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The NOVA SCOTIA MEDICAL BULLETIN

Editorial

Impaired Driving

Prosecutions for impaired driving in this Province are brought under an Act which is generally descriptive of the crime and does not specify, for example, necessary guilt in the event of a person in charge of a motor vehicle being found to have a certain numerical alcohol or drug level. The connotation of the description of faculties "impaired by alcohol or any drug or substance" has several implications for medical practitioners.

One implication of the wording of the Act is that the impairment need not be by alcohol and, while almost any drug may in certain circumstances impair, there has been a recent increase in the number of drugs which are liable to do so in normal dosage. These include sedatives, tranquilizers, muscle-relaxants and antihistamines, all in common use and the last available without prescription in cold cures. As packed by the manufacturer, these drugs usually include, somewhere in the accompanying literature, a warning, but this will ordinarily not reach the patient when the drug is supplied on prescription. A responsibility thus devolves on the physician to warn such patients that it may be dangerous to operate sewing machines or power mowers and criminal to be in charge of a motor vehicle while taking the drug. It may well become necessary for physicians themselves to give the patient a printed warning to this effect or to arrange for dispensing pharmacists to do so.

Secondly, the evidence as to impairment will ordinarily be the testimony of a police officer, possibility augmented by that of other witnesses and occasionally by an examining physician. It is unlikely that laboratory reports on the levels of alcohol or drugs in blood or urine will be presented as evidence.

Even if an accused consented to body fluids being sampled at the time and a physician cooperated in obtaining these and they were properly transmitted to a laboratory and competently analyzed, - there would be formidable difficulties in presenting these laboratory findings as proof of impairment. The court or opposing counsel would certainly object to the introduction of text-book evidence, from which the degree of impairment might be inferred from the result of the analysis. It would apparently be necessary to have a witness or a combination of witnesses who could testify from personal experience to the correlation of blood levels and impaired performance. A few such witnesses are available outside the Atlantic Provinces as the result of cooperative trials

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of effect of alcohol on driving performance conducted by police, chemists, and physicians. These witnesses are in fact occasionally called by the courts to make special interpretations but the mere knowledge that they are available is sufficient in all ordinary cases and they are not called, the lab findings are entered in evidence and the chemist or police witness is allowed to base an opinion on these.

A test case, depending on planned or fortuitous cooperation of accused, of physician and counsel in this Province might have a marked effect on future prosecutions and make quite acute the ethical and legal aspect of evidence based on body fluids obtained from accused persons.

W.A.T.

FROM THE BULLETIN OF FORTY YEARS AGO

The Medical Society of Nova Scotia Bulletin, July, 1923.

The matter of an official organ for the Medical Societies, or a Bulletin for the profession generally, should receive your careful consideration. It cannot be worth the money unless Secretaries of affiliated Branches will materially assist in its preparation. With few exceptions, little material has been furnished the Associate Secretary for publication. You want the "Bulletin" to advise you what is being done by the Society from time to time, and also as a friendly bond between doctors from one end of the Province to the other. These Bulletins cost delivered in the Post Office practically $125.00 per issue. To be worth this money it should be regarded as your Bulletin rather than that of the Associate Secretary. If anyone is inclined to minimise the work necessary in the preparation of such a Bulletin, especially with little or no co-operation, he can easily have his wrong impressions rectified, by undertaking the issue of the next two Bulletins himself. Any material that the Associate Secretary has would be gladly made available for such a volunteer editor. There can be no question whatever but that such a publication, at least quarterly, is absolutely necessary in the best interests of the profession in this Province. It is your business to see that it fills the bill.

It seems that forty years ago the Editor had an even greater problem in getting copy for the Bulletin than we do today. Nevertheless, what was true then is true today, and especially the need of help from the Branch secretaries in the way of news of a personal interest nature. All members are reminded that Dr. Nichols is always on the look out for material, and that "what interests you probably will interest other members". - Editor.)

Iron Metabolism - A Review of Current Concepts

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In order to understand the pathophysiology of practically all the major hematological disorders, a general understanding of the principles of iron metabolism is required. Moreover, some phase of iron metabolism is often disturbed in conditions in which the underlying abnormality is not primarily hematological — as infections, inflammation and chronic renal or hepatic disease.

Thirty years ago very little was known about iron metabolism and iron deficiency was not recognized as a clinical entity. During the first three decades of this century, chlorosis was commonly regarded as a form of neurosis, attributable to tight corsets, endocrine disturbance, toxemia or a variety of other diseases. Between 1930 and 1950 tremendous strides were made in the understanding of iron metabolism, but some of the conclusions must be re-evaluated in the light of modern knowledge, particularly that gained from isotopic studies.

Body Content of Iron:

The total body iron content of the normal adult is somewhere between two and six grams (a 70 kilogram man having about 4.2 grams.) Vanishingly small amounts are present in inorganic iron compounds or in ionized forms. Two general types of iron compounds are found in the body. (1) iron porphyrin (heme) compounds concerned with the transport, storage and activation of oxygen: — hemoglobin, myoglobin, cytochromes and other heme enzymes (2) non-heme compounds of iron chelated* to protein which function in the transport and storage of iron: — transferrin, ferritin and hemosiderin.

About two-thirds of the body iron is present in circulating hemoglobin and myoglobin and because of the rapid turnover of these compounds, this is the dominant role of iron. Small amounts are present in respiratory enzymes and the transport iron binding protein-transferrin. The remainder is stored in the liver, spleen, bone marrow and gastro-intestinal tract as ferritin and hemosiderin.

Nutritional Iron Balance:

Only recently, acceptable approximations of iron balance have been possible. Prior to the advent of radio-isotopes, long term balance studies were hopelessly inaccurate because of the small quantities to be analysed. However, now that naturally occurring foodstuffs can be labelled with radioactive iron, iron can be followed through absorption, utilization, storage and excretion. The over-all conclusions from these studies are that a normal individual absorbs 5-10% of ingested iron. The average diet contains 10-15 milligrams of elemental iron, so that 1-1.5 mgm. of iron is absorbed daily. This work was

*Chelation is a loose form of linkage between one compound and another, comparable with absorption.

done by Moore and has been repeatedly confirmed both by determining the amount of iron built into hemoglobin (circulating red cell) and by measuring the difference between amounts absorbed and excreted.

Iron has been referred to as a "one way" substance in its metabolic behaviour implying that it is locked into the body, once absorbed, and that loss is very restricted. This is because of the intracellular location of most of the iron in the body and because of the tight chelation of the small fraction in transit through the plasma. However, all cells contain iron enzymes and small amounts are being continually lost by desquamation and in body secretions e.g. bile. Small amounts are regularly found in sweat but this could be derived from desquamated epithelial cells. By careful balance studies with isotopes and by following the specific activity of the red cell mass after Fe^{55} labelling, the amount lost has been estimated at 0.5-1.5 mgm. per day. Therefore, in the adult male the intake balances the loss but in the growing individual, or female in the childbearing age, further consideration is necessary. Losses from menstruation, pregnancy and lactation increase requirements by another 0.5-1.5 mgm. daily making the balance extremely precarious.

Body Iron Turnover:

Since McCance and Widdowson in 1937 demonstrated that very small amounts of iron are excreted, attention centered on the role of the absorptive process in regulating body content. Generally speaking, in this process dietary iron is rendered suitable for absorption, enters the mucosal cell, is passed on to the transferrin of the plasma and ultimately is deposited selectively in certain tissues.

Iron exists in food largely as ferric hydroxide complexes, trivalent iron directly chelated to proteins, amino acids and organic acids or as heme iron complexed to proteins. It has been well demonstrated that iron is absorbed almost entirely in the divalent or ferrous state with only a small amount of trivalent ion or chelated complexes being absorbed directly. Therefore, most of the food iron is made soluble and reduced prior to absorption. It is absorbed mainly in the duodenum and upper small intestine, this being probably due to luminal factors such as pH and redox potential rather than any inherent difference in the mucosal cells. Only insignificant amounts are absorbed from the stomach. It has been suggested that gastric secretions may facilitate iron absorption by reducing the iron compounds. However, hematocrits and plasma iron levels are similar in patients with and without achlorhydria and quantitative measurements of iron absorption are normal in patients with achylia of pernicious anemia.

It has also been suggested that pancreatic juices may reduce iron absorption in the lower duodenum because they are alkaline and have a high phosphate content. Phosphates, carbonates and phytates favour the production of insoluble compounds and precipitates and markedly reduce iron absorption. Reducing substances increase iron absorption and this may be the way in which ascorbic acid in large doses functions.

