

THE NOVA SCOTIA MEDICAL BULLETIN

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The Acid Test

The day that the medical student learns that the laboratory result of a test may be in error is a significant one in the growth of the student toward the goal of becoming a physician: as so often happens at such milestones, development may then follow one of several directions. The pessimist may adopt as a permanent life-stance the attitude that laboratory tests are always wrong, and are therefore not worth ordering, or need only be ordered as a sop for the record, so that it may be entered on the chart but never looked at or regarded as a serious contribution by him as the physician in charge of the case. The optimist may feel that by and large, laboratories do a good job, and an occasional error should be overlooked. Only by putting in for every possible test that he can think of, can he possibly receive enough reports to enable him to eliminate the possibility of error, and to make quite certain that he can have enough information to make a diagnosis. The true physician-in-embryo will recognize that both he and the laboratory are fallible; he recognizes his responsibility to make a diagnosis on clinical grounds alone, and recognizes the role of the laboratory in providing the final confirmation of the diagnosis which heads his short list of possibilities.

Elsewhere in this bulletin, our attention is drawn to the fantastic growth in the demand for laboratory services in the Province, together with the multiplication of the numbers of possible tests which can be carried out on our patients. This carries very serious implications for all of us who are concerned in ordering laboratory tests as practising physicians, as well as those who are concerned in the education of the embryo physician.

As with other specialties, the growth in knowledge is increasing at a tremendously rapid rate in the specialty of Pathology, so that existing tests become out-dated and of diminished utility and significance compared with newer techniques. Tests that we

order today, and try to tell our students may be diagnostic, may be replaced by other, better tests, by the time the student graduates.

How can we cope with this problem? Up to now, the answer has been to retain the old test and add the new, to obtain more and more information from the specimens which we submit which we view with less and less certainty: there is an increasing inability to judge whether the information we have is diagnostic or not. This uncertainty leads to further demands for more tests, and an eventual total suspicion of the results of all tests.

As doctors, we pride ourselves on our individuality, and cheerfully accept the responsibility to make decisions for our patients, but it is time we learned to pocket our pride and admit that it is both impossible and inefficient for one doctor to try to master all the nuances of another's specialty. What is the purpose, what the justification, in one person spending five years studying pathology, then spending more years in specializing in one part of that field, if we as practising physicians are not prepared to ask his advice on how to solve a problem that is in his field of competence and outside our own. Instead of sending specimens to the laboratory demanding that this that or the other test be carried out, we should be sending a consultation to the pathologist requesting his opinion on the types of tests which he feels are necessary to support or refute our clinical diagnosis. Only then will we return to some measure of sanity, economy and efficiency in the use of our laboratory services.

The acid test as to whether a test is necessary should be: does the pathologist, in consultation, feel that this test will add to the information required to make a diagnosis in this patient. How many of us ever subject our laboratory test orders to this simple but effective test?

I.E.P.

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Medical Society Summer Meeting

1969

WEDNESDAY, THURSDAY, FRIDAY

JUNE 25th, 26th & 27th.

KENTVILLE, N. S.

SCHEDULE OF EVENTS

WEDNESDAY - BUSINESS (all at Cornwallis Inn)

Executive Committee Meeting
M.M.C. Board of Directors Meeting
Section for Surgery Meeting
Nominating Committee Meeting

SOCIAL

Joint Luncheon - Executive Committee & M.M.C. Board
(Cornwallis Inn)
M.M.C. Reception for Society Members (Cornwallis Inn)
Open Golf (KENWO)
Coffee Party (Cornwallis Inn)
Local Tours
Swimming (Kentville & Acadia)

THURSDAY - SOCIAL

Golf Tournament (KENWO)
Coffee Party - IOOF Hall (Artwork, Ceramic, Jewelry display)
Swimming (Kentville & Acadia)
Local Interest Visits
Outdoor Chicken Barbecue (Palmeters Country Home Motel)
"Kentville Barbershop Group Singalong Following Barbecue"

FRIDAY - SOCIAL

Golf Tournament (KENWO)
Mixed Luncheon (KENWO)
Swimming (Kentville & Acadia)
Family Dance and Carnival - Informal Attire (Cornwallis Inn)

"CARNIVAL PROFITS AND WINNINGS GO TO MEDICAL CHARITIES"

EVERYBODY WINS

A Note on the Tuberculin Test and Tuberculin Testing*

THE LATE DR. J. E. HILTZ.

The Nova Scotia Sanitorium, Kentville, N. S.

Tuberculin was first prepared in 1890 by Robert Koch, who thought that he had discovered a cure for tuberculosis; instead, he provided what is still one of the simplest and most reliable diagnostic aids in the field of tuberculosis control, widely used in individual cases and in screening.

Uses of the Tuberculin Test

The three principal reasons for carrying out tuberculin testing are:

1. *Population surveys* to detect possibly active tuberculosis, so that positive reactors to the test may be investigated further, e.g., by chest roentgenography. If a tuberculin test records falsely positive results no harm is done; but if it fails to register a positive in the case of an infected person this is a very serious matter.

In this type of survey, the Heaf test and Tine test are acceptable and very effective.

2. *The testing of an individual with a known or suspected chest lesion* to determine whether the lesion may be tuberculous.

In such cases, the Heaf and Tine tests may be too strong and a patient with a florid tuberculous lesion may contract a painful arm; or the tests may be too weak (e.g., patients with active tuberculosis but only a mild degree of tuberculin allergy), in which case they may yield falsely negative reactions.

The Mantoux tuberculin test should be used, advancing from a strength of 1 T.U. to 5, to 100, and even to 250 T.U. if the weaker doses give negative reactions. If a patient with a negative Mantoux reaction to 250 T.U. is not moribund, is not taking corticosteroids, and does not have an acute infectious disease, it is highly unlikely that his chest lesion is tuberculous. However, most physicians in chest clinics and hospitals have seen some cases of active pulmonary tuberculosis with sputum containing Niacin positive *Mycobacterium tuberculosis* but with the Mantoux reaction repeatedly negative at the 250-T.U. level.

3. *Scientific surveys* to determine the incidence in population groups of various degrees of tuberculin sensitivity, and to answer such questions as:

(a) Can the tuberculin test be used to separate those persons who show a positive tubercu-

lin reaction due to prior B.C.G. vaccination from those who have a positive test due to acquired tuberculous infection?

- (b) Should a weakly positive tuberculin reaction arouse suspicion of infection by atypical or unclassified acid-fast bacilli?
- (c) What percentage of weak reactors have active tuberculosis; or, conversely, what percentage of patients with positive sputum show only weakly positive tuberculin reactions?
- (d) By using comparable strengths of tuberculin and of antigens prepared from scotochromogens, Battery-type bacilli and avian-type mycobacteria, is it possible to indicate a community's incidence of infection with *M. tuberculosis* and atypical organisms?
- (e) Does the degree of sensitivity to tuberculin vary (as we have reason to believe) from week to week in the same person?

For these scientific undertakings, only well-standardized tuberculin is acceptable and it must be used by the Mantoux method. Old tuberculin (O.T.) is going out of favour and is being replaced by the standardized purified protein derivative (P.P.D.) of tuberculin. Table I presents information regarding the relative potency of different strengths of P.P.D. compared with dilutions of O.T.

The standard procedures for the Mantoux, Heaf and Tine Tests are as follows.

Mantoux Test

In order to standardize the reading, the area of oedema (not the erythema) should be measured accurately 48 to 72 hours after the test, holding the arm flexed at the elbow and in a good light. The size of the area of induration should always be recorded in millimeters; symbols may be used in addition to measurement but not in place of it. The accepted scale of reaction is:

Doubtfully positive	=	less than 5 mm. in diameter
+	=	5 - 9 mm.
++	=	10 - 19 mm.
+++	=	20 mm. or more
++++	=	necrosis

*Presented at the Annual Meeting, Nova Scotia, Department of Public Health, at Kentville, N. S., November 6, 1967.

Heaf Test

The strength of this multiple-puncture intracutaneous test is equivalent to 25 - 35 T.U. Reactions are best interpreted 4 to 7 days after injection of the tuberculin.

Doubtfully positive	=	Induration at 1, 2 or 3 puncture points.
+	=	Induration around 4 puncture points
++	=	Coalescence of induration points, forming a ring
+++	=	When induration involves centre of ring
++++	=	Intensive induration and even necrosis

Tine Test

This also is a multiple-puncture intracutaneous test; its strength is in the vicinity of 15 to 20 T.U.

Doubtfully positive	=	Induration less than 2 mm. in diameter
+	=	Discrete or indurated papule or papules, each 2 mm. in diameter
++	=	One or more indurated papules each 3 - 4 mm. in diameter, or two papules fused
+++	=	Plateau of induration
++++	=	When greater induration or necrosis occurs

TABLE I

Relative potency of purified protein derivative (P.P.D.) of tuberculin compared with dilutions of old tuberculin (O.T.).

STRENGTH	P.P.D.		Tuberculin units	O.T.	
	Tuberculin per tablet (mg.)	Tuberculin per dose (mg.)		O.T. per dose (mg.)	Dilution
FIRST STRENGTH	0.0002	0.00002	1	0.01	1:10,000
INTERMEDIATE STRENGTH	0.002	0.00006	3	—	—
		0.0001	5	0.05	1:2000
		0.0002	10	0.10	1:1000
SECOND STRENGTH	0.05	0.005	250	1.0	1:100

N.B. ALSO AVAILABLE ARE STABLE SOLUTIONS OF P.P.D. TUBERCULIN PROVIDING 1 T.U., 5 T.U., 10 T.U., 100 T.U., and 250 T.U., in each 0.1-ml. dose.

Recommendations

1. For tuberculin-test surveys for the purpose of case-finding, the standard and most fitting test is the Mantoux at a level of 5 T.U. However, the Heaf and Tine tests are more convenient for use in large surveys, are more acceptable by the public, and, further, the Heaf test is less expensive. They are 'stronger' than 5 T.U. and, therefore, reveal more positive reactors than does the 5-T.U. Mantoux test, as also, they detect reactions to non-specific antigens such as those from atypical mycobacteria (*e.g.*, photochromogens like *M. kansasii*, scotochromogens, and *Gause* mycobacteria) and the Battey bacilli.

All positive and doubtfully-positive reactors should have a chest X-ray examination. Doubt-

fully-positive reactors should be retested in two months, to determine whether the initial reaction reflected merely a developing allergy to tuberculin. One-plus tuberculin reactors should be retested with tuberculin at the time of the next survey as they may have been only non-specific reactors. Two-plus, 3+ and 4+ reactors may be given yearly chest X-ray examinations without repeating the tuberculin test.

2. For scientific evaluation, or for clinical evaluation of known lung disease, stable solutions of P.P.D. in strengths of 1, 5, 100 and 250 T.U. should be used. The 100-T.U. strength may be excluded, or may be the highest strength used, according to conviction or prejudice. □

Recent Advances in Laboratory Investigation

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"Why did I ask for this pathological investigation? Now that I have the result in my hand, I have no idea why I ordered it. It has, as far as I can see, no possible bearing on the case. Whatever the result, it would not influence the diagnosis or the treatment. In any case I do not know the normal values and, therefore, do not know whether the results are abnormal. My book is too out of date to mention it.

