.

During the coming summer, the regional virus laboratory at Halifax is undertaking a survey of the incidence, aetiology and distribution of encephalitis in the Maritime area, under P.H.R. Grant No. 602-7-24. The aim of this research is an attempt to determine the local causal virus or viruses of encephalitis, so that a logical approach may be made to possible preventive measures in the future, especially in the event of an epidemic.

This is a difficult field in virus research and quick results are not the rule. In most cases the causative organism is not isolated from CSF etc. and the diagnosis frequently rests on rising antibody titres, and complement fixing antibodies. Occasionally, autopsy material (brain stem, etc.) will reveal the presence of virus. One such recent case in a child admitted to a Halifax hospital revealed the causative agent to be herpes simplex.

In the U. S. A. it has taken years of clinical research to determine the pattern and distribution of viral encephalitides and the work is still far from complete, complicated by the difficulties involved in isolating the causative agent. By way of example in 1957, there were 2,135 reported cases of encephalitis in 45 states, with 6 deaths and viral diagnosis confirmed in only 139 cases.[44] (This particular report refers only to arthropod-borne encephalitis).

The collection of data and assessment of encephalitis in Canada has been complicated by the fact that the disease has not been reportable in the past, so that no true figures are available as to incidence, complications, mortality

rates, etc. Most of the available figures are from Western Canada, where the only known epidemics have occurred; caused by the arthropod-borne virus of Western Equine Encephalitis. This serotype caused epidemics in both humans and horses in Saskatchewan in 1936 and 1937, Saskatchewan and Manitoba in 1941.[45, 46]

East of Manitoba, sporadic cases only have occurred with no figures available as to incidence, cause or sequelae. It is probable however, that encephalitis of the arthropod-borne type is very rare in Eastern Canada, only two cases having been reported over the years. One of these was reported in a child from Montreal in 1957 in which there was serological evidence of infection with Western Equine Encephalitis.[47] The other, an autopsy case was recently reported from Toronto by McLean[48] in which a virus was isolated, antigenically related to Russian Spring-Summer Encephalitis, and different serologically from previously described arthropod-borne viruses in North America. Attempts are proceeding at isolation of virus from wild-caught arthropods in the region.

In the U. S. Atlantic Seaboard, Eastern Equine Encephalitis has occurred in epidemic, endemic and sporadic form, extending as far north as Massachusetts, where epidemics occurred both in humans and horses in 1938, 1955 and 1956.[49, 50].

A preliminary survey reveals that over 30 cases diagnosed as encephalitis have been admitted to two Halifax City hospitals alone, during the past 2 years, three of these cases ending fatally. Several other cases recovered but were left with serious permanent neurologic defects, including paralysis, Parkinsonism, dementia, and behavioural disturbances in children.

In the large land area encompassing the Maritime Provinces, there is no scientific information available as to the causal agents of encephalitis, and no knowledge as to whether arthropod-borne disease does occur with its concomitant animal and insect vectors. Likewise, there seems to be no evidence that cases resembling encephalitis lethargica have been recorded Economo's disease).

An attempt to accumulate this information, together with a survey of past cases from hospital records, with correlation of available histologic data from autopsy cases,and vigorous attempts at isolation of virus from all new reported cases of encephalitis, will be the subject of the proposed research of the regional virus laboratory, during the forthcoming (and succeeding) summers.

The classification of the viral encephalitides as we know them today, throughout the world, is difficult, but it is possible to group them causally for convenience. The grouping here provided is that devised by Olitsky and Casals.[51].

C.N.S. Infections caused by Neurotropic viruses which invade along axonal pathways. (According to Olitsky and Casals (1952).

Poliomyelitis
Rabies.

Arthropod-borne Encephalitides.[52]

St. Louis Encephalitis
Japanese B Encephalitis
Australian X disease
Western Equine Encephalitis (WEE)

Eastern Equine Encephalitis (EEE)
Venezuelan Equine Encephalitis
Louping-ill.
Russian Far East or tick-borne Encephalitis.

Encephalitides transmitted to man by direct contact with lower animals.

B virus (monkey)
Lymphocytic choriomeningitis (mice).

Encephalitides produced by viruses ordinarily non-encephalitogenic

Herpes simplex
Lymptogranuloma venereum
Mumps
Measles
Infectious Mononucleosis.

Viruses which are encephalitogenic in experimental animals, but not as yet known definitely to cause encephalitis in man.

A. "Tropical" viruses:

West Nile	Ilheus
Semliki Forest	Anopheles A
Bunyamwera	Anopheles B
Bwamba fever	Wyeomyia.