Some insight into the problem of defining the role of various enhancing and blocking agents can be gained by studying the absorption of ionizable salts together with food. Absorption here is reduced to half or less of what would be obtained from a comparable dose of ferrous ion. It is obvious that food causes a marked reduction in iron absorption but whether this is due to the

iron-phosphate ratio, the presence or absence of various elements or the manner of preparation is not as yet well established. Iron is present in a number of foodstuffs and tables have been constructed to indicate the relative content in various food types. The most direct data on availability of iron in different foods have been obtained by tagging individual items with radio-iron and comparing the percentage absorption to that of an equivalent amount of ferrous salt.

Influence of Mucosal Factors:

Iron is transferred across the mucosal cell as part of an active metabolic process, the individual reactions of which are not known. Copper containing enzymes and xanthine oxidase participate. One of the most striking features of iron absorption is the way in which entry of iron into the mucosal cell stimulates the production of the protein, apoferritin. Apoferritin is believed to be the acceptor substance necessary for iron absorption and is a protein that is being continually made and broken down in the mucosal cell (Granick 1956). When combined with iron, ferritin is produced which is stable and is the form in which iron is stored. It has a molecular weight of 465,000 and contains some 17-23% iron by weight. Electron microscopy reveals that intestinal mucosal cells possess a brush border and Granick believes that apoferritin molecules are located there. When small amounts of iron are present in the gut, ferrous ion enters, is oxidized to the ferric form and then diffuses to the capillary side of the cells. It is there reduced to the ferrous ion and is chelated to the iron binding protein, transferrin, of the plasma. When larger amounts of iron are absorbed, some becomes bound to apoferritin forming ferritin. The mucosal cells form temporary storage for absorbed iron as evidenced by the fact that only 50% of absorbed iron enters the plasma within 4-6 hours of ingestion. Because of the rapid turnover of mucosal cells, much of the ferritin is lost by exfoliation.

Two controlling factors in the rate of absorption are the size of the iron stores and the rate of erythropoiesis. A decrease in iron stores results in enhanced absorption of iron salt, of iron administered with food and of labelled food iron. With increased iron stores there is a corresponding decrease of absorption. When erythropoiesis is stimulated, as by hemolysis or hemorrhage, absorption increases and a corresponding decrease is seen when erythropoiesis is slowed. The fact that marrow and mucosal cell activation parallel each other suggests that the response might be due to a common stimulus as erythropoietin.

At physiological levels of intake, absorption is the result of the amount of iron available in the diet and of mucosal efficiency. At high levels of iron intake, the mucosa is capable of transferring large amounts of iron and the factors limiting the amount absorbed are the capacities of transferrin and the tissue receptors.

Iron Transport:

Once across the mucosal cells the iron is picked up by a specific transport protein. This is a B_1 globulin with a molecular weight of 90,000 variously termed transferrin, siderophilin, iron binding protein and iron binding globulin. Each molecule of protein will bind two atoms of trivalent iron, which is tightly chelated in complexes and very stable at physiological pH. Normally, there

is enough transferrin to bind about 300 μg iron per 100 ml. plasma and it is usually only one third saturated.

It is not assimilated by the receptor tissues. Abnormally high levels of transferrin are seen in iron deficiency and the highest values are seen in the last trimester of pregnancy. Low values are found in association with impaired protein synthesis as in chronic renal or hepatic disease, chronic infections or malignancies. The mechanism of iron exchange to and from transferrin is not understood.

The normal level of serum iron is 100 μg/100ml. There is normally a rather marked diurnal variation but this is sometimes lost in disease.

Tissue Iron Stores:

When present in normal amounts (600-1500 mgm) iron is stored intracellularly in reticuloendothelial or parenchymal cells. It is distributed equally between ferritin and hemosiderin in the liver, spleen, bone marrow, gastrointestinal tract and other tissues. About 50% is in the liver.

Ferriten is formed by the combination of apoferritin and iron in the mucosal cells of the gut. Its molecules are not seen on light microscopy nor do they stain with Prussian blue. It is water soluble, contains 10-25% iron by dry weight, and all the iron can be removed without destroying the apoferritin structure. Most of the iron aggregates are found within the protein molecule but a small number of ferrous ions are present on the surface of ferritin stabilized by sulfhydral groups as pointed out by Mazur. These ions are easily dissociated in the presence of suitable conditions.

Hemosiderin is a normal constituent of most tissues and the granules are larger than ferritin molecules. They can be seen by the light microscope and take up Prussian blue stain. They are insoluble in water. However, recent studies by Richter show that hemosiderin granules are large aggregates of ferritin molecules with a higher content of iron.

Functionally, there are some differences between the two compounds. Normally equal amounts of liver and bone marrow storage iron are present as ferritin and hemosiderin. As the concentration of iron in tissues rises, both fractions increase but hemosiderin does so to a much greater extent. Thus in conditions of iron overload an increasing proportion is found as hemosiderin. There is evidence that ferritin is more available for erythropoiesis and that large aggregates of hemosiderin granules are relatively unavailable.

The most direct method of assessing iron stores is examination of fragments of sternal bone marrow for stainable iron. Decreased hemosiderin represents iron depletion, and when anemia is associated with decreased or absent marrow hemosiderin it is almost always due to iron deficiency. On the other hand, a number of mechanisms lead to increased marrow deposits, for example when there is (a) a shift of hemoglobin iron into tissues, as occurs in any anemia not due either to blood loss or to insufficient iron intake, (b) impaired release from reticuloendothelial cells as occurs in infections or (c) an absolute increase in storage iron as in idiopathic hemochromatosis or transfusional hemosiderosis.

The mechanism whereby iron is incorporated into tissue storage probably depends upon energy-producing oxidative metabolic reactions associated with the synthesis of adenosine triphosphate (ATP). This reduces the iron to the

ferrous state which liberates it from its bond to attach to the acceptor sulfhydral groups on the ferritin molecule. (Mazur 1958) Mazur also proposes that the adaptive enzyme xanthine oxidase is required for mobilization of iron from ferritin stores.

Two mechanisms have been described by which iron enters into the developing red cell and is made available for hemoglobin formation. Bessis and his associates have demonstrated so-called erythroblastic islands by electron microscopy. These consist of large reticulum cells containing many ferritin molecules surrounded by immature red cells — erythroblasts. Iron granules are drawn into the red cells where they again form clusters. These cells, called sideroblasts, gradually lose their ferritin as hemoglobin is formed and thus become mature red cells. On the other hand, *in vitro* studies by Jandl, Allen and Clark, showed that iron was transferred from transferrin by competitive binding to specific receptors on the cell surface, the amount being transferred depending on the saturation of transferrin. They demonstrated that iron was preferentially transferred to immature but not to mature red cells, that the transfer was direct without iron existing in the free form and that a metabolic energy — producing process was necessary. The reticulum cells were believed to function in removing iron granules from destroyed red cells (as occurs in the spleen) rather than functioning as intermediate cells in ferritin transfer. To date, no satisfactory agreement has been reached on ferritin transfer.

The final step in iron transport is its insertion into the porphyrin ring of haemoglobin. This occurs under strict enzymatic control. There is evidence that the enzymatic activity exists in the mitochondria of reticulocytes. Derangement of iron incorporation occurs in lead poisoning, Thalassemia and the anemia of infection and inflammation.

Ferrokinetics:

Iron transport is an extremely active process and dynamic measurements can be made by the use of tracer amounts of radioactive isotopes of iron. When proper amounts of Fe^{59} are added to plasma *in vitro* the element is firmly chelated to the unsaturated transferrin. This complex can be administered intravenously and the travels and destinations of iron followed by appropriate sampling or the detection of radioactivity using externally applied directional scintillation counters.

In a normal individual, all the administered iron is in the plasma initially. Seven-ten days later 90% is in the circulating red blood cells. The rate of disappearance of iron from the plasma can be followed by serial sampling of blood. In the normal, there is a rapid exponential decrease in radioactivity during a five to six hour period. About 50% of the iron is cleared from the circulating plasma in ninety minutes. This 50% plasma clearance or plasma turnover differs considerably in different disorders.

By external tracking of the radioactive iron, it can be concluded that virtually all the iron moves rapidly from the plasma to the bone marrow where it remains for about twenty-four hours. As the iron accumulates in the marrow, the counting rate monitored over the liver and spleen decreases. Within eight to ten days, 90% of the Fe^{59} has appeared in circulating red cells in the normal individual. An increase in utilization implies a relative or absolute lack of available iron and is characteristically found in iron deficiency, apparently due to low transferrin saturation. Decreased utilization is found in iron overload, aplastic anemia, in disorders of hemoglobin synthesis, and when erythropoiesis is ineffective in terms of viable cells.