"Why did I ask for it? Could it be that I read an article about it? I have no recollection of doing so. Perhaps some of my friends suggested it, but I can't think how or why. Was it perhaps some new idea that flitted in and out of my brain? I had better ring up the pathologist and ask him about it. No, this test has occupied several man-hours in the lab. It might cause ill feeling if I now ask what is its significance. In fact I had better keep out of the way of all pathologists for the next few days in case they ask me about it."

During the last ten years knowledge in all disciplines of medicine has advanced by leaps and bounds. It is probably safe to estimate that each advance in medicine, surgery, obstetrics and gynecology has resulted in a fourfold increase in the laboratory investigational procedures associated with it. To detail the advances in clinical laboratory investigations covering the last decade would, therefore, require a large text book. In this brief review we can only briefly touch on some of the major highlights. These advances have brought in their wake problems inherent in increased use of the laboratory. It is proposed briefly to touch on these problems, some of their causes, and on some of the solutions which are being attempted.

THE PROBLEM

In the Halifax Infirmary the number of patients admitted annually rose from 10,579 in 1957 to 15,524 in 1967, an increase of 1.5 times. The average day's stay also increased during the same period from 7.5 to 10.5 days—that is patients stayed on the average 1.4 times longer. Presuming that during these extra days laboratory work would continue to be ordered at the same volume as pertained early in the illness, which is most unlikely, this might be expected to increase laboratory work 2.1 times. In actual fact there was a fivefold increase from 142,929 units in 1957 to 683,465 units in 1967, and the average number of tests per day per patient rose from 1.8 tests in 1957 to 4.3 tests in 1967.

General Causes

The increase is due in part to greater utilization of the laboratory through the widening of hospital insurance coverage, in part to the development of new laboratory tests such as tests of function and of sensitivity, histochemical procedures and immunologic procedures, in part to the institution of mass screening procedures as in the fields of exfoliative cytology and the Guthrie test for phenylketonuria or to

the institution of methods of automation, in part to the stress which has been placed on laboratory tests by the exponential growth in the urge to publish and the desire of the physician to avoid criticism. In no large measure it is due to a regrettable deterioration in clinical acumen and powers of discrimination on the part of physicians too lazy or too overworked to apply their minds to clinical problems. Much of the work of the clinical laboratory consists of repeat examinations, sometimes day after day; in our own laboratory we have received requests for repeat tests up to four times in the same day. In many cases the results are all essentially similar. Frequently four tests will be ordered together, each of which provides essentially the same information, where one would have given the diagnostic clue required. In explanation of repetitive and probably unnecessary tests of this sort, the laboratory worker must face the fact that in part it derives from a lack of confidence by the doctor in the results he obtains from the laboratory, and there may well be valid basis for this distrust. The physician must face the fact, however, that the more he overloads the laboratory with repetitive tests, the less accurate may be the individual results, though the relationship is not a simple one. For example, if a technician can perform 25 differential white counts in a day; if she receives only one every three days, her results will be less meaningful than if she is doing 15 every day, but probably no less accurate than if she is called upon to do 50.

Newer Knowledge

A few of the totally new fields which have opened up over the past decade are as follows:

(A) Autoimmunity

This is a term used to describe a state of sensitization against an individual's own tissue components which first became current in 1958 with the demonstration by Doniach and Roitt of the autoimmune basis of Hashimoto's thyroiditis² though Donath and

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Landsteiner had postulated self-immunization in paroxysmal hemoglobinuria as far back as 1925. Laboratory investigation was hampered by the insensitivity of classical immunologic methods and it is only in the last five years that gel diffusion, fluorescent and tanned red-cell techniques have become current in all large hospital laboratories. The development of these techniques has expanded the field of suspected autoimmune diseases very greatly to include many types of hemolytic anemia, purpuras, leucopenias, glomerulonephritis, hepatitis, diseases of connective tissue, ulcerative colitis, Addison's disease, myasthenia gravis and pernicious anemia but routine diagnostic applications are limited to some five of them.

CHRONIC THYROIDITIS It is well established that many types of thyroid disease are associated with the presence of a number of different thyroid autoantibodies in the serum.^{2,3} There is some correlation with the titre of these antibodies and the type and severity of disease but this is by no means perfect. Autoantibodies to thyroglobulin are highest in diffuse chronic thyroiditis of the Hashimoto type but are also encountered in primary hypothyroidism, chronic focal thyroiditis, toxic goiter and in many non-thyroid diseases such as lupoid hepatitis, nephritis, nephrosis, ulcerative colitis and diseases of collagen. These thyroglobulin-reacting antibodies can be detected by Ouchterlony or hemagglutination techniques but these methods have largely been supplanted for routine purposes by a test employing the aggregation of latex particles sensitized with thyroglobulin (T-A test, Hyland).

Immunofluorescent studies have shown that serum from cases of Hashimoto disease will react with a second antigenic fraction in thyroid colloid and also with a third component within the follicular cells.³ These reactions are much more specific but they do not lend themselves to routine use. The cellular component is found to lie within the microsomal fraction and, with preparations obtained from the microsomes of toxic thyroid tissue, it is possible to demonstrate the antibody by complement fixation. This is a sensitive test but, like the tanned red cell test it is positive in some 20 - 30% of cases of thyrotoxicosis, non-toxic nodular goiter and thyroid cancer.

As the TA test is less sensitive than these more elegant methods it gives only an occasional false positive reaction in non-thyroid conditions and is usually negative as well in thyroid disease other than diffuse thyroiditis in which condition there is over 90% positivity. It has thus considerable theoretic advantage over the more complicated procedures. There is the practical advantage that it is a simple test ideally suited to the doctor's office.

HEMOLYTIC ANEMIA Autoimmune anemia may be seen in a number of the so-called collagen diseases (disseminated lupus erythematosus, polyarteritis nodosa, rheumatoid arthritis) leukemia, lympho-

sarcoma, Hodgkin's disease, giant follicular lymphoma, sarcoidosis, multiple myeloma, carcinoma, ovarian tumors, thrombocytopenic purpuras of various types, cirrhosis, uremia, viral, or atypical pneumonia. Autoantibodies may be cold or warm reacting, complete or incomplete, and either hemolysins or hemagglutinins. Hemolysins may only react in acid medium. Both the direct and indirect antiglobulin tests are positive but, in the case of drug induced autoimmune anemias (a very small proportion of the drug-induced hemolytic anemias the Coombs test may only be positive if the test system also contains the offending drug. In addition to the usual findings of hemolytic anemia (e.g. anemia, anisocytosis, polychromasia, reticulocytosis, elevated urobilinogen—particularly fecal urobilinogen) there may be striking autoagglutination, erythrophagocytosis, and up to 20% siderocytosis. Cryoglobulins and increased or abnormal immunoglobulins may sometimes be demonstrated. All these tests have become well within the capabilities of the routine hospital laboratory during the past decade.

In contrast to the ease of investigation of autoimmune anemia, only in research institutes is it presently possible to investigate cases of suspected autoimmune leucopenia or thrombocytopenia by a search for leucoagglutinins, the performance of Coombs tests on white cells or platelets, antiglobulin consumption test or tests for cytotoxicity. One of the by-products of the present impetus in tissue transplantation techniques is the search for ready methods of leucocyte typing and it is probable that well within the next five years methods of stabilizing these delicate cells will be developed so that it will be possible to make them "hold still" long enough to be tested in the routine hospital laboratory.

PERNICIOUS ANEMIA It has long been known that mucosal atrophy and a chronic plasma celled and lymphocyte infiltrate of the gastric submucosa invariably accompanies pernicious anemia but only in the last ten years has it been possible to demonstrate that this is accompanied by autoantibodies, one of them directed against gastric mucosal cells, demonstrable by complement fixation or fluorescent antibody methods and the other against human intrinsic factor demonstrated by the Ouchterlony technique.⁴

Early enthusiasm for these tests has subsided and they remain research tools only, having been supplanted by microbiologic assay methods for serum B₁₂ and folic acid.

RHEUMATOID ARTHRITIS Research into the basic abnormality in rheumatoid arthritis has received a great impetus as the result of newer knowledge of the nature of immunoglobulins particularly as derived from papain fractionation, ultracentrifugation, chromatography on DAE cellulose and fluorescein conjugation but these remain research tools. The classical time consuming Rose Waaler test using sensitized sheep cells in a hemolytic system

has largely been replaced during the past decade by the coated polystyrene latex test of Singer and Plotz. This is now available as a commercial preparation (R A test, Hyland). The test comprises the mixing on a glass slide of diluted serum with a suspension of latex particles which have been coated with human gamma globulin. A positive result is indicated by agglutination of the latex particles and is, in contrast to the classical Rose Waaler test, very easy to read. The R A test appears, in our hands, to be more sensitive but less specific than the Rose Waaler test and the chance of missing significant elevation of the rheumatoid factor is not great. Owing to its sensitivity, however, a positive result is not diagnostic of rheumatoid disease and false positives may be seen in syphilis, sarcoidosis or viral hepatitis in which conditions the classical Rose Waaler reaction is usually negative. Recently a further set of moieties known as the Gm - InV system has been described following the demonstration that human group O Rh positive cells coated with incomplete anti-D may be agglutinated by some rheumatoid sera. Not only is there a difference in reactivity of sera but also a variability in the avidity of different anti-D coats so that a large spectrum of results may be obtained whereby cases may be grouped into Gm (a), Gm (b), and InV classes. The matter is further complicated by the fact that agglutination of cells with certain anti-D coats can be inhibited by some but not all normal sera. As a result the Gm and InV groups may now be further divided into Gm (a+), Gm (a-), Gm (b+), Gm (b-), InV (+) and InV (-). From time to time the laboratory receives requests for such testing but the complexity is so great and the results of so little practical value that we have not established the methods in our own laboratory.

DISSEMINATED LUPUS ERYTHEMATOSIS It is twenty years since Hargraves, from the Mayo Clinic, described the L. E. Cell phenomenon and this remains the standard reference test in this disease though it is only diagnostic if strongly positive. Weaker degrees of positivity may sometimes be seen in cases of lupoid hepatitis, Sjogren's syndrome, other connective tissue disorders, penicillin allergy and in asymptomatic relatives of cases of D.L.E.

The test is nearly always positive in true D.L.E. but is subject to considerable technical variation and positive results may only be seen on repeated testing. It reverts readily to a negative reaction under corticoid therapy or if the patient develops uremia.