Others being studied in Africa and South America.

B. California:—
Durand's disease.
Pseudolymphocytic choriomeningitis
Encephalomyocarditis family. (Warren, Smadel and Russ).
Col. S. K. virus infection, Col. M. M. virus infection,
Encephalomyocarditis, 1945, and Mengo encephalomyelitis

Coxsackie group.

Neurologic maladies possibly having a viral etiology but for which as yet no infective agent has been identified:—

von Economo's disease (encephalitis lethargica, sleepy sickness)
Guillain-Barre syndrome (infectious polyneuronitis)
Herpes zoster.

Demyelinating encephalitides for which viral etiology has been proposed without convincing evidence:—

Acute primary haemorrhagic encephalitis or leuko-encephalitis.
Disseminated encephalitis.
Post-infection or post vaccination encephalitides occurring after:—
Measles
Influenza
Mumps
Chicken pox
Small-pox vaccination

Rabies vaccination
Infectious hepatitis
Dengue
German measles
Yellow fever
Lymphocytic choriomeningitis.

It is obvious that many of the exotically named conditions in the above listing do not constitute a problem in North America, but they are printed here merely for general information, and to give an idea of the scope of the problem of encephalitis, both causally and geographically.

It must be remembered that encephalitic syndromes may be produced by chemical substances (alcohol, barbiturates, etc.) protozoa, fungi, bacteria, spirochaetes and rickettsiae.

Encephalitis can also be divided into "epidemic" and "sporadic." Examples of epidemic encephalitis are St. Louis, Eastern and Western Encephalitis, Japanese B and Australian X disease. Sporadic cases of encephalitis include the post-infectious and post-vaccination group, herpes encephalitis, and so-called hemorrhagic leuko-encephalitis.

Mode of transmission forms another basis of classification. Thus, equine encephalitis, St. Louis encephalitis, Japanese B and Australian X are all spread by mosquitoes. Louping ill and Russian far eastern encephalitis are tick-borne. The method of transmission of encephalitis lethargica (if indeed this condition still exists as an entity), is not known.[53]

Casals[54] has shown recently that the arthropod-borne viruses may be placed into at least 3 immunologically distinct groups—A, B and C, on the basis of their hemagglutination-inhibition reactions in which the capacity of convalescent sera to inhibit the agglutinating effect of virus suspensions, is titred. In North America, group A members are, Eastern and Western Equine viruses, while St. Louis Encephalitis is the only group B member known to infect man.

The clinical features of encephalitis are of little help in classifying them. Brewis, in a study of over 90 cases of encephalitis in children, found no relation between the clinical features and the etiologic category.

In the world-wide family of virus encephalitides, there are many related strains, and this forms the basis of interesting speculation on the spread of these diseases throughout the world, and suggests that they may have had their descent from relatively few precursor organisms. For example, there is an antigenic relationship between West Nile, Japanese B encephalitis, and St. Louis Encephalitis.[55] Smithburn[56] found that Japanese B immune sera neutralized both the St. Louis and West Nile viruses, that St. Louis immune sera neutralized the West Nile virus, but not the Japanese B, and that West Nile immune sera failed to neutralize either the St. Louis or Japanese B Viruses. Of interest in this respect, is the report of McLean[48] from Toronto of the Powassan virus, antigenically related to the Russian Spring-Summer disease, and the first such case reported on this continent, especially in view of the similarity in climate, geography etc. between Canada and Russia. Murray Valley encephalitis, which is probably a recent recurrence of the Australian X disease of 25 years ago, is very closely related antigenically to Japanese B virus, and may indeed be the same virus.

Hammon in 1948 suggested that the whole group of arthropod-borne encephalitides may be related and indeed derived from one common stem

virus.[57] The clinical manifestations are similar.[58] Following an incubation period of from 4-21 days, the onset of illness is acute with severe headache, dizziness, photophobia, nausea and vomiting, and fever which may be low-grade, usually lasting one to two weeks. Some cases do not develop definite signs of involvement of the central nervous system, but in typical cases, these symptoms at the onset of illness are followed by encephalitic symptoms with neck rigidity and mental confusion; then nerve paralysis, especially affecting the muscles of the eyes, causing squints and diplopia, may develop. Aphasia may occur. Often the patient becomes stuporous and even comatose. Death occurs in approximately one-third of the cases, nearly always within 2 weeks of onset. Two-thirds approximately of the non-fatal cases, recover completely. The remainder are left with sequelae, such as headache, irritability, loss of memory, lethargy and Parkinsonism.