"IRON METABOLISM — PART 2"

Iron Deficiency:

Iron deficiency is probably the most common cause of anemia in the world and certainly represents a major cause of morbidity and mortality. On the basis of the general principles of iron metabolism mentioned earlier, the situations in which deficiency may occur can be accurately delineated. Since intake and per cent absorption are limited, situations increasing iron requirement, as periods of rapid body growth, pregnancy and lactation and heavy menstrual loss, will deplete iron stores. When iron loss exceeds absorption as in chronic blood loss, iron deficiency will occur. This is usually occult or overt bleeding from the gastro-intestinal or genito-urinary tracts but can result from bleeding from many different sites.

Rarely, iron deficiency can be caused by paroxysmal nocturnal hemoglobinuria or other hemolytic anemias in the form of hemosiderin test from the renal tubules or by primary pulmonary hemosiderosis, a rare entity in which there is hemorrhage into the lung tissue. Malabsorption over prolonged periods may upset the balance as in steatorrhea or poor absorption following gastric surgery. As long as the excretion is about one mgm. a day, a pure deficiency secondary to inadequate intake would take at least five to six years and is for practical purposes never seen in adults in this country.

Although iron deficiency has often been considered synonymous with hypochromic microcytic anemia, it is important to appreciate that the changes induced by iron depletion depend on the rapidity with which it develops and it is helpful to consider the changes induced by gradual depletion. In the initial phase, body iron stores become progressively reduced. This is referred to as latent iron deficiency and can be detected by histological assessment of the hemosiderin content of reticuloendothelial cells in the marrow. As long as there is enough storage iron to supply bone marrow requirements, the plasma iron and transferrin levels remain normal. At this stage the rate of iron absorption rises, as demonstrated by a plasma iron tolerance or turnover test. The second phase commences when stores are exhausted so that the bone marrow needs are not being satisfied. The plasma iron falls while the level of circulating transferrin rises and its saturation falls. Once the plasma ironfalls to about 50 mg% or the saturation of transferrin to below 15%, the impairment of hemoglobin synthesis leads to the production of red cells with a decreased hemoglobin content. The marrow, in an attempt to compensate, produces many small cells which are poorly filled.

Other rare causes of microcytic hypochromic anemia should be ruled out. Thalassemia is a rare familial anemia and is usually distinguished by the elevated bilirubin and reticulocyte count and normal or increased plasma iron. A similar picture can be caused by chronic infection or inflammation, lead poisoning or rheumatoid arthritis but here the underlying condition is usually obvious. Several cases of pyridoxine responsive microcytic hypochromic anemias have been reported and these can be diagnosed because of the increased marrow hemosiderin and plasma iron level and by the response to pyridoxine.

The treatment of iron deficiency is now one of the best understood and most effective means of therapy available to the physician. The basic objectives of treatment are to supply optimal amounts of iron for use by the bone marrow in the production of red cells and at the same time avoid toxic reactions from the iron itself. When the rate of blood loss is equal to, or exceeds the regenerative capacity of the marrow or the severity of the anemia threatens life, iron therapy can be supplemented by blood transfusion.

Optimal iron requirements by the erythroid marrow are between 0.3-0.8 mgm/kilogram daily and sufficient oral iron must be given to ensure that these amounts are absorbed. Ferrous salts are the standard preparations employed and these various salts — sulfate, gluconate, succinate and fumerate —are equally well absorbed. In general, the rate of hemoglobin response is over 0.2 gram/100 ml. daily in subjects with uncomplicated iron deficiency anemia when the initial hematocrit is less than 20%, with lesser degrees of response with higher hematocrits. In a patient who is not bleeding, a rise of hemoglobin in excess of 2 gram% should occur on oral therapy within the first three weeks. At the present time, there is little evidence that any iron compound is superior to ferrous sulfate or related ferrous salts and these are no indications for ascorbic or succinic acids because ferrous salts are absorbed so well when given alone. **Preparations containing other so-called hematinics are universally condemned** because of the expense and the confusion as to the specificity of the response obtained.

Several preparations are available for parenteral administration, either intravenously or intramuscularly. These iron complexes are removed from the plasma by reticuloendothelial cells where the iron is split off and becomes bound to transferrin in the plasma. When parenteral iron therapy is given to adults with iron deficiency anemia the hemoglobin level rises about 0.15-0.30 gm% daily. It has been well documented that the hemoglobin response does not differ with oral, intravenous or intramuscular administration of iron. Both local and general reactions to parenteral iron occur and Richmond reported the induction of sarcomas in rats given iron dextran by intramuscular injection.

In general, parenteral iron therapy is indicated where oral therapy is either not tolerated or ineffective. In some situations, it is desirable to replenish the body stores and in such circumstances parenteral iron may be indicated. However, it should be remembered that, once bleeding has been effectively managed, stores are gradually reconstituted from a normal dietary intake of iron over a prolonged period.

Iron in excessive amounts can cause death and **ferrous sulfate ranks next to aspirin as the most important single childhood poison.** These children die in acidosis and shock and have markedly increased levels of plasma iron partially bound to transferrin but also to albumen and globulins. Treatment with chelating agents orally e.g. EDTA or DTPA and supportive measures are indicated.

Iron Overload:

By adulthood about 1 gm. of storage iron is present in the body and this changes very little. An absolute increase in total body iron signifies increased absorption or the introduction of iron by some other route and the excess iron is laid down in stores, mostly as hemosiderin. Excessive iron absorbed from the gut is laid down in parenchymal deposits and parenteral iron is mostly taken by reticuloendothelial tissue. Hemosiderosis refers to increased storage iron without tissue damage whereas hemochromatosis implies that such damage exists.

Types of Mechanisms of Iron Overload:

(a) **Parenchymal Stores**

1. Failure of normal regulatory mechanism for absorption — idiopathic hemochromatosis.
2. Dietary overload — Bantu of South Africa
3. Excessive absorption in response to increased and usually ineffective erythropoiesis.

(b) **Reticuloendothelial Stores**

1. Transfusional siderosis in refractory anemias.

(c) **Focal Iron Stores**

1. Parenchymal as in the kidneys in paroxysmal nocturnal hemoglobinuria
2. Reticuloendothelial as in idiopathic pulmonary hemosiderosis.

Idiopathic hemochromatosis appears to be due to an inborn error of metabolism in which there is a slow increase in the total body content of iron. There is a markedly increased absorption of dietary iron in the range of two-four mgm. daily, the cause of which is unknown. There is an increased familial incidence of the disorder suggesting a genetic basis. A definite association with alcoholism and Laennec's cirrhosis has been found but it is probable that the liver damage of hemochromatosis is merely potentiated by these factors.

Pathologically, there is a marked increase in total body iron in the range of 60-80 grams. In the fully developed case, there are striking changes in most organs particularly the liver, spleen, pancreas, heart and skin. However, very little is known of the findings in the long latent period during which iron is steadily accumulating. Studies done to date using liver biopsies reveal that the liver is subjected to the major impact in the early stages.

Clinically, cirrhosis of the liver is present in all advanced cases, and diabetes mellitus, cardiac failure and skin pigmentation are usually present. Males predominate in the incidence in a ratio of 10:1 possibly related to the blood loss of females in pregnancy, lactation and menstruation.

The only definitive diagnostic test is a liver biopsy. The plasma iron is usually over 200 mg% and the transferrin is completely or almost completely saturated. Examination of a bone marrow smear for increased hemosiderin is a helpful diagnostic aid and the response to repeated phlebotomies will demonstrate the presence or absence of increased tissue iron. The treatment consists of repeated phlebotomies over a period of several years.

Iron overload in the South African Bantu has been proven to be due to an abnormally high absorption from the gut. It has been shown that the amount of absorption increases with the size of the dose of iron presented to the gut. The high iron content present in the food of the Bantu and in their kaffir beer comes mainly from their iron cooking utensils. Histological changes are most marked in the liver and reticuloendothelial system. There is a close correlation between the amount of portal siderosis and the diffuse portal fibrosis and when cirrhosis appears there is a widespread distribution of iron in other tissues very similar to those in hemochromatosis. The incidence of diabetes mellitus in the affected Bantus also is significantly increased.

For the most part, subjects with refractory anemias who receive repeated transufsions do not show similar pathological changes, presumably because the iron is taken up by the reticuloendothelial system, and is, therefore, more inactive because it is slowly released. However, cases are reported where changes similar to those of idiopathic hemochromatosis are found in transfusional siderosis.

Controversy still exists over the relationship between idiopathic hemochromatosis and hemosiderosis. Some contend that they are variants of the same condition while other feel they are entirely different entities. In any event, there seems to be no doubt that when excessive parenchymal deposits of iron are present for a long period characteristic pathological and clinical features may develop. Since excessive iron is the only common feature in these conditions, it seems reasonable to suppose that it is important in the production of tissue changes.