In an attempt to provide a more sensitive testing procedure, approximately ten years ago Holborow et al⁵ developed a fluorescent antibody method to demonstrate antinuclear factor based on the incubation of cryostat sections with test sera and subsequent exposure to fluorescein-conjugated antiglobulin serum. This method will detect virtually any antinuclear antibody and is nearly always positive in D.L.E. False positive reactions however occur in from 50 - 95% of cases of other connective tissue disorders and from 10 - 50% of cases of rheumatoid

arthritis and the technique varies widely from laboratory to laboratory. This would be a good screening test were it not for the fact that it requires the services of a full time technician and is therefore suitable only to research establishments.

Serum from cases of D.L.E. will react by complement fixation not only with whole cell nuclei but also with isolated D.N.A., D.N.A.-histone and D.N.A. - protein (D.N.A.P.) Lawlis⁶ showed that formalized red cells may be coated with pure D.N.A. and used as a very specific test positive in some 80% of patients with active D.L.E. A commercially available slide test employing D.N.A.P. coated latex (L. E. test, Hyland) has been under study in our laboratory for the past five years. We have found it somewhat less sensitive than the L.E. test but this lack of sensitivity, approximately of the same order as the Lawlis test, gives it a fairly high specificity for true disseminated lupus. A negative test does not rule out the disease but in contrast to positive L. E. cell preparations false positive reactions are almost never seen.

(B) Chromosomal Studies

Since 1910 progress in karyotyping has been entirely confined to the last decade. Prior to 1956 even the number of chromosomes in man was uncertain but was thought to be 48. In that year Tjio⁷ established for the first time that the true number was 46. Early methods based on the tissue culture of fetal lung were quixotic and difficult to carry out and it was not until 1960 when lymphocyte transformation in peripheral blood samples incubated *in vitro* in the presence of phytohemagglutinin was discovered⁸ that the method became applicable to even large hospital laboratories. Although a vast amount of information regarding chromosomal abnormalities has accrued in the last eight years we are still on the threshold of our potential knowledge and at present our methods can detect only the grossest changes consisting of abnormality in number, unsure identification of individual chromosomes and very gross abnormalities of chromosomes such as fractures or loss of large portions.

The technique of chromosomal study presently employed involves the preliminary culture of lymphocytes in a tissue culture medium containing phytohemagglutinin. After some two to three days there is a remarkable burst of mitotic activity then colchicine is added. This both arrests the mitoses in mid-phase and prevents spindle formation so that they are not bound tightly together as in normal cell division. The cells must then be swollen in a hypotonic solution under careful control so that, although the individual chromosomes separate from one another, they remain enveloped by the cytoplasmic membrane and are not lost for study. They may then be fixed and transferred to a slide for staining and study. To enable this they must be flattened either by controlled pressure or by careful air drying of tiny drops. This last step requires considerable

technical skill. Even in the best preparations only some 4% of the cells will be in mitosis and only a small proportion of these mitoses will be satisfactory for analysis. The test therefore is a tedious one to carry out and is by no means within the competence of all. It is usual, and in our view almost essential, to prepare enlarged photographic prints of ten or more mitoses of perfect quality for meaningful analysis. Study of an individual case requires about a week's work. This is by no means an "emergency" test though more than once it has been requested from us "stat".

Present methods of karyotyping are comparable with viewing a tissue section with the unaided naked eye and at present it is quite impossible to demonstrate the lesions of Mendelian inherited disorders such as hemophilia, phenylketonuria, sickle cell trait and the like. Nor is it probable that present methods of study, including future use of electron microscopy, will ever be any more successful in this regard as these disorders probably involve the transposition or replacement by a single amino acid or purine base in the vast convoluted molecule of D.N.A. within the much larger gene lying in the relatively colossal chromosome - which latter we cannot even see clearly. It is as though, at a distance of ten miles we were attempting to pick out a single grey hair or as Lennox puts it—like "hoping to detect a single false note in a recording of a symphony speeded up so fast that we hear the whole in a second".⁹ Chromosomal studies remain a research tool of very limited application.

(C) Electrophoresis

1. SERUM PROTEINS Prior to 1958 routine electrophoresis in the clinical laboratory was virtually limited to the analysis of serum proteins on a filter paper support. Better separation was obtainable by means of the moving boundary (Tiselius) apparatus but the equipment and technique were too elaborate for hospital use. During the past decade the introduction of cellulose acetate, agar gel, starch block and acrylamide supports have given a striking impetus to other applications and have brought these within the technical competence of any hospital laboratory. What was once a semi-research method has now become a routine tool and in our laboratory electrophoresis on cellulose acetate is now performed whenever serum protein estimation is requested. Electrophoresis of hemoglobin is also now routine and may be performed with equal success either by the starch block or cellulose methods.

2. ISOENZYMES The isoenzymes of lactic dehydrogenase may be separated electrophoretically either by a commercially available agar gel kit or by techniques employing cellulose acetate. It is almost axiomatic that in medicine when a new test is developed the cry of "publish or perish" goes up, there is a spate of papers in the literature and the nomenclature becomes, for a while, chaotic. The situation with LDH has been no exception. It was early ap-

parent that five isoenzymes were recognizable¹⁰ and these were labeled both by American and European workers as LDH₁, LDH₂ . . . LDH₅. Confusion at once developed because the Europeans numbered them starting with the fastest moving component (as is current in the electrophoresis of serum proteins or hemoglobins) whereas Americans at first numbered them the other way. The European practice has now been generally adopted. Further confusion also developed when it was found that the five isoenzymes were probably composed of two subunits which were designated H and M, these being present in varying proportions so that LDH₁ was designated H₄ and the others were labelled through H₃M₁, H₂M₂ etc to M₄ (LDH₅). The fact that the letter "H" occurs under two different meanings (i.e. H-subunit and H-hydrogenase) has suggested to us that the electrophoretic bands are best designated LD₁, LD₂ etc and it is our practice to report them as such.

The clinical value of LDH isoenzymes derives from the fact that their distribution in specific tissues varies. Thus heart muscle and red blood cells are rich in LD₁ and LD₅, liver contains almost pure LD₁ and adrenal is largely LD₃. Necrosis of each of these tissues whether it be the heart, liver or red blood cells releases the enzyme into the serum for detection.

The isoenzymes in addition to differing electrophoretic mobilities also show variable substrate specificities and may be separated by the ability of LD₁ to utilize hydroxybutyrate instead of pyruvate, its ability to withstand heat inactivation and its inhibition by low concentrations of oxalate whereas LD₄ and LD₅ are heat labile, resistant to oxalate but inhibited by urea. During the past year a differential assay method has been developed as a commercially available kit (Profile LDH, Warner Chilcott) which may render electrophoretic separation no longer necessary. If this is so it will result in a saving of laboratory time of some 24 hours.

Attempts to separate the isoenzymes of alkaline phosphatase specific for bone disease on the one hand and liver metastasis on the other by heat inactivation, phenylalanine inhibition and electrophoresis have proven only of limited application to date but it is probable that during the next few years the field of isoenzyme estimation will expand greatly.

3. LIPOPROTEINS Normal serum contains mainly β -lipoprotein together with a small amount of α -lipoprotein. By the use of a modified technique of paper electrophoresis¹⁰ employing an albumin buffer it is possible to distinguish up to four lipoprotein bands representing α , pre- β , β -lipoproteins and chylomicrons in different cases of hyperlipemia. When taken in conjunction with ultracentrifugal studies and assay of cholesterol, phospholipids and triglycerides, it is possible to group the hyperlipemias into five classes. The use of the ultracentrifuge is essential and this limits meaningful study to large research institutes. It is tempting to

attempt study without this elaborate tool but, despite claims in the literature, paper electrophoresis still leaves much to be desired. We are presently investigating a method employing cellulose acetate.

Beta-lipoproteins may be estimated in a semi-quantitative manner by a precipitin technique and this is the method presently employed. It is a simple and rapid screening tool, positive results correlating closely with elevated cholesterol and triglycerides.

4. IMMUNOGLOBULINS The concept of immunoglobulins has developed during the past eight years. The term refers to those globulins (β and γ) taking part in immune reactions but does not include complement or properdin. It is not generally appreciated that the term alpha, beta or gamma globulin does not refer to a homogeneous chemical or ultracentrifugal entity and that even chemically similar globulins may show completely different immunologic patterns. As a result of classification based on these different parameters a most confusing terminology rapidly developed based on Svedberg constants, electrophoretic mobility, salt fractionation, cold ethanol fractionation and precipitin patterns. For research purposes terms such as 7S γ , β_2A and γ_2K_2 retain some value but it does not seem necessary for the practicing physician to attempt their elucidation and he may safely follow the recommendations of the Committee on Nomenclature of the World Health Organization that they be classified on their immuno-chemical properties as Ig followed by an upper case roman letter. The four main classes of immunoglobulins are, by this classification, designated IgG, IgA, IgM and IgD. By papain cleavage it is possible to show that each of these classes has a basic molecule composed of heavy and light chains. The heavy chains are designated μ , α , γ and δ but these terms are better avoided for fear of confusion with the globulins detected by electrophoresis which represent quite different moieties. The light chains are designated K and L. Antigenic specificity resides in the heavy chain and common antigenic determinants in the light chains. As normal globulins of each class contain both light chains (though not on the same molecule) and as there is cross reaction between immunoglobulins on light chain analysis this is seldom indicated except in some cases of dysproteinemia (*vide infra*).

Abnormalities of immunoglobulins may be either quantitative (increased or reduced) or qualitative (dysproteinemias). In most cases the presence of a quantitative abnormality is apparent in the routine protein electrophoretogram and, if this is normal, immunoglobulin assay is probably not indicated unless there is a very strong clinical suspicion that the pattern is masked.

IgG comprises 85 - 90% of the immunoglobulins in adult serum; published values for the normal level varying from 700 - 1,600 mgm/100 ml. It neutralizes toxins and viruses and is actively trans-

ported across the placenta. IgA migrates either as a slow moving β or a fast moving γ globulin and is present in body secretions as well as serum. The normal blood level is given by some workers to be as low as 55 mgm/100ml. and as high as 420 mgm/100 ml. by others. In our rather limited experience we have found the normal level to lie between 130 - 400 mgm. %. IgM is the chief class synthesized in response to initial stimulus and the major immunoglobulin formed during the neonatal period. As IgM does not pass the placenta its presence in cord blood is indicative of an intrauterine infection.

Qualitative abnormality of immunoglobulins is seen in the dysgammaglobulinemias such as myelomatosis, Waldenström's macroglobulinemia, Franklin's heavy chain disease, light chain disease and in some apparently normal, old persons. Unfortunately these abnormal immunoglobulin-like proteins have been designated "M-components" (after Myeloma and Macroglobulinemia) and this has undoubtedly given rise to some confusion with the notation IgM to which it bears only peripheral relationship as these M-components may show antigenic similarity to any one of the four major immunoglobulins. In our view the term M-component is best avoided and we recommend that it be replaced by one of the terms "gammopathy," "gamma-dysproteinemia" or "disgammaglobulinemia".