It will be noted that many of these encephalitides are relatively rare in occurrence and represent types of disease not seen on the North American continent. The fact remains that there is abundant clinical and pathological evidence however, that encephalitis does occur with frequency in North America. In Nova Scotia, encephalitis is lpresent but the aetiological background here, as in many other areas of Canada, is not known.

In the Atlantic Provinces of Canada, it is logical to assume that, if arthropod disease does occur, and this must be rare, the virus to be suspected would be that of Eastern Equine Encephalitis, which has been seen in epidemics in Massachusetts as recently as 1955. This disease, though usually diagnosed in epidemic times, can also occur sporadically. To our knowledge, no epidemic encephalitis has ever occurred in the Maritime area, except for two outbreaks of aseptic meningitis due to Echo 9 virus, reported by this laboratory in 1958. In view, however, of the number of ocean ports in this area, one would have to be constantly on the lookout for imported disease from other parts of the world.

At this point a brief discussion of a recently described epidemic illness of possible viral aetiology, might be worthwhile, especially in view of reports coming in from widely scattered areas of the world, all in temperate climates. This disease, variously labelled Iceland disease, Akureyri disease, benign myalgic encephalomyelitis, epidemic neuromyasthenia, was first described in an outbreak in the town of Akureyri, Iceland by Sigurdsson et al.[59] 465 cases simulating poliomyelitis were listed out of a population of 6900, the attack rate being 6.7%. Paresis was observed in 129 cases, with no deaths, and the incidence was highest in the age group 15-19.

The incubation period is about one week[60] with symptoms of insidious onset. Initially there is low fever with headache, especially in the back of the head and nape; and pains in the back and shoulders are also common.

The painful muscles are usually tender to the touch—sometimes extremely so. The patient complains of tiredness, particularly after even slight exertion. These symptoms usually disappear in a few days to a few weeks, but may persist for months or even for years, and the chronicity of this epidemic illness is part of its special interest. Many patients complain of insomnia, nervousness and loss of memory, with vertigo and postural giddiness. Persistent neurasthenic complaints seem to be most common in those patients with a prominent antecedent history of psychoneurosis.

In some cases, paresis develops from 2 days to four weeks after the onset of the disease, or may improve and then recur The paresis, usually limited to one muscle or muscle group, may be accompanied by diminish-

ed tendon reflexes. The recovery may be very slow. Paresthesias and numbness or hyperesthesia and hypoalgesia are sometimes observed in the affected limbs.

Examination of the spinal fluid may reveal slightly elevated protein, with cells being in the normal range in most cases.

Recent epidemic outbreaks of a similar illness have been reported in institutions in England and South Africa.

Faeces have been tested for poliomyelitis virus and Coxsackie virus, but no consistant findings have been reported. To our knowledge no cases of this type have been reported in Canada.

Encephalitis in the Maritime Provinces, is sporadic only in its occurrence, and a preliminary analysis of 30 cases admitted to two Halifax area hospitals in the past two years indicates that there is little seasonal variation in incidence with cases occurring through the 4 seasons of the year.

Sporadic encephalitis has received much less attention in the world literature than the epidemic form, possibly because of the multiplicity of its causes, only a few of which are known definitely to be due to specific neurotropic viruses.

In this group is the encephalitis caused by herpes simplex, a rare and fulminating complication of a virus which is very common and widespread, being found in such conditions as the common herpes labialis and herpetic gingivo-stomatitis, often seen in epidemic form among young children in summer months. Serological surveys show that about 60% of the general population has antibodies to herpes, giving some idea of its prevalence.

Primary herpetic infection in infants may be very severe, especially in those who lack passive immunity from their mothers. Fatal cases with lesions in liver, adrenals and central nervous system have been described.[61] One recent such case occurred in Halifax with a child dying after only 4 days of encephalitic symptoms. Herpes virus was grown from brain tissue taken at autopsy. In a series of 854 cases of aseptic meningitis reported by Adair et al,[62] herpes simplex was diagnosed serologically 6 times.