REFERENCES

INTRODUCTION:

Beutler, E. Iron Metabolism, Annual Rev. Med. 12: 195, 1961.
Bothwell, T. H. and Finch, C. A. Iron Metabolism, Little, Brown and Co., 1962.
Harris, John W. The Red Cell, Western Reserve School of Medicine, Cleveland, 1963. Harvard University Press.

BODY IRON TURNOVER:

Brown, E. B., Dubach, N., Moore, C. V. Study in Iron Transportation and Metabolism, J. Lab. and Clin. Med. 52: 335, 1958.
Moore, C. V. The Importance of Nutritional Factors in the Pathogenesis of Iron Deficiency Anemia. Am. J. Clin. Nutrition 3: 3, 1955.
Granick, S. Metabolism and Function of Iron, Report of the Nineteenth Ross Pediatric Research Conference 1956.
Hahn, P. F. et al. Radioactive Iron Absorption by Gastrointestinal Tract J. Exper. Med. 78: 169, 1943.
Stevens, A. R. et al. Iron Metabolism after Partial Gastrectomy. Annals of Surgery 149: 534, 1959.

IRON TRANSPORT:

Laurell, C. B. Plasma Iron and the Transport of Iron in the Organism. Pharm. Rev. 4: 371, 1952.

TISSUE IRON STORES:

Mazur, A. et al. Mechanism of Release of Ferritin Iron in Vivo by Xanthine Oxidose' J. Clin. Invest. 37: 1809, 1958.
Richter, G. W. A Study of Hemosiderosis with the Aid of Electron Microscopy. Bull. New York Acad. Med. 34: 134, 1958.
Bessis, Marcel C and Breton-Gorius, J. Iron Metabolism in Bone Marrow as Seen by Electron Microscopy. Blood. 19: 635, 1962.
Jandl, J. H. et al. Transfer of Iron from Serum Iron-Binding Protein to Human Reticulocytes. J. Clin. Invest. 38: 161, 1959.

FERRO KINETICS:

Huff, R. L. et al. Ferro Kinetics in Normal Persons and in Patients Having Various Erythropoietic Disorders. J. Clin. Invest. 30: 1812, 1951.

IRON DEFICIENCY:

Conrad, M. E. and Crosby, W. H. The Natural History of Iron Deficiency Induced by Phlebotomy. Blood 20: 173, 1962.
Rickers, J. N., Brown, C. L. and Sprague, C. C. Pyridoxine Responsive Anemia Blood. 19: 304, 1962.
Kinney and Co. Inc. Iron Toxicity Annonated Bibliography Columbus Ind. 1959.
Richmond, H. G. Induction of Sarcoma in the Rat by Iron Dextran Complex Brit. M. J. 1: 947, 1959.
Beutler, E. Ratson, M. J. and Bettenwieser, G. A Comparison of the Plasma Iron, Iron-Binding Capacity, Sternal Marrow and Other Methods in the Clinical Evaluation of Iron Stores. Ann. Int. Med. 48: 60, 1958.
Coleman, D. H. et al. Rate of Blood Regeneraton After Blood Loss, Arch. Int. Med. 92: 341, 1953.

IRON OVERLOAD:

FINCH, S. C. and FINCH, C. A. Idiopathic Hemochromatosis. Med. 34: 321, 1955.
MACDONALD, R. A. Idiopathic Hemochromatosis. Arch. Int. Med. 107: 606, 1961.
OLIVER, R. A. M. Siderosis Following Transfusions of Blood. J. Path and Bact. 77: 171, 1959.
SOERGEL, F. H. and SOMMERS, S. C. Idiopathic Pulmonary Hemosiderosis. Pediatrics 19: 1101, 1957.

The Prescribing of "Physio"

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Those of us who graduated from our Medical Undergraduate Courses locally more than 10 years ago, had little opportunity to observe the workings of an active Physiotherapy or Occupational Therapy Department. Our acquaintance with these things has therefore been acquired, in many cases rather casually, in our post-graduate years, and we may never have had any formal instruction in this field. There are now some 28 Physiotherapists practicing in Nova Scotia in a variety of settings, and we have to prescribe Physiotherapy for our patients from time to time. It may be considered redundant to say that accurate diagnosis of the patient's condition is essential to intelligent prescribing of anything. Beyond this an understanding of the mechanism of production of the pain or other symptom is helpful in deciding what form of Physiotherapy is likely to be beneficial. One must also have a clear conception of what a Physiotherapist can do and cannot do. In some instances the advice of a Specialist in Physical Medicine and Rehabilitation is available, and the writing of the actual prescription can be left to the Consultant, but in many other instances the prescribing of "Physio." rests with the patient's personal Physician.

(1) Has the Physiotherapist a contribution to make? It is important to bear in mind that although the patient's condition may be one which can ordinarily benefit from physical treatment, the disease may have passed the stage where physical measures can be expected to accomplish much for the patient, or the problem may be of such magnitude that very intensive care in a special unit may be required. It is very frustrating for the Physiotherapist to be loaded with a large quota of patients for whom she is not able to accomplish much. There should be a reasonable likelihood that treatment of the kind and duration ordered will produce improvement for the patient. The Physiotherapist should not be prescribed for the same reason for which the baby is given a "pacifier".

(2) Neither is it sufficient to write on a piece of paper "Please give this patient Physiotherapy times 2." This is inviting the Physiotherapist to prescribe the treatment, and is equivalent to sending the patient to the Druggist with a blank prescription slip signed by you. You should try to envison what you expect the Physiotherapist to do, and in what way it will help the patient. You can then issue intelligent instructions.

(3) Realizing that the prescribing of Physiotherapy is an unfamiliar procedure to many Doctors, attempts have been made to design some physiotherapy prescription forms in such a way that a minimum of effort is involved in filling them out, a maximum of suggestions are made for the Physician's

consideration, and in at least one instance, discussion between the Physician and Physiotherapist after the Physiotherapist's first contact with the patient is suggested.

(4) In general the Physiotherapist can minister to the patient through such measures as the employment of heat, cold, exercises of various kinds, massage, splinting and manipulations. The particular manner in which these modalities are to be employed constitutes the Physiotherapy prescription. In general, cold will only be prescribed in conditions with pain and swelling of a few hour's duration. Thereafter heat is apt to be more effective in relieving the patient's pain and muscle spasm. Heat will be much more often prescribed than cold since it is unusual for the patient to be seen by a Physiotherapist within a few hours after an injury or the development of an acute condition. Heat is prescribed in a variety of ways divided into superficial (dry), deep (moist) and deep (electrical). Of those moist heat should probably be most commonly employed because it is (a) easy to administer, (b) penetrating, and (c) usually as effective as any. It can be employed by means of hot baths for the whole body, hot wax for an extremity or hot packs for a part of the trunk for a part of an extremity.

(5) Exercises can be active, passive or the Physiotherapist can assist the patient with active movements. This form of treatment has been extremely popular in the last few years and deservedly so. In general the greater the patient's active participation the greater the strengthening value of the exercise and the less chance of doing damage to the patient, since his own discomfort limits his activity. Exercises are mainly designed for strengthening and for maintaining and increasing range of movement of musculo-skeletal structures. The detailed prescription may therefore include the designation "Passive movements", "Active assisted exercises", or "Active exercises", and a description of whether one is aiming primarily for range or primarily for increased strength. In the event that increased strength is an objective, consideration should be given to ordering "Progressively resisted" exercises. Such resisted exercises can be done by graduated manual resistance or by the use of progressively increasing amounts of weight.

(6) Massage and manipulations have such limited and specialized values that they need scarcely be dealt with in this brief and general discussion.

It must always be borne in mind that the Doctor is asking a skilled colleague to participate in the care of his patient, and that good communication between colleagues is the keystone of effective treatment.

Eradication of Tuberculosis in Children*

Pediatricians must be aware of the danger of tuberculosis in children and use chemotherapy and the tuberculin test as their principal tools in the campaign to wipe out this disease.

A group of authorities in various fields of medicine met at Arden House in Harriman, N.Y., in November, 1959, at the joint invitation of the United States Public Health Service and the National Tuberculosis Association. The conferees agreed that the elimination of tuberculosis as a public health problem was a practical goal but recognized that this objective was not achievable for the country as a whole within the immediate future.

Therefore, recommendation was made for the establishment of intermediate goals. Two such goals have been proposed - an active case rate by 1970 of not more than 10 per 100,000 population (the case rate in 1950 was 80), and control of infection in each community to the point where not more than 1 per cent of the children at age 14 react to tuberculin. For children, the objective is for tuberculosis to become as uncommon as diphtheria or smallpox.