Both the myeloma and macroglobulin peaks tend to be very sharp and narrow as they represent a homogeneous, if abnormal substance. Accompanying the increased abnormal globulin there is almost invariably suppression of the other normal immunoglobulins so these disorders are said to be "monoclonal". In some cases which we have studied the abnormal protein has appeared to be identical with Bence Jones protein. This substance is composed purely of one or other light chain and it does not combine with the antisera reactive to the immunoglobulins. In such cases light chain analysis is of great assistance.

There are a number of procedures available for immunoglobulin assay. Of these single diffusion in antibody agar enables quantitation with a precision of $\pm 10\%$ and is the simplest and most useful. Considerably more complex is immuno-electrophoresis usually performed in agarose gel. We are presently developing a method employing cellulose acetate.

(5) HAPTOGLOBINS Haptoglobins are a special group of glycoproteins which combine rapidly with free oxyhemoglobin and which migrate as α_2 globulins on cellulose acetate. The haptoglobin content of the blood is increased in such a large variety of conditions that the diagnostic value of increased concentration is negligible. Serum haptoglobin reduction however is a highly sensitive and quantitative method for the detection of intravascular hemolysis and it is of considerable value in the differential diagnosis of anemia and in the investigation of transfusion reactions. Until recently

methods for estimating this substance gave quixotic results but several methods employing electrophoresis have been published recently and we are presently investigating them.

(D) Enzyme Studies

Prior to 1958 enzymatic methods in the clinical laboratory were limited to the study of amylase, trypsin, alkaline and acid phosphatases, and occasionally lipase. Studies of glutamic oxaloacetic transaminase were just coming into use. In the interim there has been an amazing proliferation of enzymatic tests, some of which have stood the test of time such as SGOT, SGPT, LDH and CPK whereas others such as cholinesterase, leucine amidopeptidase, 5' nucleotidase, aldolase and malic dehydrogenase have not proven of great value. Hydroxybutyric dehydrogenase and isocitric dehydrogenase are presently under evaluation.

Until the value of an enzymatic procedure is established there is a tendency to order other enzyme studies along with it at the same time partly because clinicians are not yet sure of the relative value of the new test and partly working on the assumption that if one test is good, four tests must be very much better. It is now common for the laboratory to receive an emergency requisition for four or five different enzymatic studies simultaneously. Doctors who do this do not realize the complexity of these tests. Many factors affect enzyme activity including substrate concentration, temperature and pH. Since primary standards are not available it is imperative that the conditions be duplicated exactly for each run and that one or more control sera be analysed at the same time. Timing of the reaction is mandatory and of extreme importance. None of these tests is of the type where "A" is simply added to "B" and colour is developed with "C"; instead each step requires incubation and split-second timing. In most cases the enzyme will retain its activity overnight in the refrigerator.

Four conclusions derive from the foregoing:

(a) Due to the complex nature of these tests and the time involved in estimation of them, they are not ideally emergency procedures.

(b) Due to differing incubation times and the necessity for precision in performance it is not possible for an emergency technician to carry out four different enzymatic procedures simultaneously with accuracy. This means that all other emergency tests must cease while she carries out a consecutive series of enzyme incubation each of which confirms the results of the others where the estimation of one, carefully selected, would have provided the necessary information.

(c) Clearly these tests lend themselves ideally to the "batch" approach whereby the laboratory sets up the estimation of a number of different sera at one time including several control sera and then, having performed say twenty estimations of SGOT, carries out a similar set of estimations of LDH.

(d) In many cases it is not the *absolute* level of enzymatic activity which is of significance but rather the *change* in activity. Thus CPK is elevated more rapidly than SGOT following infarction but returns more rapidly to normal whereas LDH elevation persists longer than either of the other two. In our opinion more meaningful information is obtained by holding the emergency specimen overnight and carrying out the investigation along with a fresh sample with the routine run the next morning.

Finally a few brief words in an attempt to correct the present deplorable "shot gun" methods of using enzymatic studies.

1. SGOT. Oxaloacetic transaminase is a sensitive but nonspecific index of tissue damage. It is elevated in acute and chronic diseases of the liver and necrosis of large parenchymal organs such as occurs in infarction of the heart, kidney, lung and pancreas but not usually in cases of dissecting aortic aneurysm. Differentiation of these disorders is not possible by this test. As with alkaline phosphatase, SGOT is elevated in cases of hepatic metastasis but the test has the additional advantage that it is normal in cases of metastasis to bone.

2. SGPT. Pyruvic transaminase is elevated greatest in acute hepatic necrosis and is therefore commonly thought of as "the liver enzyme". This impression is quite false as there may be little or no elevation in chronic liver disease or cirrhosis nor does it have any additional diagnostic value over SGOT in differentiating hepatocellular from obstructive jaundice. SGPT usually remains normal in cases of myocardial infarction yet it is almost routinely loaded into the shot gun in cases of suspected myocardial infarction the reason for which is obscure. The simultaneous occurrence of diffuse hepatic necrosis and myocardial infarction is not a common clinical problem and when the two do coexist one is clearly dominant therefore there is little routine need to differentiate liver disease from heart disease every time an enzyme test is ordered. In acute hepatitis SGPT elevation is almost invariably accompanied by SGOT elevation so there is no need even in this condition to order both. Finally, whether recovery occurs from the attack of hepatitis or it becomes chronic, SGPT will fall. This is not the case with SGOT which only becomes normal on recovery, and even then this return to normality occurs later than is the case with SGPT. It would seem to us that estimation of SGPT levels is rarely essential and certainly it is not indicated as a routine.

3. LDH. Lactic dehydrogenase elevation occurs later than SGOT elevation in both liver disease and parenchymal infarction. It may not therefore be elevated in a very early myocardial infarct. It is just such cases which may require emergency tests. If SGOT is not elevated in a myocardial infarct there is little chance that LDH will be elevated and so

seant indication for ordering it on an emergency basis. On the other hand LDH elevation persists longer than GOT elevation and in an infarct of some days' duration GOT may have reverted whereas LDH remains high. It is in such cases that the test is of great value. The ability of the lab to fractionate into LDH isoenzymes of the distinctive LD₄ - LD₅ or "H" pattern in myocardial infarct and the LD₁ or "L" pattern in liver disease renders it the best laboratory test for differentiating heart disease from liver disease.

Elevated LDH isozymes of the "H" pattern are also seen in pernicious anemia and to a lesser degree in any hemolytic anemia, but not in iron deficient or aplastic anemias, and this may be of differential help. Both GOT and LDH are elevated in the C.S.F. in cases of encephalomalacia. There is no need to order both as a routine. We have had no experience nor have we read any reports of the isoenzyme pattern in the C.S.F. in other cerebral diseases.

4. CPK. Creatine phosphokinase is an enzyme present in muscle and nervous tissue, but not in the liver, lung or kidney. In the absence of encephalomalacia or necrosis of skeletal muscle, elevated CPK is virtually diagnostic of a recent myocardial infarct, though elevation is seen in some cases of hypothyroidism. The test returns rapidly to normal following a myocardial infarct but as this remission has no prognostic significance, there is little indication for repeating the test unless a second infarct is suspected. A normal CPK with elevated GOT would be suggestive confirmatory evidence of pulmonary infarction if performed in the first 36 hours but not thereafter. Serum CPK is also elevated in a variety of muscle disorders, mainly dystrophies and acute necroses, but also to some degree in muscular atrophies. It is said to be elevated in some women who are asymptomatic carriers of the gene of muscular dystrophy.

This should be a valuable tool but unfortunately the test is expensive and very complex, taking some four times as long to perform as does the SGOT. At present determination of CPK activity is indicated only when special diagnostic problems present.

(E) Other Fields

DIABETES The term diabetes mellitus means the running through of urine sweet to the taste—we have come a long way since this method of diagnosis was employed, and it is now appreciated that undue emphasis has been assigned to the diagnostic value of glycosuria. It is now known that glycosuria is dependent not only on the concentration of blood sugar, but also on glomerular filtration rate, maximum tubular reabsorptive capacity (glucose T_m) as well as the state of hydration and electrolyte balance. In coma, therefore, when plasma glucose is very high, concentration of glucose in urine is dependent on the maximum osmotic work the kidneys can carry out, and there will be no direct relationship to blood glucose level. In some cases of diabetic coma with renal impairment and salt deficiency there may be no

glycosuria. The accurate estimation of urine sugar is, therefore, unnecessary and may be misleading. Similarly the relationship between ketone bodies in the urine and blood ketones is a very complicated one. Acetone is a non-threshold substance whereas β-hydroxybutyric and acetoacetic acids are only excreted above a certain renal threshold. Plasma bicarbonate is unrelated to the level of ketones other than acetoacetic acid, but it provides an accurate index of the severity of the acidosis in the initial stages of diabetic ketosis when the pH of the body fluids remains in the normal range. In the later stages the fall in plasma bicarbonate may fail to compensate for the acidosis, and the blood pH falls below the lower limit of normal. This fact can only be appreciated by actual pH measurements. Severe loss of both serum sodium and phosphate may be completely masked by dehydration and may only become apparent on rehydration.

Ten years ago tests for fasting blood sugar were routinely ordered in screening for diabetes, but it has become increasingly apparent that this test is dangerously insensitive and unreliable, and tests for fasting blood sugar have almost entirely been replaced by the two-hour postprandial estimation. We have switched our blood sugar determinations to plasma levels to eliminate the variability of patient hematocrit. For screening purposes on outpatients one questions whether a formal glucose tolerance curve provides any more meaningful information than the simple two-hour postprandial estimation. In the case of the former, the ambulatory subject, frequently a wage-earner, is required to miss both his morning meal and lose a half or whole day's wages while a glucose tolerance curve is followed, whereas the two-hour test requires only that he have his breakfast at 7:00 A.M. and attend the laboratory for ten minutes at 9:00 A.M.

MALABSORPTIVE STATES For an excellent review of the laboratory investigation of states of malabsorption we would refer the reader to the paper by McKiggan in the penultimate Symposium Issue of *The Bulletin* sponsored by our hospital.¹² We should like to reiterate the considerable diagnostic superiority of the D-xylose test over the study of fecal fat, the uselessness of making separate estimations for split, unsplit and neutral fat, and of estimations based on the percentage per hundred grams, and the considerable value of properly controlled fat balance studies.

In our laboratory we have found that a simple increase in serum optical density following a standard fat meal compares very favourably with results obtained by the very much more complicated use of radioiodinated triolein. This test consists of the administration of 60 ml. peanut oil and 20 grams of a barium meal in the fasting state, followed by hot tea and two crackers. Blood samples are obtained at 0, 3, 4, 5 and 6 hours following the meal, and a flat plate of the abdomen is taken at four and one-half hours to check on gastric emptying. Normal persons show an optical density index of from 25 to 130, whereas in steatorrhea the index is from 0 to 9.