At least three other rare varieties of sporadic encephalitis, with possible virus etiology have been described.[63] (1) Acute hemorrhagic leukoencephalitis, an usually fatal illness featured by fits, paralyses and coma, with histologic changes in blood vessels showing capillary necrosis with concomitant hemorrhages in the brain, marked leukocytic infiltration and widespread perivascular and focal demyelination. A hypersensitivity mechanism, involving the C.N.S. has been suggested as the cause. Two such cases, one of which survived, were reported in 1957 from the Halifax area by McLetchie and Stevenson.[64] (2) Subacute inclusion body encephalitis is a chronic progressive illness with personality changes, mental deterioration, optic atrophy, convulsions and progressive paralysis. Large eosinophilic inclusions are found in nerve cells and neuroglia. Demyelination is noted in the white matter of the brain. (3) Subacute sclerosing leukoencephalitis is a histologically similar condition, which may in fact be identical. Herpes virus has been isolated from a case similar to type (2) above. Post infectious and post-vaccination encephalitis should be classified under sporadic causes of encephalitis especially in childhood. Although often associated with outbreaks of contagious disease the syndrome occurs sporadically and rarely within these epidemics.

The illness usually begins five to fourteen days after the primary infection, and takes the form of an acute disseminated encephalomyelitis, with histological

features of perivascular lymphocytic cuffing, hemorrhage and oedema of brain substance. Demyelination of the white matter may occur. The spinal cord may be similarly involved resulting in cases of lower or upper motor neuron type of paralysis.

This illness has been described following measles, rubella, influenza, mumps, infectious mononucleosis, small-pox vaccination, very rarely after immunization with typhoid or pertussis vaccine, and anti-tetanus serum. Rabies vaccine will occasionally result in a neuroparalytic accident due to axonal degeneration above and around the area of vaccination.

Mumps encephalitis, because of the known neurotropic tendencies of the mumps virus is the only one of these conditions which may be a true encephalitis. The remainder of these conditions, with the possible exception of chicken pox may constitute a group of hypersensitivity reactions involving the central nervous system. Some clinicians, on this basis, favour treating these conditions with steroids.

Mumps encephalitis deserves special mention here, because a preliminary survey indicates that it is a relatively frequent cause of encephalitis in the Maritime area.

It is felt by many that mumps is a viremic illness with a predilection for glandular and nervous tissue. The mumps virus has definite neurotropic tendencies, and mumps virus can be isolated from the spinal fluid of patients with mumps meningoencephalitis. The buccal cavity can be the portal of entry for the virus but the long incubation period suggests that the virus does not reach the parotid glands via Stenson's ducts. The mumps virus, like that of rabies may reach the C.N.S. by way of the peripheral nerves.

In a report of approximately 250 cases of mumps in a rural area of Saskatchewan studied by Bowers and Weatherhead[65] the authors felt that approximately 25% of all cases of mumps might be expected to manifest mumps meningoencephalitis with a large proportion being found in those cases of mumps showing high fever, vomiting and complaining of headache. In fact, it could be said that transient meningeal irritation may be a feature of many cases of mumps and that if lumbar puncture were done routinely in such cases, there would be a large percentage showing lymphocytic pleocytosis. The diagnosis of mumps encephalitis today requires the isolation of virus from the spinal fluid, which should not prove too difficult in those cases where material (CSF) is received early in the illness. The mumps complement fixation test may be used to confirm the diagnosis. Infection with the mumps virus which has two antigens "S" and "V" results in the formation of antibodies which may be designated anti-S and anti-V. Anti-S is often present in the sera of mumps patients before there is any appreciable level of Anti-V. Rising titres of Anti-S and Anti-V in two-phase acute and convalescent sera, which should be at least four-fold suggest recent mumps infection.

While mumps encephalitis carries a good prognosis and permanent sequelae are uncommon, occasional cases with apparent demyelination have been reported in which permanent muscular weakness or paralyses occur, following the infection.

Although studies of sporadic encephalitis are infrequent in the medical literature, one of the best reviews on the subject was published by Adair et al in 1953.[62] They reviewed 854 cases submitted over a period of 11 years, occurring among military and veteran personnel in the United States. They found that approximately 9% of their cases were caused by infection with lymphocytic

choriomeningitis virus and 12% with mumps virus. Studies on a portion of the patients in their series indicated that herpes simplex was responsible for about 5% and the leptospires for about 7% of their total group. They found no specific aetiological agent in approximately three-quarters of the cases of sporadic aseptic meningitis studied. Since the publication of this work newly developed diagnostic procedures and techniques may be expected to reduce the size of the undiagnosed group.

Clinical symptomatology which should arouse suspicion of possible encephalitis include the following:—

(a) Sudden unexplained death in infants.
(b) Febrile fatal illnesses in children accompanied by convulsions, coma, lethargy, altered sleep rhythm.
(c) Febrile illness in children or adults associated with headache, mental confusion, meningeal signs, positive Kernig, Brudzinski sign, abdominal pain and gait disturbances.
(d) Low grade febrile illness in children or adults associated with personality changes, psychotic behaviour, anorexia, somnolence with unexplained ocular or other cranial nerve palsies, upper or lower motor neurone paralyses, or weakness of extremities.
(e) Any prolonged unexplained fever with irritability and anorexia.
(f) Any case in which lumbar puncture reveals a pleocytosis without evidence of space-occupying lesion or bacterial causes.