Chemotherapy the First Tool

The most important tool to attain this objective is chemotherapy. The public health reason for treating adults is to render them noninfectious. In children the suppression of contagion is not of public health interest. Even where there is marked roentgenographic evidence of primary tuberculosis, a very small population of bacilli is usually found in cultures from gastric lavage of children. Furthermore, most children with primary tuberculosis are free from symptoms, including cough. Isolation may not, therefore, be necessary, and some health departments permit a child with primary pulmonary tuberculosis to attend school if he is free from symptoms.

However, when possible, a child with newly discovered primary pulmonary tuberculosis should be admitted to a hospital for one or two days to obtain cultures from gastric lavage or from bronchial secretions. As the rate of tuberculosis falls, this procedure will become more important to identify bacilli resistant to the usual drugs. Prolonged hospitalization of children may be traumatic.

The main purpose of administering isoniazid to children with primary tuberculosis is to *prevent* complications.

Isoniazid is the only antimicrobial agent which prevents the development of complications. It is inexpensive and easily administered and should be given for at least one year in doses of 10 to 15 milligrams per kilogram of body weight.

The present trend in most parts of the world is to use combined therapy, that is, para-aminosalicylic acid (PAS) with isoniazid. In uncomplicated primary tuberculosis, and for use in secondary prophylaxis to prevent complications, there seems to be no reason why isoniazid should not be given alone.

Recent converters, very young children with reactions to tuberculin, all children with roentgenographic evidence of manifest primary tuberculosis, and children with complications of primary tuberculosis or with chronic pulmonary tuberculosis should be given specific therapy.

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Tuberculin Test the Second Tool

The second and most important tool for eradication of tuberculosis in children is the tuberculin test. The emphasis should be on the number of tuberculin tests and, in children with previously negative tests, on the frequency of their repetition.

The tuberculin test is extremely valuable in diagnosis but it is not infallible. A Mantoux test will produce a skin reaction when tuberculous infection is present, provided the testing material is fresh, the test is properly administered, and read and the individual tested is not moribund, convalescent from measles, or receiving steroid therapy. However, some skin reaction to tuberculin may occur in those who have never been infected with tubercle bacilli. Sometimes such reactions can be recognized as atypical. A Mantoux which is red but not indurated is not called positive. Measurement of the Mantoux is important. Less than 5 mm. in diameter is definitely negative and 10 mm. or more positive. Between 5 and 10 mm. there is indecision and the test should be repeated with the same or a slightly larger dose. A test with 5 TU of PPD (the intermediate strength) should select 99 per cent of positive reactors.

Another tool for the eradication of tuberculosis is roentgenography. In children this tool should never be used for surveys, but every child with a positive tuberculin test should have a roentgenogram. If the child has obvious tuberculosis, sufficient films should be taken to guide the physician in the care of the patient.

Other approaches to the prevention of infection in children, aside from treatment and segregation of infectious adults, are attempts to alter the resistance of uninfected children by vaccination or the use of isoniazid as primary prophylaxis. There is no doubt that increased resistance to exogenous infection can be obtained by vaccination, the BCG strain of attenuated bovine bacilli being the agent commonly used. This is of value in countries with a high incidence of tuberculosis, especially when given to newborn children. From a public health point of view, the artificial sensitivity produced by BCG interferes with the use of the tuberculin test in case finding. In areas of low morbidity this is a strong argument against the use of BCG.

Role of Pediatrician

The prevention of tuberculous infection by the administration of isoniazid has been proved in experimental animals. The data from the prophylaxis study of the Public Health Service, when published, should show whether or not this method of prevention can be applied to human beings.

There are many contributions which the pediatrician can make to a tuberculosis control program. First, the negativism about tuberculosis must be overcome. Obviously, with a decreasing rate of infection there will be less tuberculosis and fewer tuberculin conversions. But the pediatrician must continue to be aware of the possibility of tuberculosis. Where there are tuberculous adults there are infected children. All children must be tested repeatedly in infancy and at least once a year ad infinitum or until conversion occurs; prompt treatment with isoniazid should follow conversions.

Tuberculosis is preeminently a social disease. It increases where living conditions are poor and homes overcrowded. Any measures to relieve poverty and its attendant evils of inadequate nutrition and crowding will help in the basic control of the disease. The pediatrician must function not only as a physician but also as a public-minded citizen intent on securing for every child the right to be protected from a preventable communicable disease.

Prescalene Fat Pad Biopsy In Thoracic Diseases*

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Since the original description by Daniels in 1949, biopsy of the prescalene lymph node has become an established procedure, both for the diagnosis of otherwise obscure intrathoracic disease and also in the assessment of operability of bronchogenic carcinoma. In the past decade, numerous reports have appeared in the literature concerning the use of the procedure. Most of these attest to its considerable value, while a few suggest that unless palpable cervical nodes are present very little information will be gained by simple removal of the fat pad.

At the Nova Scotia Sanatorium, the first scalene node biopsy was done on February 22, 1950, and up to and including October 19, 1962, the procedure has been used in 75 patients. It is the purpose of this presentation to discuss this method of diagnosis and describe our experience with it.

As noted above, following the original publication of Daniels[1], biopsy of the prescalene fat pad came into rather widespread use, the lymph drainage of the thorax was re-studied and in some centres the limits of the dissection were extended well down into the mediastinum. Shefts, Terrill and Swindell[2] were able to report positive findings in 67 of 187 patients on whom they carried out the procedure, a yield of 35.8%. Harken and his co-workers[3] in 1954 advocated extending the simple fat pad dissection into the mediastinum, and as would be expected, obtained significantly better results in diagnoses. Seghers, Orie, Hadders and Hunderhout[4], Piper[5], Odelberg[6], and Connar[7] all published findings suggesting that the procedure was a most efficient auxiliary diagnostic method in diseases of the chest. Scott[8] in 1957 stated that in his experience scalene lymph node biopsy was a useful procedure, particularly in case of hilar adenopathy and diffuse bilateral disease. Higgins and his co-workers[9] had quite acceptable results so far as positive findings were concerned as did Gaurie and Friedell[10]. At the other extreme, Morgan and Scott[11] with a yield of only 12.4% in 441 consecutive biopsies and only 8% in their last 281 cases state that scalene fat pad biopsy is a procedure of limited value in patients without palpable supraclavicular lymph nodes.

On reviewing the rather voluminous literature on the subject, one is impressed by the variety of results obtained by the different authors. The reason for this discrepancy becomes obvious on further study. Some reports include patients in whom nodes were palpable, and some are of cases in which was employed the radical technique of exploring the mediastinum through the small supraclavicular incision as described by Harken. In both these instances, the yield of positive findings will be high. On the other hand, if one is confined to carrying out the simple procedure originally described by Daniels, the lymph

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nodes will reveal abnormal findings in a lower percentage of cases. Thus we have the procedure reported as yielding positive diagnostic findings in 60% of cases all the say down to 10%.

At this institution, it has been policy to carry out the simple operation as originally proposed by Daniels and in discussing results it is inferred that palpable supraclavicular nodes were not present. It is felt that when the procedure is extended in the way described by Harken, it is no longer a simple operation without danger to the patient. It would seem that exploring the mediastinum blindly through a small supraclavicular incision under local anaesthesia is a practice fraught with hazards.

To clarify the rationale of prescalene fat pad biopsy, it might be well to review briefly the lymphatic channels to the scalene lymph nodes.

The right scalene nodes receive lymph from the entire right lung, the left lower lobe and a portion of the lingula of the left upper lobe and that the left scalene nodes drain only the upper division of the left upper lobe and the rest of the lingula. However, in some cases, there is a slight variation in that lymph drainage from the lingula and even from the upper portion of the lower lobe on the left will proceed to the left scalene nodes. In determining the side on which to carry out the biopsy, the right fat pad will be removed where the pulmonary lesion is (1) anywhere in the right lung or perihilar region, (2) in the left lower lobe, and (3) in the lingula of the left upper lobe. A left scalene biopsy will be done when the disease involves the upper division of the left upper lobe. Because of the above-mentioned variations in lymph drainage of the left mid-lung region, whenever a right scalene node biopsy gives negative findings it is advisable to proceed with a left-sided operation for removal of the fat pad.