PREGNANCY TESTS During the past five years serological tests for pregnancy have completely replaced the Aschheim-Zondek, Friedman, and frog tests. A number of serological methods have been developed, varying from agglutination inhibition of sensitized red cells (Prepuerin, Burroughs-Wellcome, Pregnosticon, Organon), slide tests involving agglutination inhibition of latex (Brevindex, Ortho), and recently a slide test employing the direct agglutination of latex (DAP Test, Bell Craig). The slide tests have the great advantage that they may be read within two minutes, but they are more difficult to read than are the tube tests, and we have obtained positive results on occasion with tube tests when the slide test has remained negative. As in many other fields of laboratory investigation, our interpretation is greatly hampered by an almost total absence of "feedback" from the clinical departments, so that we are unable to assess whether our more sensitive methods are giving us false positive results. A vast amount of information is potentially available in the laboratory and it is indeed tragic that so little clinical information accompanies the specimens. This obtains throughout and probably has many causes. In some cases it may derive from an actual resentment of the attending physician to other persons' entering into the sacred doctor-patient relationship—we heard of one case where the request by a pathologist for some clinical notes to enable him to interpret a problem slide was returned by the angry physician with the comment, "None of your damn business," but this degree of medical secrecy must surely be unusual. The communication gap may well be due to the fact that modern medical practice leaves the physician very little time to discuss his case with the pathologist, but, in our opinion, in most cases it results from the fact that the physician is apt to delegate the responsibility for the completion of requisitions to a nurse who is often no more aware of the clinical state of the patient than is the pathologist. Meanwhile potentially valuable information is accumulating in the laboratory, and with our modern methods of data retrieval this reservoir should be utilized much more efficiently. This can only be accomplished if there is very much closer liaison between clinical and laboratory departments.

OTHER SEROLOGICAL METHODS A large number of serological methods, completely new in the last decade, have been developed, such as the TPI test and slide test for the differential diagnosis of infectious mononucleosis, to mention only two. Recently two rapid methods for estimating C-Reactive Protein, the Hyland Latex Anti-CRP Test and Test of Sylvana, have been introduced. We have compared the results of these in parallel with the classical precipitin test in 200 consecutive sera, and find the Sylvana test to be a very sensitive method. In our opinion this test may well replace sedimentation rates in the near future, and we are presently conducting a comparison.

Summary

The foregoing point out some of the complexities which have developed in laboratory methods entirely during the past decade. These tests represent only a small corner of the vast area of progress. Fortunately the major advances in the field of endocrinologic investigation have already been covered in the Infirmary Symposium by Nicholas,¹² far better than I could do. In my own short review I have not attempted to cover any of the many advances in the fields of microbiology, virology, or histology, nor the study of inherited amino acid and enzyme abnormalities (e.g. phenylketonuria, galactosemia or glucose 6-phosphate dehydrogenase deficiency), methods for investigation of Rh sensitization, the study of serum electrolytes and acid-base balance, newer methods of studying normal and abnormal hemoglobin or defects in blood coagulation, nor the methods which have been developed for the investigation of the cells of the blood to mention only a very few. Every one of the foregoing tests which I have omitted to discuss, which still represent only a small proportion of studies completely new in the past decade, is now a part of our routine armamentarium. I have said nothing of newer methods of investigation such as thin-layer chromatography, fluoroscopy, absorption spectroscopy, or gas chromatography which, although still research methods, are already becoming routine in larger laboratories. The omission of discussion of these is imposed on me because of lack of space, but it renders my present review incomplete.

THE SOLUTION

I. Automation

Proliferation of laboratory work has resulted during the past twenty years in the development of mechanical and electrical aids which not only release the technician for other work, but which in many cases are capable of greater precision and are less subject to random or individual variations. These particularly have come to the fore during the past decade.

GLASS WASHERS Many aids are now available for decreasing the drudgery and increasing the efficiency of glass washing, from simple siphon-operated pipette washers to modern programmed machines of the familiar dish-washing variety.

AUTOMATIC DISPENSERS Many of these function by means of a piston and suitable valve arrangement. They may be combined with automatic dilution or the addition of programmed reagents.

FLOW-THROUGH COLORIMETERS Flow-through cells have become available for installation into most colorimeters and spectrophotometers. They greatly shorten the time taken to read a large number of specimens and clearly they are of much less practical value when specimens arrive in the laboratory one by one throughout the day. They have the big advantage that the same cuvette is used for all measurements and they thereby eliminate errors due to unmatched cuvettes.

DIGITAL READ-OUT INSTRUMENTS During the last five years instruments displaying results on a digital counter have replaced many of the older instruments employing conventional microammeters or galvanometers. Examples are the Coulter Counter in hematology and the I.L. Flame Photometer. Such digital read out eliminates the manual recording of results and subsequent calculation or reading from a graph and the consequent chance of error.

AUTOMATIC BALANCES During the last few years the classical analytical balance has given way to single pan balances employing a pre-loaded beam, digital readout and magnetic damping, so that operations which previously took several minutes can now be accomplished in seconds.

THE AUTOANALYSER There can be little doubt that the introduction of automatic systems of analysis into the clinical chemistry and hematology laboratories has had far more far-reaching consequences than any other single recent development. There are a number of automatic systems presently employed, such as the Robot Chemist (Warner-Chilcott), Mecolab system (Joyce, Leobl) and Auto-Chemist (AGA), but the most commonly used instrument is the Auto Analyser (Autotechnicon Corporation). The principle upon which this instrument operates is a revolutionary one in two regards. Firstly, instead of pipetting sera and reagents in absolute volumes, e.g. microliters or milliliters, they are mixed in amounts relative to each other by a peristaltic pump which milks tubes of various calibers simultaneously. Time delay and consecutive adding of reagents are accomplished by introducing tubes of various lengths and the solutions are mixed by introducing air bubbles into the system. These air bubbles also serve to separate one sample from the next. Secondly, the normal step of protein precipitation and centrifugation is avoided by interposing a dialysis bath in the system so that only a protein-free filtrate is analysed. By the introduction of extra modules it is possible to carry out either the simultaneous or the sequential analysis of up to 12 constituents from each sample.

For each system of analysis there are five essential components as follows:

1. **THE SAMPLING UNIT.** This consists of a metal disc with forty holes in its periphery, holding small plastic disposable cups with serum samples, control sera and standard solutions. Mounted near the periphery is a sample pickup tube which dips into each cup in turn, aspirates a sample, and then a large air bubble to separate this sample from the next.

2. **PERISTALTIC PUMP.** Metal rollers or fingers held on the sprocket chains of the pump milk polyethylene tubes leading from up to eight reagent bottles or from the air. By various plumbing connections these may be combined to produce sequential mixing. After each addition there is usually a horizontal glass mixing coil.

3. **DIALYZER.** The pump moves the diluted, segmented sample into a dialyzer consisting of a cellophane sheet compressed between two plates which have grooved channels through which the fluid is pumped. Usually the diluted sample moves through one channel and the protein-free constituents pass through the membrane to combine with reagents circulating in the channel on the other side of the membrane under controlled temperature conditions.

4. **HEATING BATH.** The reaction stream now usually passes through a heating bath for colour development or an incubation bath in the case of enzymatic reactions, and then reagents may finally be added to stop the reaction.

5. **RECORDING COLORIMETER.** The flowing stream which has now attained its final colour development next passes through a de-bubbler to a dual-beam colorimeter where the electrical output from a photocell behind the flow cell is compared with that from a reference diaphragm. This difference is then traced as percent transmittance on a chart recorder and the specimen passes into a drain. As the specimen leaves the flow cell it is followed by a hiatus corresponding to a large air bubble and the recorder returns to 100% transmittance, ready for the next sample.

At the present time the Autoanalyser has been programmed for a large number of methods, including fluorimetry and flame photometry, in addition to colorimetric methods and it may also be employed for hematology, including cell counting and electrical estimation of hematocrit, and also for blood bank serology. The new SMA 12 will give an automatic print out of twelve different analyses on each blood sample. If this last-named instrument gains wide acceptance, it will produce far-reaching changes in our concepts of laboratory medicine — changes which may or may not be desirable.

For one thing we shall rapidly acquire information of the levels of a number of constituents in normal persons and various disease states which we have never investigated adequately before. Full utilization of this potential will only be possible with wide application of computer techniques. If the hypothesis is true that for many diseases there is a presymptomatic stage showing biochemical abnormalities, it is just by such data processing techniques that these will be brought to light.

On the other hand, physicians will be bombarded with information they have not requested within which will be buried the information they seek. It is certain that unexpected abnormal findings will be uncovered by this unsolicited information, but if the, admittedly low, proportion of false laboratory results remains constant, multiplying the tests by twelve will result in a numerical increase in these falsely misleading results. There is a danger that clinical cerebration may become further attenuated.

II. Kit Methodology

Ten years ago most laboratories prepared their own standard solutions, reagents, buffers and enzyme substrates. This was a time-consuming process and also productive of such marked variation from laboratory to laboratory that it was difficult to compare results from two institutions. The last few years have seen the advent of commercial kits in clinical chemistry and serology whereby, often by simple reconstitution with water, laboratories are furnished with active standardized reagents and control substances. There seems little danger that the use of such kits will result in laboratories relinquishing their responsibility for the accuracy of their results to a commercial house, as the manufacturers vie with one another for the very lucrative trade so that accuracy is retained and expense is kept to the minimum.

III. Specialization

The time when grade 12 education followed by an eighteen-month course qualified a laboratory technician to carry out all the known methods of clinical laboratory technology passed long since. As in clinical medicine there has been an ever increasing degree of specialization within the laboratory. The "general practitioner pathologist" is probably also on the way out. Even amongst the junior technicians it has been necessary, in the interests of efficiency, to limit the scope of work which each one is called upon to carry out regularly.

In most laboratories, therefore, technicians may normally work only within one discipline, hematology, clinical chemistry, bacteriology and so forth, and often only within one small area of this (e.g. the Autoanalyser, estimation of blood gases, electrophoresis, hormonal analysis, etc.). This has three main consequences:

1. Efficient utilization of such persons and the specialized equipment which they use requires the *batch approach* whereby a number of sera are examined at one time or in one session. Having dealt with this set of problems, the technician can then move to another area of the laboratory where she carries out a different type of analysis on another batch of specimens, and then elsewhere for another set of analyses. If, on the other hand, test samples are transmitted to the laboratory irregularly throughout the day, the analyst may be kept continuously busy setting up the first test afresh and will be unavailable for the other tests.

2. The technical staff of the clinical laboratory is largely recruited from the nubile section of the population, and it is seldom permanent. It takes some time to train a specialist technician and when she leaves, this is apt to introduce a temporary hiatus in the laboratory routine which it may be difficult to fill for some time.

3. The fact that the number of varieties of tests offered by the modern clinical laboratory has almost doubled during the past decade, that many

of them are elegant procedures requiring special knowledge outside the competence of general technologists, that others are very time consuming and it is inefficient to perform them singly, and that laboratories are striving to maintain a high degree of quality control means that only a small proportion of the total number of laboratory tests can be performed efficiently out of regular hours. It is felt that in most cases emergency tests may be confined to the estimation of hemoglobin, white blood count and differential, examination of a stained blood film, partial thromboplastin and prothrombin times, thrombin time for fibrinogen, C.S.F. examination, amylase, barbiturates, salicylates and sugar, blood urea nitrogen, serum electrolytes, bilirubin estimation in infants, bromsulphthalein excretion and blood bank serology.