SPECIMENS REQUESTED FROM CASES OF SUSPECTED ENCEPHALITIS

Since we do not know what virus or viruses we expect to find, in our Atlantic Province survey, nor in what tissues they are likely to be found, the following specimens should be submitted.

(a) From EARLY acute febrile patients, collect 5 cc. of blood to which 1 ml. of a 1 percent solution of heparin should be added to prevent coagulation of blood. DO NOT use citrate or oxalate as anticoagulant. Such blood will be inoculated intracerebrally in mice. The blood should be shipped frozen, since haemolysis of red cells does not appear to injure the infectivity of virus.
Also collect 15 cc. of 2 two phase acute and convalescent blood samples (not less than 3 weeks apart) from which the sera should be separated, as in the case of Echo infections, and these should be frozen and shipped to the Laboratory.
(b) Cerebrospinal fluid. Ship frozen in dry ice.
(c) Stools—Ship frozen in sterile screw-capped jar packed in dry ice.
(d) Saliva, sputum, throat washings—Should be gathered in a sterile screw-capped jar, and shipped frozen in dry ice.
(e) Autopsy material. The main reason why more is not known about sporadic encephalitis is because the diagnosis is frequently not made until the pathologist has examined microscopic sections of brain. By this time all the tissue is usually fixed in formalin and none is available for virus culture. To overcome this difficulty, many pathologists in the U. S. A. make a routine of placing fresh pieces of brain and other tissues in sterile containers and freezing same until histological examination of formalin fixed tissue has been completed.

A second reason why little virus research has been carried out on sporadic encephalitis is because, in suspected cases, material has not been removed at autopsy with aseptic surgical precautions, so that if and when a virus is isolated, no reliance can be placed on the result.

Material desired at autopsy, preferably 2 to 3 hours after death, should include cerebral cortex, mid brain, pons, spinal cord, liver, lung, spleen, salivary gland and segment of tied-off large bowel. All these should be placed in sterile screw-capped jars, packed in dry ice and shipped to the Laboratory.

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CANADIAN LIFE INSURANCE MEDICAL FELLOWSHIP FUND

Financial assistance from the Canadian Life Insurance Medical Fellowship Fund has been granted to thirteen medical research workers at ten medical schools of Canadian Universities. The aggregate amount awarded by the Fund this year is in excess of $64,000 and the individual fellowships range in value from $3,500 to $6,000.

Five of the thirteen are new investigations and the other eight are renewals from previous years. All fellowships are for the period July 1, 1959 to June 30, 1960. Included among the fellowships awarded is one to Doctor J. J. Sidorov, Dalhousie University, for the continuation of a research project on obesity.