To those who in other days carried out operative procedures on the phrenic nerve for the treatment of pulmonary tuberculosis, the region occupied by the scalene fat pad is a very familiar one. The operation is carried out under local anaesthesia with the patient supine, a pillow under the shoulders and with the head rotated away from the side of the operation. An incision approximately 4 cm. long is made 2 cm. above and parallel with the clavicle, its mid-point being at the lateral border of the sternocleidomastoid muscle. The skin and platysma are divided and retracted. The anterior cervical fascia is then incised, after which the fat pad becomes visible. Roughly, it lies in an area bounded medially by the internal jugular vein, inferiorly by the subclavian vein and superolaterally by the inferior belly of the amohyoid muscle. Its floor is the fascia-covered belly of the scalenus anterior muscle and lateral to this a portion of the scalenus medius muscle. The fat pad is grasped with an Allis forceps and elevated. Then by a combination of blunt nnd sharp dissection, clamping and ligating before dividing, as much as is feasible of the pad is removed. In the inferior portion of the wound branches of the transverse cervical and inferior thyroid vessels can be injured. If so, they are ligated. However, the structure most exposed to damage is the thoracic duct which can readily be torn in left-sided operations if it is not retracted out of harm's way. If the duct is torn and the injury recognized, it should be clamped and ligated. Care should be taken also to avoid injury to the phrenic nerve. The incision is closed in layers. The operation should have no ill effects on the patient and should cause no interruption in his usual activities.

As previously noted, at the Nova Scotia Sanatorium, since February 22, 1950 prescalene fat pad biopsies were carried out on 75 patients.

Table I

In Table I will be noted the distribution of patients with regard to sex and age. There were 42 males and 33 females. The youngest patient was 9, the oldest 76. Two-thirds of the patients were in the age group of 30 to 59 with a calculated average age in the males being 51.4 years and that of the females 39.8 years.

In all cases the biopsy was performed for diagnosis. No patient with known bronchogenic carcinoma was subjected to the operation and the reason for this in retrospect does not appear clear. When bronchogenic carcinomas have metastasized to the scalene lymph nodes, thoracotomy is obviously contraindicated as it is felt that even in such cases where resection is technically possible, the amount of palliation obtained does not justify the operation.

All operations were done under local anaesthesia and there were three complications. These consisted of two minor wound infections which occurred within three weeks postoperatively in 1953. Both cleared up spontaneously in a matter of days. In a third individual, during the dissection of the fat pad medially, it would appear that the internal jugular vein was torn with profuse bleeding. The haemorrhage was temporarily controlled by pressure, general anaesthesia administered and the bleeding point ligated.

Table II

Table II summarizes the findings of the histological examination of the resected fat pad. It will be noted that a diagnosis was made by the pathologist in 17 or 22.6% of cases. Forty-one specimens contained lymph nodes showing evidence of a non-specific adenitis and in 17 cases the tissue was normal. There were 14 cases in which sarcoidosis was present, primary carcinoma was noted in two and Hodgkins Disease in one. The striking feature of this table would appear to be the high percentage of sarcoidosis in the positive cases, and the apparent ease with which sarcoidosis can be diagnosed by scalene node biopsy. Indeed, 73.7% of the patients in this series in whom a diagnosis of sarcoidosis was eventually made had sarcoid tissue demonstrated in the scalene fat pad.

Table III

Table III relates the final diagnosis to the findings in the resected scalene fat pad as mentioned in the previous paragraph. Fourteen of the 19 cases with sarcoidosis had a positive scalene node biopsy. Of the 13 primary bronchogenic carcinoma, two were diagnosed by the finding of malignant cells in a scalene node, an incidence of only 15.4%.

If one peruses this table carefully, it will be seen why the biopsy was reported as showing either normal or non-specific findings in a considerable proportion. One would not expect to find changes in the fat pad in the case of a pneumonitis, lung abscess, rheumatoid lung, mitral stenosis, hypertensive cardiovascular disease, pulmonary fibrosis or fibrothorax. It will also be

TABLE I
SEX AND AGE

Age Group	Both Sexes	Male	Female
0 - 9	1	0	1
10 - 19	0	0	0
20 - 29	10	2	8
30 - 39	15	7	8
40 - 49	17	10	7
50 - 59	18	11	7
60 - 69	11	9	2
70 +	3	3	0
All Ages	75	42	33

Youngest: 9 years
Eldest: 76 years
Date of first operation: February 22, 1950
Date of last operation: October 19, 1962
Calculated average age (males): 51.4 years
Calculated average age (females): 39.8 years

TABLE II
TISSUE DIAGNOSIS OF RESECTED FAT PAD

Sarcoidosis	14	
Carcinoma, primary	2	Positive 17 or 22.6%
Hodgkins Disease	1	
Non-specific reactions	41	
Normal tissue	17	Negative 58 or 77.4%
All cases	75	

Specimen diagnostic	17	or 22.6% of all cases
Specimen non-specific	41	or 54.7% of all cases
Normal tissue	17	or 22.7% of all cases
All cases	75	

TABLE III

FINAL DIAGNOSIS RELATED TO PATHOLOGICAL DIAGNOSIS OF RESECTED SPECIMEN

	Pathological Diagnosis of Resected Specimen					
Final Diagnosis	All Cases	Normal Tissue	Non-Specific	Sarcoid-osis	Carcinoma Primary	Hodgkins Disease
Pneumonitis	4	1	3			
Sarcoidosis	19	1	4	14*		
Tuberculosis	9	3	6			
Mycosis	1		1			
Carcinoma, primary	13	3	8		2**	
Carcinoma, secondary	3	1	2			
Hodgkins Disease	1					1
Silicosis	2	1	1			
Farmer's Lung	2		2			
Lung abscess	1		1			
Rheumatoid lung	1		1			
Mitral Stenosis	1	1				
Hypertensive cardiovascular disease	1		1			
Pulmonary fibrosis	3	1	2			
Fibrothorax	1		1			
Not diagnosed	13	5	8			
All Cases	75	17	41	14	2	1

* 73.7% of all sarcoid cases biopsied
** 15.4% of all cases of primary carcinoma biopsied

TABLE IV

DISTRIBUTION OF LESION RELATED TO THE PATHOLOGICAL FINDINGS IN RESECTED SPECIMEN

Distribution of Lesion	All Cases	Normal Tissue	Nonspecific Reaction	Diagnostic Reaction
Localized Unilateral	28	9	16	3
Localized Bilateral	18	3	12	3
Disseminated Unilateral	1		1	
Disseminated Bilateral	28	5	12	11
All Cases	75	17	41	17

2 Carcinoma in Localized Unilateral
1 Hodgkins Disease in Disseminated Bilateral
All other positive findings were Sarcoidosis

TABLE V

SITE AND DISTRIBUTION OF LESION RELATED TO THE SIDE OF BIOPSY

Site and Distribution of Lesion	All Cases	Side of Biopsy	
		Right	Left
Localized - right	21	21	
Localized - left	7	4	3
Localized - bilateral	18	15	3
Disseminated - right	1	1	
Disseminated - left	0		
Disseminated - bilateral	28	25	3
All Cases	75	66	9

Number diagnostic 17 15 2
Left — 2 carcinoma in "Localized left".
There were no sarcoids biopsied on the left.

noted that 13 of the patients in the series are listed as undiagnosed, all methods used in an attempt to determine the nature of a condition present having been unsuccessful.

Table IV

Table IV summarizes efforts to determine whether one is more likely to obtain a diagnosis by scalene biopsy in a disseminated pulmonary disease than in the localized lesions. While the numbers are too small for any valid deductions, it would appear that scalene node biopsy is more likely to produce a diagnosis in the disseminated bilateral type of lesion.

Table V

The site and distribution of the lesion as related to the side of the biopsy are shown in Table V. It will be noted that 66 operations were done on the right side and only nine on the left. The reason for this should appear obvious if one recalls the course of lymph drainage from the lungs which indicates a right-sided biopsy in all bilateral disseminated lesions and in all cases confined to the right lung or left lower lobe. An interesting fact is that two patients in whom the diagnosis of bronchogenic carcinoma was made by the scalene node biopsy had left-sided fat pad biopsies in the presence of left apical disease.

Discussion:

With the exception of a few dissenters, biopsy of the prescalene fat pad is now accepted as a valuable auxiliary procedure in the diagnosis of obscure intrathoracic disease. The procedure is a simple one and should have no significant complications. At the Nova Scotia Sanatorium it is usually the final diagnostic measure undertaken before exploratory thoracotomy. Needless to say, it is only one of the many measures which are available for the diagnosis of a chest lesion. Others include a careful history and general physical examination, search of the sputum for organisms and cells, cytology and bacteriology of pleural fluid when present, skin tests, all available X-ray studies including planigraphy and bronchography, bronchoscopic examination with biopsy of any visualiz-d bronchial lesion and the aspiration of bronchial secretion for cytological examination.

It is felt that the operation defeats its purpose unless it is kept to the removal of the immediately available fat pad within the limits of the small incision. If one has to blindly dissect deep into the mediastinum in order to obtain lymph nodes, it is much safer to open the chest and assess the pathology under direct vision.