It is seriously suggested that this core of some fourteen estimations encompasses all but a very few tests which can properly be considered of an emergency nature. If requests for emergency tests could be limited to them, we should have very few problems out of hours. The only alternative solution is to divide the laboratory staff into three eight-hour shifts and to train three specialist technicians for each one presently employed. This is the practice followed in industry and it might have some advantages. The present state of technician supply does not, however, permit it.

IV. Microtechniques

Fourfold increase in the number of tests now being performed on each patient raises problems regarding the size of specimen required. In pediatric work this may be of serious consequence. Prior to 1958 the majority of methods for biochemical analysis required 1 ml. or more of blood for a single determination, but during the past ten years methods have been developed for routine estimations on 0.2 ml. or less, and in the case of many tests, notably serum protein estimations, serum electrolytes, blood gases, bilirubin, glucose, serum calcium, and a great many others, valid analyses can now reliably be performed by ultra-microtechniques employing ten to twenty microliters of blood or serum — that is, less than a single drop.

V. Batch Processing

The advantages, indeed the necessity, of processing specimens in batches has been referred to above. This applies not only to specialized techniques, but also to the more mundane procedures such as hemoglobin assay and blood glucose determination. Very few laboratories have multi-channel autoanalysers, and in most it is necessary to re-program the single instrument for each different test. This involves switching the eight-tube manifolds, reagent bottles, incubation baths and filters, and re-stabilizing the instrument. This may take an hour.

It is, therefore, essential for efficient operation that the laboratory perform all the tests of one sort together once or twice daily. This is not an ideal

situation either for the attending physician or for the laboratory, but financially it is not possible to operate otherwise. The wider use of multichannel analysers will correct the problem to some degree, but will not abolish it as it is clearly impossible to house a sufficient number of machines, each of which costs some \$70,000, to provide continuous assay of the over one hundred different laboratory procedures presently performed in the hospital clinical laboratory.

VI. Change in the Role of the Clinical Pathologist

Increased complexity of clinical laboratory practice has resulted in a change in the role of the pathologist. No longer is he a "moribund anatomist" who peers by the hour down his microscope, giving only occasional side-long glances at the operation of the clinical chemistry, hematology or serology departments. There is a serious overtone to the quotation from the Peripatetic Correspondent which heads this article. Proliferation of laboratory tests often leaves the clinician a little confused regarding the value of each, and only the clinical pathologist can help him. The indiscriminate ordering of a number of laboratory tests is not only wasteful of the laboratory efficiency and the taxpayer's money, but also it may delay the clinical diagnosis.

Each patient presents as a clinical problem which must be unravelled in an orderly fashion. Some of this sorting will take place at the bedside, some in the X-ray department, and some in the laboratory. In each of these areas the patient will find a doctor expert in his field who also knows a fair amount of the operation of the other fields, but not so much as the local expert. Ideally then, the problem should be presented to each of these authorities — in the case of the laboratory this would be "anemia," "possible cirrhosis of the liver," "unexplained purpura," rather than "saline fragility," "S.G.O.T.," or "clotting time." These, too, are relatively random lists, but they illustrate a valid point, as in actual fact the test detailed in the second list would in many cases be normal in the clinical problems preceding them.

We have already outlined in the pages of *The Bulletin*¹⁴ the sort of orderly laboratory approach to clinical problems which we recommend and Cooper¹⁵ has given an account of the vast

amount of information which can be extracted from individual tests in hematology. The indiscriminate approach is similar to that of the man who closes his eyes and fires a shotgun wildly in the hope that one pellet will find its mark.

CONCLUSION

The advances in laboratory methods of investigation during the last ten years are too vast to be more than touched on in a simple review article. They have unveiled totally new vistas and we have barely placed our feet on the threshold of these. They have brought with them problems of volume and the necessity to discriminate. It is time we took stock and planned for the even wider fields which are to come. We should review in our minds the primary role we see for the clinical laboratory. Is its function to be the performance of as many tests as possible of a few varieties, or a lesser number of tests of as many types as possible? Is it primarily to be for the performance of as many of a routine nature as can be accomplished, or should more of its time be devoted to more elegant research procedures such as the investigation of glycoproteins, chromosomal abnormalities, isoenzyme estimations, and the like?

Only the medical staff of each hospital can decide these questions for themselves, but they must face the fact that the answers are mutually exclusive; we cannot have all. □

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PLAN TO ATTEND

THE 1969 SUMMER MEETING - KENTVILLE, N. S.

JUNE 25th, 26th & 27th



the decisive analgesic

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TABLETS

For effective relief of moderate to severe pain,
there's nothing quite like 292 Tablets.

Each tablet contains:

Acetylsalicylic acid 3½ gr. (0.22 Gm.)
Phenacetin 2½ gr. (0.16 Gm.)
Caffeine citrate ½ gr. (32 mg.)
Codeine phosphate 1/2 gr. (32 mg.)

Dosage: One or two tablets two or three times daily as required.

Contraindications: Gastrointestinal ulceration or sensitivity to ingredients. Large doses taken for prolonged periods may induce nephrotoxicity or gastrointestinal disturbances.

Full information on request.

Ⓞ Narcotic; telephone prescription permitted.



Medical Society Summer Meeting

Wednesday, Thursday, Friday

June 25th, 26th, and 27th

KENTVILLE, N. S.



Action: phenothiazine derivative possessing a specific antipruritic action; IT RELIEVES ITCHING REGARDLESS OF CAUSE.

Dosage: should be adjusted to the severity of the symptoms and the patient's response; a low dosage is generally effective. Here is a brief guide of average doses:

Oral route — adults: 2.5 or 5 mg twice daily after meals, plus 5 mg at bedtime; in predominantly nocturnal conditions, a single dose of 5 to 10 mg at bedtime; **children** (from 2 to 12): 2.5 or 5 mg at bedtime plus 2.5 mg twice a day after meals if necessary. Daily dose should rarely exceed 15 mg.

Parenteral route — particularly indicated in emergency cases or when rapid results are required; **adults:** 25 mg in deep I.M. injection repeated within 24 hours if necessary; **children:** 10 to 25 mg (2 to 5 ml) according to body weight.

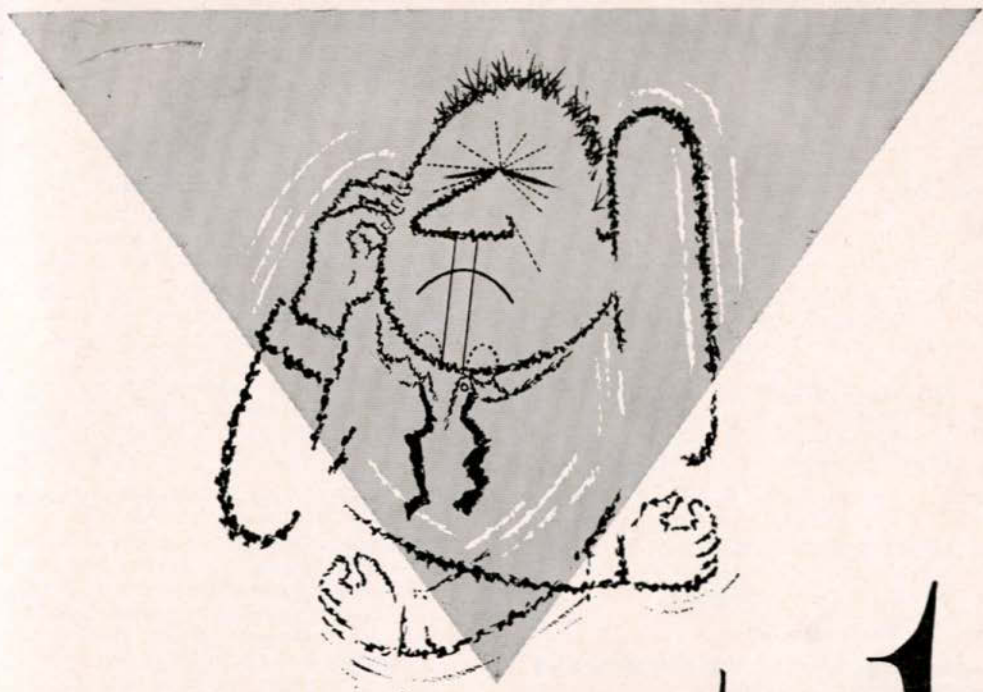
Contra-indication: comatose states due to barbiturates or alcohol.

Tolerance and precautions: usually well tolerated but should be administered under medical supervision; mild drowsiness may occur at the beginning of treatment; it generally disappears within 24 to 48 hours. Patients should be cautioned against driving a car or operating machinery until drowsiness has subsided.

Overdosage — treatment: no specific antidote; therapy must be based on symptomatic relief; gastric lavage; nor-epinephrine infusion if necessary.

Presentations: tablets of 2.5, 5 and 10 mg; ampoules of 5 ml, 25 mg (5 mg per ml) and vials of 10 ml, 5 mg per ml for deep I.M. injection; liquid, 2.5 mg per tsp. (5 ml).

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The Medical Advisory Committee on Driver Licensing

ANNUAL REPORT, 1968

General

The Medical Advisory Committee on Driver Licensing completed its seventh year of operation in December 1968.

Membership

The Committee consisted of the following:

- Mr. J. C. Douglas - Chairman
Dr. H. Kenneth Hall - nominated by The Medical Society of Nova Scotia
Dr. Alan J. MacLeod - nominated by The Medical Society of Nova Scotia
Dr. H. D. Beach - nominated by the Association of Psychologists of Nova Scotia
Mr. D. J. Tully - Registrar of Motor Vehicles
Mr. C. E. Pass - Secretary

Regional Representatives

The following are Regional Representatives of the Medical Advisory Committee:

- Dr. R. Sers, Antigonish
Antigonish - Guysborough Medical Society
Dr. P. R. Little, Truro
Colchester - East Hants Medical Society
Dr. H. C. Still, Halifax
Halifax Medical Society
Dr. R. G. A. Wood, Lunenburg
Lunenburg - Queens Medical Society
Dr. J. N. Park, New Glasgow
Pictou County Medical Society
Dr. F. W. Morse, Lawrencetown
Valley Medical Society
Dr. B. C. Trask, Sydney
Cape Breton Medical Society
Regular monthly meetings of the Committee were held during 1968.

Proceedings

During the year, 77 individual cases were studied by the Committee. On some of these, further information was required with the result that some cases were referred back to the Committee on more than one occasion. The total number of referrals to the Committee, as the result of this, was 87.