INFECTIOUS DISEASES—NOVA SCOTIA
Reported Summary for the Month of April, 1959

Diseases	NOVA SCOTIA 1959 C	NOVA SCOTIA 1959 D	NOVA SCOTIA 1958 C	NOVA SCOTIA 1958 D	CANADA 1959 C	CANADA 1958 C
Brucellosis (Undulant fever) (044)	0	0	0	0	11	0
Diarrhoea of newborn, epidemic (764)	0	0	0	0	10	0
Diphtheria (055)	0	0	0	0	3	0
Dysentery:						
(a) Amoebic (046)	1	0	0	0	1	0
(b) Bacillary (045)	0	0	0	0	48	0
(c) Unspecified (048)	0	0	0	0	3	0
Encephalitis, infectious (082.0)	0	0	0	0	1	1
Food Poisoning:						
(a) Staphylococcus intoxication (049.0)	0	0	0	0	0	0
(b) Salmonella infections (042.1)	0	0	0	0	0	0
(c) Unspecified (049.2)	0	0	0	0	34	0
Hepatitis, infectious (including serum hepatitis) (092, N998.5)	20	0	25	1	299	0
Meningitis, viral or aseptic (080.2, 082.1)						
(a) due to polio virus	0	0	0	0	0	0
(b) due to Coxsackie virus	0	0	0	0	0	0
(c) due to ECHO virus	0	0	0	0	0	0
(d) other and unspecified	0	0	0	0	9	0
Meningococcal infections (057)	4	0	1	1	23	30
Pemphigus neonatorum (impetigo of the newborn) (766)	0	0	0	0	0	0
Pertussis (Whooping Cough) (056)	0	0	19	0	351	358
Poliomyelitis, paralytic (080.0, 080.1)	0	0	0	0	0	2
Scarlet Fever & Streptococcal Sore Throat (050, 051)	54	1	192	0	1902	694
Tuberculosis						
(a) Pulmonary (001, 002)	30	6	18	2	515	424
(b) Other and unspecified (003-019)	0	0	4	0	0	41
Typhoid and Paratyphoid Fever (040, 041)	0	0	0	0	190	24
Venereal diseases						
(a) Gonorrhoea — Ophthalmia neonatorum (033)	0	0	0	0	0	0
All other forms (030-032, 034)	12	0	16	0	1070	1005
(b) Syphilis — Acquired—ordinary (021.0, 021.1)	0	0	0	0	0	0
— secondary (021.2, 021.3)	2	0	0	0	0	0
— latent (028)	2	0	0	0	0	0
— tertiary — cardiovascular (023)	0	0	0	0	0	0
— „ — neurosyphilis (024, 026)	0	0	0	0	0	0
— „ — other (027)	0	0	1	0	150*	170*
Prenatal—congenital (020)	0	0	0	0	0	0
Other and unspecified (029)	0	0	0	0	1	0
(c) Chancroid (036)	0	0	0	0	0	0
(d) Granuloma inguinale (038)	0	0	0	0	0	0
(e) Lymphogranuloma venereum (037)	0	0	0	0	0	0
Rare Diseases:						
Anthrax (062)	0	0	0	0	0	0
Botulism (049.1)	0	0	0	0	0	0
Cholera (043)	0	0	0	0	0	0
Leprosy (060)	0	0	0	0	0	0
Malaria (110-117)	0	0	0	0	0	0
Plague (058)	0	0	0	0	0	0
Psittacosis & ornithosis (096.2)	0	0	0	0	0	0
Rabies in Man (094)	0	0	0	0	0	0
Relapsing fever, louse-borne (071.0)	0	0	0	0	0	0
Rickettsial infections:						
(a) Typhus, louse-borne (100)	0	0	0	0	0	0
(b) Rocky Mountain spotted fever (104 part)	0	0	0	0	0	0
(c) Q-Fever (108 part)	0	0	0	0	0	0
(d) Other & unspecified (101-108)	0	0	0	0	0	0
Smallpox (084)	0	0	0	0	0	0
Tetanus (061)	0	0	0	0	0	0
Trichinosis (128)	0	0	0	0	0	0
Tularaemia (059)	0	0	0	0	0	0
Yellow Fever (091)	0	0	0	0	0	0
Pneumonococcal Meningitis	1	0	0	0	0	0
OTHER (haemphilus influenza Meningitis)	1	0	0	0	0	0

C — Cases D — Deaths

*Not broken down

Society Meetings

Halifax Medical Society

Since last reporting on the activities of the Halifax Medical Society we have completed the 1958-59 meetings and a new slate of officers has been elected for 1959-60. They are -

President - Doctor J. W. Merritt.
Vice-President - Doctor D. M. MacRae.
Secretary - Doctor H. C. Still.
Treasurer - Doctor R. W. M. Ballem.

Other members of the Executive—Doctors L. A. Rosere, J. R. MacLean, J. H. Charman, R. L. Aikens, J. S. Robertson and R. J. Weil.

The names of the following members were nominated to be Representatives on the Executive of The Medical Society of Nova Scotia—Doctors J. W. Merritt, D. M. MacRae and A. M. Marshall.

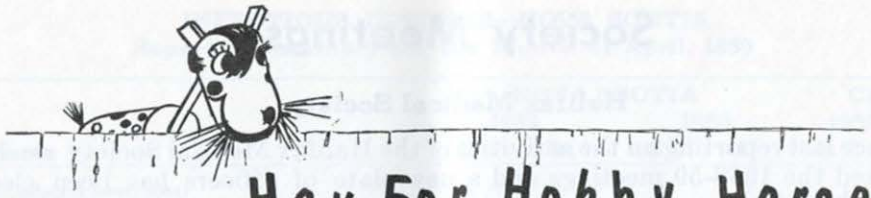
The Annual Business Meeting of the Society at which these nominations were approved took place on Thursday, April 30th at the Dalhousie Public Health Clinic, and the President and Officers were officially installed at the Annual Dinner Dance held at the Lord Nelson Hotel on Wednesday, May 6th.