In this series, for some uncertain reasons, no operations were done to determine the operability of a proven bronchogenic carcinoma. It is in the patient's best interest, however, to know before opening his chest that a surgical resection of the lung for cure can probably be carried out. This is obviously not the case if the scalene nodes harbour malignant cells. If the fat pad biopsy shows that the carcinoma cannot be removed curatively, the patient should be spared the more major surgical procedure as it is now generally accepted that palliation can be provided just as effectively by radiation as by resection of the tumour-containing lung.

The high proportion of cases in which proven sarcoid changes were present

in the scalene nodes is quite impressive in this small series. From the review of the literature, this is quite generally the finding and it would appear that this procedure has its greatest application in the diagnosis of pulmonary sarcoidosis.

Summary:

1. In the past 12 years, 75 patients have undergone prescalene fat pad biopsy at the Nova Scotia Sanatorium. In all cases, the procedure was carried out as an adjunct to diagnosis and in no instances to assess the operability of a previously proven bronchogenic carcinoma.

2. Positive findings were obtained in 17 or 22.6% of these surgically removed specimens. In 14 of the 17 cases, sarcoidosis was present.

3. Operative complications occurred in three cases. One was an operative haemorrhage which was controlled with some difficulty, the other two were wound infections of a minor nature which resolved in a short time.

4. Prescalene fat pad biopsy is a valuable auxiliary measure in the diagnosis of obscure intrathoracic disease.

REFERENCES

1. Daniels, A. C. A Method of Biopsy Useful in Diagnosing Certain Intrathoracis Diseases. Dis. of Chest, 16: 360, 1949.
2. Shefts, L. M., Territt, A. A., and Swindell, H. Scalene Node Biopsy. Am. Rev. Tuberc, 68: 505, 1953.
3. Harken, D. E., Block, H., Clauss, R. and Farrand, R. E. A Simple Cervicomediastinal Exploration for Tissue Diagnosis in Intrathoracic Disease. New Eng. J. Med., 251: 1041, 1954.
4. Seghers, K. K., Orie, N. G., Hadders, H. N., and Hunderhout, J. M. Daniels' Biopsy in Diagnosis and Treatment of Pathological Processes in Lungs and Mediastinum. Arch. Chir. Neerl., 6: 57, 1954.
5. Piper, C. A. Scalene Node Biopsy in Diagnosis of Diseases of the Chest. Am. Pract. and Digest of Treatment. 5: 3, 1954.
6. Odelberg, A. The Technique and Value of Retroclavian Lymph Node Biopsy. Annales Chirurgiae et Gynaecologie Fenniae, 43: suppl. 5, 1954.
7. Connar, R. G. Prescalene and Deep Cervical Lymph Node Biopsy. Surg. Gynec. and Obstet., 101: 732, 1955.
8. Scott, S. M. A Critical Review of One Hundred and Sixty Consecutive Scalene Node Biopsies. Am. Rev. Tuberc., 76: 1002, 1957.
9. Higgins, G. A. and Brownlee, W. E. Prescalene Fat Pad Biopsy. J. Thor. Surg. 38: 402, 1959.
10. Gaurie, M. D., and Friedell, Gilbert H. Scalene Node Biopsy, Cytological Studies and Other Diagnostic Methods in Intrathoracic Disease. J. Thor. and Cardiovasc. Surg., 38: 235, 1959.
11. Morgan, S. Wesley and Scott, Stewart, M. A Critical Reappraisal of Scalene Fat Pad Biopsies. J. Thor. and Cardiovasc. Surg. 43: 548, 1962.

Knee Meniscus Injuries

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Introduction

The purpose of this article is to review the diagnostic features and the general principles of the treatment of soft tissue injuries of the knee with particular reference to those of the meniscus. At Camp Hill Hospital in Halifax the charts of 112 patients were reviewed, 85 of whom were operated with the diagnosis of a torn meniscus. Some conclusions drawn from this investigation also will be discussed.

Types of meniscus tears:

In general there are two types of tears involving either medial or lateral meniscus, longitudinal tear and transverse tear. A longitudinal tear may be located at the periphery of the meniscus where it adheres to the synovial membrane. This is called marginal tear. It may be located more centrally in the meniscus body, then if it involves anterior, middle as well as posterior segment of the meniscus, it is called bucket handle tear. A transverse tear may extend into the periphery of the meniscus or it may not. This detail is important to know as we shall see in the treatment of meniscus tears. It is interesting that athletic injuries in youth usually causes longitudinal tears. In middle aged and older persons the tears are caused usually by much less severe trauma like turning around suddenly or getting up from a kneeled position, for the meniscus has been weakened by wear and tear. These tears are usually transverse.

The injury causing a meniscus tear may also rupture one of the collateral ligaments and/or one of the cruciate ligaments. The combination of a medial meniscus tear with ruptures of medial collateral and anterior cruciate ligaments is called "the unhappy triad", for it is a very serious injury from the standpoint of prognosis. Therefore it is very important that the extent of the injury should be properly assessed during the initial examination of the patient in order that proper treatment may prevent future disability.

Diagnostic features:

Depending on the type of trauma, the extent of injury, the age of the patient and the length of time passed since the injury, the signs and symptoms may vary to a certain extent.

Symptoms:

1. Immediate incapacity:

In traumatic meniscus injuries the patient is incapacitated immediately so that usually he will be unable to continue the game or the work he was doing.

2. The initial snap:

At the time of incident the patient may feel something gave way in the knee joint, often with a sickening feeling and may also hear a snap.

3. Initial and subsequent swellings:

The initial swelling occurs if the tear extends to the periphery of the meniscus, thus injuring the vessels which supply the peripheral margin. The subsequent effusions are due to the irritation of the synovial membrane.

4. Locking:

It is important to differentiate the true locking from the inability to move the knee because of muscle spasm. The true locking has a springy feeling and occurs in between 10° to 40° short of full extension. Besides an interposed segment of a torn meniscus, it may also be caused by a loose body or a pedunculated synovial growth. It may occur initially when the meniscus is torn or subsequently if a small tear becomes more extensive. The tear of the posterior horn may cause a catching feeling only.

5. Pain:

Quite often it is localized on the medial or the lateral aspect of the knee depending upon which meniscus is torn.

6. Giving way:

It is a feeling of sudden instability of the knee, often causing the patient to fall down. It occurs during walking on rough ground or turning suddenly on the leg. The knee may give way also if there is quadriceps muscle insufficiency, flexion contracture or anterior cruciate ligament rupture. However, in these conditions the giving way occurs usually on going downstairs.

Signs:

1. Swelling:

The swelling may be diffuse due either to hemarthrosis if the patient was seen soon after the injury, or to synovial effusion. Initially it may not be present if the tear did not extend to the periphery of the meniscus for blood vessels are present only at the peripheral margin. In posterior horn tears there may be a soft tissue swelling just posterior to the collateral ligament only due to the local tissue edema. The cyst of a meniscus, which is more frequent on the lateral side may cause a local prominence.

2. Tenderness:

The tenderness may be anterior or posterior to the collateral ligament or where the ligament crosses the joint line. In injuries of collateral ligaments usually the proximal insertion site, less frequently the distal one, is tender when palpated. Also the cartilage of the patella and the femoral condyles should be palpated to detect chrondromalacia or osteochonditis dissecans.

3. Range of motion:

The patient may be seen with a locked knee joint. In some other cases, flexion or extension may be limited. Quite often the limitation of last few degrees of extension is an important finding leading to the diagnosis of a torn meniscus.

4. The stability of the knee:

It is very important that the stability of collateral and cruciate ligaments should be checked. In acute cases if necessary the tender spot should be injected with xylocaine and a stress film should be taken.

5. Quadriceps muscle atrophy:

The circumference of the thigh should be measured 5" above the patella and compared with the normal side. In knee mechanics the wasting of the vastus medialis is very important for its role in the locking of the knee in full extension.

6. McMurray's sign:

With the patient lying supine, the knee is bent fully, then the leg is rotated externally and extended for medial meniscus injuries, rotated internally and extended for lateral meniscus injuries. One may even hear a click or patient may complain of pain only at the injured meniscus site.

7. X-ray films:

Avulsion and other type fractures, loose bodies, osteochondritis dissecans and arthritic changes are ruled out.

8. Examination of the joint fluid:

It is a very useful procedure in chronic cases to differentiate traumatic synovitis from rheumatoid, gouty or infectious arthritis.

In children and women with similar symptoms first recurrent dislocation of the patella and congenital discoid meniscus should be ruled out.