The following actions were taken as the result of recommendations made by the Committee:

- Twenty-seven persons had their licenses recommended as medically fit.
Twelve persons had their licenses suspended for reason of medical unfitness.
Fourteen persons were found to be medically fit but were required to be re-examined as a driver.
Five persons were recommended for restrictions on their licenses.
One person had his license suspended for visual impairment.
Five persons were found to be medically fit but were required to be re-examined by a Driver Improvement Officer at that time and again in six months.
One person was found to be medically fit but was required to be re-examined by a Driver Improvement Officer at that time and again in one year.
Two unlicensed persons were refused licenses on the grounds of medical unfitness.
Three persons were required to submit a medical report before renewal of license.
Seven cases are awaiting further information.
The above report re the activities of the Medical Advisory Committee on Driver Licensing during 1968 is respectfully submitted.

J. C. Douglas,
Chairman -
Medical Advisory Committee
on Driver Licensing. □

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Established 1929

5511 Spring Garden Rd.

The Erythrocyte Sedimentation Rate

ROBERT F. SCHARF, M.D., C.M., F.R.C.P.(C)

Halifax, N. S.

As medical knowledge increases, more specific, elaborate and accurate laboratory tests increasingly assist in diagnosis and treatment. In many situations the availability of sophisticated investigation is limited or there is delay in getting the results: meanwhile, simple laboratory tests are frequently forgotten. Admittedly, some are not specific, but this should not be allowed to hide the fact that many can be almost diagnostic when coupled with an alert appreciation of clinical possibilities. For instance, increase in the uric-acid level in the serum in a rather confused case of supposed local thrombophlebitis, and either a similar elevation or an abnormal glucose tolerance curve in a patient of 45 with tender heels, may be diagnostic of the soft-tissue reactions of gout or diabetes, respectively.

We have found the erythrocyte sedimentation rate (ESR) valuable in several situations. In chronic or low-grade osteomyelitis, the persistently elevated or progressively increasing values obtained with this simple test may be the only abnormal laboratory finding. For example, two patients who were seen recently had mild persistent pain in the operative area after bone operations at other hospitals. The roentgenographic appearances were compatible with the trauma suffered and its treatment, and the pain was not abnormal for the stage of recovery from initially severe injuries. In both cases the progressive increase in ESR — to 40, 50, and 60 mm. in 1 hour — enabled us to make an accurate prognosis and prescribe appropriate therapy before roentgenography or the clinical course indicated bone infection. Persistent increase in the ESR after severe injuries should lead one to suspect the presence of intra-abdominal abscesses in cases of abdominal trauma, and osteomyelitis if bony injury has occurred — especially in cases of open reduction or compound fracture.

The young male adult who presents at the outpatient department, complaining of persistent or recent low-back pain, worse in the mornings and easing in the afternoons, all of whose laboratory findings are negative except a raised ESR, can be

diagnosed with almost complete confidence as having early ankylosing spondylitis. The roentgenological finding of sacro-iliac sclerosis, or the presence of any restriction of spine or chest motion that otherwise is unexplained, will verify the diagnosis. A normal ESR in these circumstances in the untreated symptomatic patient virtually excludes this diagnosis.

So valuable do we find an ESR that at our Forces' hospitals we admit any patient with back pain and a persistently elevated ESR — to 40, 50, (or more) mm. in 1 hour — and he is treated as an outpatient only after tuberculosis, chronic bone infection, and malignancy of the common sites have been excluded as far as possible by careful observation and testing. In most cases in which the clinical course is satisfactory but the ESR remains elevated, twelve months later we re-check all of our findings.

The ESR provides a simple method for the routine checking of the resolution of a chronic abdominal abscess or of treated severe diverticulitis. True, an elevated level could be due to other causes but an increasing level coupled with increased clinical signs is ominous, and subsiding or normal levels are very encouraging.

Many patients with a torn knee meniscus give no history of injury. Slight warmth and swelling of the knee, seemingly not due to injury, may be due to mechanical causes; however, this should not be accepted until other causes have been excluded. A normal ESR rules out most rheumatoid causes, and an otherwise unexplained elevation should lead to careful medical investigation.

Many puzzling cases in which we should have ordered regular ESR tests to elucidate changes have been resolved when the ESR has finally been studied. The test is simple to perform, requiring only a few glass tubes, a watch, blood samples and a trustworthy observer. Its more frequent employment in a wide variety of cases may yield surprising dividends to the surgeon — or indeed, to any physician. □

**HAVE YOU MAILED YOUR
ACCOMMODATION APPLICATION FORM
FOR
THE 1969 SUMMER MEETING?**

Correspondence

Dear Sir:

The paper describing the patient with pulmonary embolus, reprinted in the Bulletin, February, 1969, page 21, was clearly written before lung scanning became a routine examination.

Whilst it is agreed that this examination is not available in every locality, it is generally accepted today that where it is available it forms an essential part of the diagnostic process in suspected pulmonary embolism. I would submit that most cases of fatal pulmonary embolus will be averted if the following regime be instituted:

1. Always suspect pulmonary embolus in the high risk group.
2. Any patient who develops unexplained chest pain or dyspnoea in this group should have one dose of anticoagulant.
3. Chest X-ray.
4. Lung scan should be done immediately.
5. The diagnosis can now be made, often with assistance from EKG, and necessary treatment continued.
6. Where the embolus is thought to be massive, pulmonary arteriography must be done before considering embolectomy.

J. F. Filbee, M.B.

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For precautionary statement regarding toxicity to liver and pancreas, please consult your Vademecum International.

Full information available on request.



Public Health News

Water and Sewage Works Operators Course

A Water and Sewage Works Operators Course for operators of sewage treatment plants and water treatment facilities in the four Atlantic Provinces was held in Halifax April 21 to 25 at the Halifax County Vocational School.

Attended by approximately 30 persons, the course was sponsored by the American Water Works Association with financial aid coming from the Nova Scotia Department of Public Health, the New Brunswick Water Authority, and the Prince Edward Island Water Authority. The Nova Scotia Water Authority decided not to render any assistance.

The course is the first of several expected to be held in the next few years.

Camp Tidnish in Operation This Summer

Summer camps for handicapped children and young adults will be held again this summer at Camp Tidnish, 15 miles from Amherst. Dates for the camp, operated by the Rotary Club of Amherst, are:

Young adults (16 and over) June 22 to July 5

Seniors (13 - 16) July 6 to 19

Juniors (8 - 12) July 20 to August 5

For further information contact the Canadian Rehabilitation Council for the Disabled, 2004 Gottingen Street, Halifax.

Diabetics May Receive Little Diet Instruction

Persons diagnosed as diabetic in hospital or at the doctor's office may receive very little diet instruction. Mrs. Maudie Haley, nutritionist, told the annual staff meeting of the Fundy Health Unit in Windsor.

She said such persons are usually quite startled to learn they have diabetes. It is in this confused state that the public health nurse usually first sees the person.

Mrs. Haley suggested that the nurse first talk a little about diabetes to the person. She said there was a need to explain what the disease was and how the oral tablets and insulin worked.

The nurse also had to reassure the person that diabetes was not a dreaded disease and that by following good eating habits, that person can continue to live a normal happy life.

Mrs. Haley said a new Diabetic Team has been formed at the Children's Hospital. This team included a social worker, nurse, dietitian, intern from the Metabolic Unit, and specialist Dr. Bruce Morton. Diabetic children may be referred by their family physician to the Metabolic Clinic Monday afternoons.

Chronic Obstructive Airway Disease

Two clinical types may be recognized in patients with chronic airway obstruction. One is the emphysematous type, designated as "PP", and the other the bronchial type, called "BB". Differences are found in the cardiac output of the two types of patients.

Chronic airway obstruction has usually been classified on the basis of physiologic measurements of lung function or on destructive parenchymal lesions found at autopsy.

However, another approach to classification is suggested by clinical features. These indicate that some patients with chronic airway obstruction—ones at opposite ends of a wide clinical spectrum—may be classified as either "pink puffers" (PP) or "blue bloaters" (BB).

A cardiopulmonary classification can be formulated for these patients on the basis of differences in ventilatory and circulatory responses to the demands for tissue oxygenation, and anatomic and pathologic characteristics.

In the study reported, 112 patients were selected from an "Emphysema Registry" maintained at the University of Colorado Medical Center. They were classified as PP if they were thin or had a history of major weight loss, had narrow cardiac shadows on their roentgenograms, a hematocrit less than 55 per cent, and no history of heart failure or of phlebotomy. Patients were classified as BB if they had no marked weight loss except terminally, had cardiac enlargement, had had at least three treated episodes of heart failure, a hematocrit repeatedly greater than 60 per cent, and had had 10 or more phlebotomies.

In addition to clinical examination, standard pulmonary function tests were made. These included maximum breathing capacity (MBC); vital capacity (VC) and forced expiratory volume (FEV₁); test of inert gas distribution; arterial blood and gas exchange measurements; exercise tests; cardiac catheterization; and, in the case of 20 patients who died, pathologic examination.

The range of ventilatory impairment was similar in both types, as were several measurements of gas exchange. Alveolar ventilation was not significantly different in the two types. However, when alveolar ventilation was expressed as per unit of oxygen uptake, the ratio was significantly lower in BB patients than in PP ones.

The overall pulmonary ventilation was greater in PP patients than in BB ones, and arterial oxygen saturation was much lower in BB patients both at rest and during exercise.

At autopsy examination of the 20 patients (evenly divided between PP and BB patients), the 10 PP patients were all found to have had severe emphysema; only two had mucous gland hyperplasia in their bronchi. On the other hand, seven of the 10 BB patients had mucous gland hyperplasia and two did not have severe emphysema.

While physiologic measurements in chronic pulmonary disease are useful in guiding therapy, by themselves they provide little information of differential diagnostic importance and may be misleading if not properly interpreted.

In the present series, the total lung capacity of PP patients was greater than that of BB patients. In BB patients emphysema appears to be somewhat less severe than in PP patients, and mucous gland hyperplasia seems to be more common.

Physiologic Findings

Striking differences were found between PP and BB patients in their cardiac outputs. The arteriovenous oxygen difference was consistently smaller in BB patients, meaning that cardiac output, for a given oxygen uptake, was consistently higher than in PP patients. Since the patients in this series were separated into two types which do not depend on strictly "pulmonary" signs, it is not surprising that ventilatory measurements do not yield the distinguishing features provided by the cardiac outputs.

In both types of patients, exercise brought about a comparable rise in cardiac output in the absence of congestive failure. However, when the BB patient was in congestive failure, the cardiac output fell with exercise. In heart failure both types of patients were severely hypoxemic, and the BB patients remained so in cardiac compensation. In the PP patient the arterial saturation was lower at rest than during exercise when in failure; in the BB patient the saturation was lower at rest than during exercise when not in failure.

The amount of oxygen delivered to the lungs per minute is greater in PP patients than in BB patients because their ventilation is greater. This becomes significant when expressed as a ratio of ventilation to oxygen uptake.

A difference between the oxygen output transport system in the two types of patients is that the

Giles F. Filley, M.D.; Henry J. Beckwith, M.D.; John T. Reeves, M.D.; and Roger S. Mitchell, M.D. *The American Journal of Medicine*, January, 1968.

¹Reprinted from the Abstracts of the National Tuberculosis Association, June 1968.