At the Business Meeting reports were heard from the Secretary, the Treasurer and Auditors, from one of the Representatives on the Executive of The Medical Society of Nova Scotia (Doctor F. A. Dunsworth), from the Chairman of the Mediation Committee, and from a Representative on the Board of Maritime Medical Care, Doctor F. Murray Fraser. Doctor Fraser outlined some of the changes proposed by Maritime Medical Care which will be implemented on July 1st. He was congratulated by several speakers on the excellence of his report and the hard work which he had put in since becoming President of that organization.

Other meetings during 1959 were held at Camp Hill Hospital in January, Children's Hospital in February, R.C.N. Hospital in March, and Nova Scotia Hospital, Dartmouth, in April. This was the first meeting to be held at the Nova Scotia Hospital for a number of years. A clinical programme was presented in the form of a symposium on "Modern Methods of Psychiatric treatment in use at the Hospital," with various members of the hospital staff taking part. Subsequently interested members were taken on a tour of the newly completed hospital.

During the year concern was expressed at the poor attendance at regular meetings, averaging less than forty out of a total membership of over two hundred, and a Committee under the chairmanship of Doctor A. B. Crosby has been set up "to explore ways and means of improving attendance at regular meetings of the Society."

H. C. STILL, M.B.,
Secretary.



Hay For Hobby Horses

THE 106TH ANNUAL MEETING

The column for July will celebrate the 106th Annual Meeting of The Medical Society of Nova Scotia held at Keltic Lodge, Ingonish Beach, Cape Breton. We are the oldest medical society in Canada and one of our own, Sir Charles Tupper, was the first President of The Canadian Medical Association. (I had to be told these interesting things by Art Peart, the amiable assistant secretary of The Canadian Medical Association).

The Medical Society of Nova Scotia can be a pacemaker in Canadian medical affairs, despite its relatively small size numerically speaking, if enough of us keep vigorous and responsive to the important issues confronting us. We have had evidence of hard work, clear thinking and a flexible approach in the conduct of our Society in the matter of chiropractic and hospital insurance legislation. However, our effectiveness depends on the willingness of the majority of our members to keep informed and hold themselves responsible for the decisions reached in the name of the Society. This willingness is expressed by activity at the branch levels and attendance **and participation** in the business sessions of the annual meeting. The handwriting on the wall is there for all to read "Physician—Act to-day or to-morrow Big Brother will act for you."

The profession is caught up in a variety of complex problems in a socio-economic atmosphere that can, and does, change rapidly. Unless we are alert, informed and ready to respond to these trends promptly we may awaken to find our chance to mold the future lost by default.

The reports of the standing and special committees and representatives of The Medical Society of Nova Scotia ran to seventy pages this year. It is a good production and our executive secretary and his staff deserve our thanks. The reports deal with many topics, some of critical importance to every practising physician. Unfortunately there was scant time to deal with many of these topics in the general meeting. The most important function to be served by these annual meetings is deliberate examination of the business of our provincial society. The warning given by Hal Devereux during his address as retiring president was pertinent. "Don't leave the affairs of the society in the hands of the executive." I am sure no one would endorse this warning more heartily than do past and present members of the executive.

The Canadian Medical Association declared for the principle of pre-paid health care almost three decades ago.

However, approval in principle and passive good will are not enough—the medical profession charged with the responsibility for health care must play a large part in designing and implementing health care plans. This view of the future places on us onerous, and for most physicians, unfamiliar burdens. The alternative to the greater participation in pre-paid health care by organized

medicine is greater participation by "third-party" agents. The basic fact of the modern political scene is this "the public will get what it wants in health insurance—if not through us, then in spite of us."

The Medical Society of Nova Scotia sponsored its own pre-paid medical plan ten years ago. Physicians in this province have had mixed feelings about Maritime Medical Care Inc. "The initial premium was much too low for the services provided." "We (the profession) have been subsidizing medical care for ten years." "It is only bought by people who need the protection of prepayment least" etc. Despite miscalculations and misadventures our "baby" has survived and even grown a little but it must increase five or six fold in the next few years in order to fulfil its capacities. The time has come when we must make a real effort to bring a higher percentage of the people of Nova Scotia under Maritime Medical Care coverage at a lower premium wherever possible. In addition, the medical profession must evolve a health insurance programme to enable us to compete, wherever necessary, with large commercial carriers.