General principles of treatment:

In acute cases the knee should be aspirated under strict aseptic conditions if there is hemarthrosis to lower increased intra synovial pressure. This will relieve the pain and prevent the harmful effects of the blood in the joint space. A compression bandage is then applied. Local cold application is helpful in the first 24 hours. If the patient comes with a locked knee due to torn meniscus, primary surgical treatment is indicated. The marginal tears heal well because of the rich blood supply at the periphery. If a transverse tear extends into the peripheral margin it may fill in with fibrous tissue, however this is usually a weak point and may cause further trouble requiring surgical excision. If diagnosis is not definite, a three weeks period of non weight bearing with isometric progressive quadriceps strengthening exercises is advised. Then the patient should be reassessed. The exercises should continue till both thighs are equal in circumference. The detection of ligamentous injuries is very important. If stress films show opening of the joint space for more than 15°, the general trend is now to do a primary surgical repair of the collateral ligament. Otherwise a knee cylinder cast is applied for 6-8 weeks and quadriceps exercises are done during and after immobilization. The primary repair of a cruciate ligament is considered only if it is avulsed from the anterior tibial spine and a gap is present suggesting that the fragment won't unite.

If a patient with a torn meniscus is not operated upon, the recurrent effusions, and giving way cause progressive slackening of ligaments leading to an unstable joint. Even in cases with some radiographic evidence of arthritis the excision of a torn meniscus retards the progress of the arthritic process.

The study done at Camp Hill Hospital will be published in detail. It seems to me it would be worthwhile to mention some conclusions drawn from that study.

1. Quadriceps muscle atrophy:

Throughout the study it was evident that if the patient had a strong quadriceps muscle, his disability was considerably less and he was able to do his work. Here the importance of pre- and post operative progressive resistance exercises becomes evident.

2. Instability of the knee:

The instability was a significant factor in causing the symptoms. Ligamentous injuries should be diagnosed when the patient is first seen and treated properly.

3. Interval:

Patients who had their injury diagnosed adequately at the earliest moment and treated properly had the best results. A rather long period of discomfort in the knee with recurrent effusions and giving way lead to traumatic synovitis, further quadriceps muscle atrophy, instability of the knee and eventually to traumatic arthritis.

Halifax, May 12, 1963.

Personal Interest Notes

LUNENBURG-QUEENS MEDICAL SOCIETY

Dr. and Mrs. Russell Zinck, Lunenburg have recently returned from a holiday in Europe.

Dr. George C. Jollmore, who graduated from Dalhousie this year has commenced a practice in Chester.

Dr. R. J. Gonsalves has opened an office in New Ross, a great boon to this community where for over a year those seeking medical aid have had to travel to Kentville, Chester or Bridgewater.

The last quarterly meeting of the Lunenburg-Queens Medical Society was held at Boscowan Manor, Lunenburg, on June 6th. Dr. Clyde Marshall and Dr. S. H. Kryszek were guest speakers. The fall meeting will be held in September at Kedge Lodge.

IN THE NEWS

ANTIGONISH: — The board of trustees at St. Martha's Hospital has announced the appointment of Dr. Peter Delva to the medical staff. A paediatrician, Dr. Delva is a graduate of London University, England. He was senior resident at the Children's Hospital, Halifax, until June 1962. Since then he has been assistant paediatrician at the Babies' and Childrens' Hospital in Cleveland, Ohio, and also instructor in Paediatrics at the University.

OTTAWA: — Dr. Murchie McPhail, a native of Kilburn, N. B., and former head of Pharmcology, Dalhousie, has been named Director of Biosciences Research at Defence Research Board Headquarters, effective Aug. 1, 1963. A specialist in physiology, endocrinology and in the defensive aspects of chemical warfare agents, his recent post is head of the physiology section at Suffield Experimental Station, Ralston, Alta. Dr. McPhail succeeds Dr. Morley G. Whillans, who has been named defence research member on the Canadian joint staff in London. Dr. Whillans was also on the staff of Dalhousie Medical School at one time.

Another former medical professor at Dalhousie, Dr. R. W. Reed has recently been in Halifax as one of the main speakers at the four day conference of Can. Society of Laboratory Technologists. His paper was entitled "Laboratory Diagnosis of Tuberculosis" and discussed the new methods of isolation of the tubercle bacillus.

Dr. Reed is a native of Nova Scotia and was chairman of the Department of Bacteriology at Dalhousie from 1950-55, associate provincial bacteriologist and bacteriologist at the Victoria General Hosital. He is presently bacteriologist at the Royal Victoria Hospital, Montreal.

HALIFAX: — Dr. Helen Hunter spent ten days of June in London, England, attending the First British Academic Conference in Otolaryngology held by the Royal College of Surgeons of England. She attended meetings in Paedo-Audiology. Dr. Hunter is paediatrician of the Hearing and Speech Clinic recently established in Halifax.

Dr. Arthur Shane has also spent some time this summer in the United Kingdom.

Congratulations

To those doctors whose many hours of service to St. John Ambulance have won them the following recognition by the Order.

Officer (brother): Dr. Charles Lorway MacLellan, Sydney.

Priory Votes of Thanks have been awarded to: Dr. Joseph Cairns, Halifax; Col. J. E. H. Miller M. D., Halifax; Dr. J. T. Snow, Kennetcook and Dr. Dewis Robert Davies, Oxford.

The President-Commissioner for Nova Scotia in the Order is Dr. C. B. Weld, and the Provincial Vice-President is Dr. S. H. Keshen. Dr. W. A. Condy and Dr. J. E. Hiltz are on the Board of Management while the names of many doctors throughout the province are on the Provincial Executive Committee.

The second annual meeting of the Atlantic Society of Obstetricians was held in the Lecture Room of the Pathological Building, Saint John, N. B. on May 25, 1963. Twenty-two active members, one Honorary Member and four guests attended the successful morning and afternoon business and clinical meetings.

The officers elected for the ensuing year are: —

Past President — Dr. Frank Wanamaker, Saint John, N. B.; President — Dr. John Maloney, Charlottetown, P.E.I.; Vice-President — Dr. Frank O'Dea, Saint John's, Newfoundland; Sect-Treas. — Dr. Donald Smith, Halifax, N. S.; Members of Council — N. B. — Dr. Victor McLaughlan, Moncton, N. B.; N. S. — Dr. Patrick Gardiner, Glace Bay, N. S.; P.E.I. — Dr. Kent Irvin, Charlottetown, P.E.I.; Newfoundland — Dr. C. M. R. Lovey's, Saint John's, Newfoundland.

Thirty-four guests, members and wives attended a reception and dinner at 7 p.m., at the Admiral Beatty Hotel. A very fine after dinner address was given by the Chief Anaesthetist of the D.V.A. Lancaster Hospital, Dr. Jennings. The next annual meeting will be held May 30, 1964 in Charlottetown.

Births

To Dr. and Mrs. M. E. DeLory, a daughter on June 21, 1963, at the Grace Maternity Hospital.

Dr. and Mrs. Fred W. Prince, a son, Christopher James on June 28, 1963, at Dawson Memorial Hospital, Bridgewater, N. S.

Dr. and Mrs. Wylie Verge, a daughter, Alice Margaret, at the Grace Maternity Hospital on June 29, 1963.

Marriages

Our best wishes go to Dr. and Mrs. William C. Nicholas who were married in the United Baptist Church, Sydney. Mrs. Nicholas is the former Miss Sheila Marie Bonnell, only daughter of Mr. and Mrs. John R. Bonnell of Sydney. The bridegroom is the son of Mr. and Mrs. Elias Nicholas, Canso and Halifax. Dr. and Mrs. Nicholas leave shortly for London where Dr. Nicholas will continue his postgraduate work in Internal Medicine.

Deaths

We regret to record the death late in June of this year of Dr. Louis J. Giovanetti, for fifty years one of Newfoundland's most prominent physicians. A native of Port Morien, he graduated from Dalhousie University in 1900. During the next fifty years, he practised medicine in several Newfoundland communities.

Surviving him are his wife, a daughter and three sons, including Dr. Joseph L. Giovanetti of Newcastle, N. B., and Reginald Giovanetti of Dartmouth, to all of whom we extend our sympathy.

We extend sympathy to the family of Dr. John Edminston Park, who died recently at All Saints Hospital, Springhill, following an operation. Dr. Park was a graduate of McGill University and served overseas as Captain of the Medical Corps in the First World War. He practised medicine in New Glasgow and in Newcastle, N. B., before coming to Oxford in 1931.

Coming Meetings

PLEASE REMEMBER:

September	23-27.	Short Course in Anaesthesia.
November	4-7	Dalhousie Refresher Course
November	20-23	Can. Cardiovacular Soc. and Can. Heart F'dtion at Toronto.

HERE'S A DATE TO BEAR IN MIND — MEDICAL BALL
LORD NELSON HOTEL

DECEMBER 6 at 9 p.m. (Get your baby sitter early.)