Such a matter as the future role of Trans-Canada Medical Plans can be ignored only at the risk of our corporate security. F. Murray Fraser has shown qualities of statesmanship in dealing with the perplexing problems of Maritime Medical Care and national affairs of Trans-Canada Medical Plans. His approach to the future of prepaid health care schemes is both realistic and farsighted. My understanding of the current problems in the provision of health insurance on a larger scale is this: The public wants health insurance with emphasis on ancillary services such as nursing, ambulance service and drugs. They are more apt to buy commercial plans that provide these services at the expense, or even complete neglect, of physicians' services. The public has only a rudimentary understanding of the essentials of a comprehensive health care plan. The medical profession acting through non-profit health insurance agencies, such as our own Maritime Medical Care Inc. must provide physicians' services plus the ancillary services in a package that will compete with the attractive, but incomplete plans of commercial carriers. Physicians' care must be the cornerstone of health insurance even though it maybe undervalued in the public mind and in the market place. The health insurance to be provided for groups like the Federal Civil Service may not include adequate provision for physicians' services unless the medical profession assists in the planning.

Hal Devereux made a very fine impression on your correspondent in his presidential address. When a man speaks from the heart his message overcomes any defect in style or expression. I did not see the newspaper account of his address but I carried away from it the strong impression that Hal Devereux has taken a realistic view of our progress and defects. His remarks about the future of medical care plans are reflected in the paragraph above. I am sure the incoming executive will have his words in mind as they pursue their deliberations. The Medical Society of Nova Scotia is fortunate to have a man like Hal Devereux available for future service.

High Spots and Random Jottings. These meetings are good for us all. The bonds of sympathy between our members are strengthened as they come to know each other better in a beautiful spot like Keltic Lodge. Most of the mistrust, suspicion and dissent that threatens to separate us can be dispelled by this one prescription; "Get to know your fellow physician better." This salutary benefit of improved intra-professional relationships would justify our meetings even if there were no important business to transact.—Martin Hoff-

man proved once again that he is a superb teacher. He avoids the stilted and soporific device of slides and relies on his vigorous delivery to carry the subject. Very few physicians could have come away without some benefit even though the topics "Diabetes" and "Common symptoms in office practice" were familiar to us all.—The mixed panel discussions on "The Medical Professions—How is it viewed by the Public" and "Health Insurance" were a worthwhile innovation. The local guests on the first panel, Mrs. J. Louis Dubinsky and Mr. Dan Joe MacIsaac, both of Glace Bay, made distinctive contributions. The ladies in the audience were obviously proud that Mrs. Dubinsky represented the distaff with such charming competence. Dan Joe handled one or two "hot grounders" with dexterity and finesse. Without mentioning the contentious name of Hoffa he compared labor unions with the doctor who operates successfully many times only to be damned for his occasional lack of success in a dramatic case. I hope for Mr. MacIsaac's sake and the sake of the nation that his analogy is accurate. Dan Joe got the following question from someone in the audience. "Why does John Doe pay the TV repair man $5.75 per call on the spot and complain when a new scale of fees for the medical profession will pay the physician less?" Dan Joe replied "People don't call the TV repair man unless they have $5.75." Nicely done!—Frank Dunsworth displayed a hitherto unsuspected knowledge of the mysteries of pharmacology and therapeutics, to a fascinated audience he described a new triumph of medical science called Bigbaxin. This is a subtle compounding of a muscle relaxant and an aphrodisiac that solves an hitherto unsurmountable difficulty in later life. He also described Span-Tran and other novel dosage forms of a well known happiness drug. The best story I heard at the convention was told by Hal Baker and concerned the situation in which an executive was showing his niece through an extremely well equipped Cadillac.

A few of our brethren who arrived late on Tuesday evening had to navigate Cape Smoky in dense fog. Ian and Patsy MacGregor in station wagon and trailer manned by a crew of seven made the spine tingling circuit.—Jim Reid's prescription for the nervous on Smoky is "let the air out of your tires so you won't slide and turn out your lights so you won't be scared."—The Lobster Party on the beach featured a mixed choir from the Pictou County Medical Society under the direction of Doctors Granville and Parker—a few lobsters—and a hungry and disgruntled band of golfers who tarried too long on the 19th hole—the Keltic Coffee Shop was inundated by hungry chilled boisterous merry-makers immediately after—coffee shop harmony was provided by Jack and Shirley Kerr, Hal and Kay Read, Clarence and Doris Young, Hugh and Mary MacDonald, with the Tompkins clan in the background.—

I was happy to be present when John C. Ballem, Dean of the Pictou County Medical profession was made a senior member of The Canadian Medical Association—his action in asking his fellow practitioners to stand with him was characteristic.

All in all it was a grand meeting—hope to see new friends and old at the 107th next year.

Fraternally yours,

BROTHER TIMOTHY.