Printed through cooperation Nova Scotia Tuberculosis Association.

hypoxemic BB patient has a lower total ventilation and a higher cardiac output. The PP patient, regardless of his metabolic or cardiac status, has a higher ratio of total ventilation to cardiac output. In the BB patient, arterial hypoxemia is associated with low-ventilation to cardiac output values.

Although a chronic cough usually develops early in both types of patients, the history of cough is of longer duration in the BB than in the PP patients. Both types are dyspneic, but the dyspnea is more severe and disabling in PP patients than in BB ones.

Arterial Blood

The arterial blood of the BB patient is less saturated than that of the PP patient but his tissues are probably less hypoxic. His heart fails when he has a pulmonary insult such as acute bronchitis, bronchiolitis, pneumonia, pulmonary embolism, or excessive sedation.

The simple and practical criteria by which these types can be distinguished not only have diagnostic

value but also raise questions about several general physiologic responses to different types of pulmonary interference with oxygen transport.

Two general mechanisms are available for adjusting to oxygen deficiency. They are by decreasing the rate of oxygen consumption and by increasing both the rate of oxygen delivery to the tissues and the rate of oxidative metabolism. The PP patient, with his weight loss, small consumption of oxygen, and low cardiac output, appears to be "adapting," while the BB patient, consuming more oxygen and with a higher cardiac output, seems to be putting up more of a "struggle."

The importance of the distinction between hypoxia and hypoxemia must be emphasized. Perhaps the PP patient, with arterial saturation almost normal, is only superficially "pink" and the hypoxemic BB patient is only superficially "blue." When direct methods become available for determining which type has the more severe hypoxia in the body tissues, these labels may need to be reversed. □

13th Annual Scientific Assembly of THE COLLEGE OF FAMILY PHYSICIANS OF CANADA

Host, The Ontario Chapter, College of Family Physicians

Guests, The Royal College of General Practitioners of Great Britain

Royal York Hotel, Toronto, Ontario

September 29th - October 2nd, 1969

Appreciation

Joseph Earle Hiltz

During the early evening of March 22, 1969, while, as Vice-Chairman of the Board of Governors of Acadia University, he was about to attend the dinner in honour of the first Chancellor, death came suddenly to Dr. Earle Hiltz. He had planned to do a lot more but his contributions to his profession, the community at large, and humanity in general, were such as only a few men are privileged to give.

Joseph Earle Hiltz was born in Truro, March 15, 1909. He received his early education in his home town and entered Dalhousie University, at which institution he obtained his science degree in 1930 and from which he graduated in medicine in 1934. He was Resident Physician at the Victoria General Hospital from 1934 until May 1935. His intention at that time was to enter general practice and to obtain some training in the diagnosis and treatment of tuberculosis, he came to the Nova Scotia Sanatorium for three weeks. He was to remain for 34 years.

He was appointed staff physician at the Sanatorium in 1935 and became Assistant Medical Superintendent in 1937. From 1944 to January 1946, he was Acting Superintendent at the Victoria General Hospital in Halifax. In January 1946, he went to Shelburne where the Royal Canadian Naval Hospital had been made available to the Province. He established it as Roseway Hospital for the treatment of tuberculosis and with a small general hospital wing. From September 1946 to May 1947, he attended the School of Public Health and Hygiene at the University of Toronto, obtaining his Diploma in Public Health in May 1947. Preparatory to his return to the Nova Scotia Sanatorium, he spent the summer of 1947 on tour of tuberculosis treatment centres in Canada and the United States. On October 1, 1947, he was appointed Medical Superintendent of the Nova Scotia Sanatorium, a position he continued to hold until he died.

While he was most desirous of doing everything possible to restore the health of people with tuberculosis, he was equally insistent that every effort should be made to prevent tuberculosis developing in the individual. At the Nova Scotia Sanatorium he gathered around him a loyal and capable staff and, over the years, making the best use possible of rather primitive buildings, he made certain that every worthwhile advance in the diagnosis and treatment of tuberculosis and, later, of all respiratory diseases was utilized to the fullest advantage. In 1956, he became Administrator of Tuberculosis Control for the Province of Nova Scotia, and the

various Health Unit Directors who are responsible for the actual control routine will bear witness to his zeal in tuberculosis prevention.

His formal duties were only a part of the tremendous effort he put forth throughout all his professional life. The Nova Scotia Tuberculosis Association knew him well, he organized the Nova Scotia Thoracic Society, he was President of the Canadian Tuberculosis Association, and had a great deal to do with the formation of the Canadian Thoracic Society. He was a very active member of the International Union Against Tuberculosis and his biennial vacations were busman's holidays to wherever in the world the meeting of the International Union was being held. Few committees having to do with the subject of tuberculosis or respiratory diseases did not count Earle Hiltz either as chairman or a prominent member, were they provincial, national, or international. Yet he found time to lecture to the affiliate student nurses at the Sanatorium, the medical students at Dalhousie University, to the students of the Dalhousie School of Nursing, and he did not neglect research. His contributions to the medical literature, provincial, national, and international, totalled at the time of his death some sixty scientific articles. He was certified in Internal Medicine by the Royal College of Physicians and Surgeons of Canada, he was a Fellow of the American College of Chest Physicians, and a member and past director of the American Thoracic Society.

He was a very active figure in organized medicine. He was disturbed by the attitude held concerning salaried physicians by many of their medical confreres and did much to alter it. He seemed to be continually a member of committees of the Valley Medical Society and The Medical Society of Nova Scotia and rarely missed a meeting of these organizations. He was a prime mover in the setting up in The Medical Society of Nova Scotia of the Section for Salaried Physicians.

While it might be considered that such an involvement with his profession would be enough to keep any man fully occupied, Dr. Hiltz found the time to accomplish many other things. He was a past chairman and a continuing member of the Board of Directors of the Fundy Mental Health Centre; he was a member of the Board of Trustees of the Maritime School of Social Work; he was a past chairman of the Institute of Pastoral Training, and he was keenly interested in the activities of the Nova Scotia Institute of Science. For many years,

the Valley Chapter of this Institute has held its March meeting at the Nova Scotia Sanatorium. He was long actively engaged in the work of the St. John Ambulance Association and, at the time of his death, was Provincial President, Nova Scotia Council.

While he had never attended Acadia, the University occupied a very special place in his affection. He had long been a member of the Board of Governors and for the past several years was vice-chairman of the Board. He had been Chairman of the Acadia University Institute since its inception. He worked hard for Acadia particularly during the period of rapid expansion of the University which has been going on for the past fifteen years. The appointment of the first Chancellor whose installation took place just before Dr. Hiltz died was a source of particular gratification to him.

Civic responsibilities did not escape him. He served two terms as president of the Kentville Gyro Club and was past chairman of the Board of Stewards of the United Church of Saint Stephen and Saint Paul of Kentville, N. S. He was a member of the Kentville Board of Trade. Up until 1959 when he ceased to have any spare time he was an ardent

curler and remains one of two skips in the history of the Gloucester Curling Club who negotiated an eight-end.

He was one of Canada's best-known philatelist and possessed the most complete collection of Danish West Indies stamps in existence. He was a director and past president of the Valley Stamp Club, a member of the Royal Philatelic Society of Canada and Canadian Armed Services Stamp Exchange Club.

When a man has accomplished so much usually he has had the help of a good woman and Earle was fortunate in having one of the best. He married Eileen MacKay, New Glasgow, N. S. in 1937. She and his sister Margaret, Mrs. E. G. Jarvis, Halifax, survive him.

It is going to be very difficult to get along without Earle Hiltz. He undertook many tasks and strove for perfection in all of them. His enthusiasm, his example, his leadership could not but inspire those associated with him to try to excel in all they did. He would wish us to carry on to the goals he had set for himself and for us. That, we shall endeavour to do.

J. J. Quinlan □

NEW MEMBERS

The Physicians listed below have joined The Medical Society of Nova Scotia between October 1, 1968 and April 30, 1969. A most cordial welcome is extended from the Society.

F. A. Dunsworth, M.D.,
President.

DR. J. P. ANDERSON	Halifax	DR. B. S. LIU	Halifax
DR. D. W. ARCHIBLAD	Halifax	DR. D. C. MASILAMANI	Dartmouth
DR. B. W. D. BADLEY	Roekingham	DR. J. D. MEEHAN	Freeport, Digby Co.
DR. M. BERGIN	Dartmouth	DR. N. M. MEHTA	Bass River
DR. G. E. BOYD	Halifax	DR. R. T. MICHAEL	Halifax
DR. P. BRIGHT-AZARE	Armdale	DR. E. A. MOORE	Halifax
DR. R. L. BROWN	Halifax	DR. A. F. J. MORETON	Halifax
DR. C. BUGDEN	Roekingham	DR. A. S. MURRAY	Dartmouth
DR. J. F. CANTWELL	Halifax	DR. A. C. MacDONALD	Halifax
DR. DOROTHY C. CHEN	Halifax	DR. C. J. MacDONALD	Halifax
DR. P. P. CHOW	Don Mills, Ont.	DR. D. A. MacDOUGALL	Antigonish
DR. HELEN M. CUNNINGHAM	Dartmouth	DR. A. R. MACNEIL	Halifax
DR. H. W. EDSTROM	Halifax	DR. A. S. PARKER	Halifax
DR. P. L. EMENAU	Armdale	DR. R. G. PETRIE	New Waterford
DR. R. C. FORBES	Lunenburg	DR. C. S. PRICE	Halifax
DR. R. J. FRASER	Musquodoboit Harbour	DR. WM. RICHMOND	Goldboro, Guys. Co.
DR. JUDITH H. GOLD	Halifax	DR. M. D. RIDING	Armdale
DR. J. D. GRAHAM	Halifax	DR. R. G. RITCHIE	Hantsport
DR. M. P. GUPTA	Ottawa, Ont.	DR. K. I. ROBB	Roekingham
DR. R. GUZMAN	Halifax	DR. D. K. RUSHTON	Fairview
DR. O. A. HAYNE	Halifax	DR. A. SAMAD	Dirby
DR. L. P. M. HEFFERNAN	Roekingham	DR. V. E. SANGALANG	Halifax
DR. B. H. HOAR	Antigonish	DR. R. F. SCHARF	Dartmouth
DR. C. HOBEIKA	Halifax	DR. MARLENE J. M. SCOTT	Halifax
DR. J. E. HOWARD	Halifax	DR. A. D. M. SMITH	Shubenacadie
DR. J. R. JACKSON	Halifax	DR. I. R. SUTHERLAND	Sandy Cove, Digby Co.
DR. A. J. JOHNSON	Halifax	DR. E. S. SYLWESTER	Halifax
DR. A. W. KUSHNER	Halifax	DR. M. A. THOMAS	Glacé Bay
DR. PAH-GIN KWA	Halifax	DR. W. D. TILLER	Roekingham
DR. W. H. LENCO	Halifax	DR. R. C. TSANG	Halifax
		DR. W. C. WOOD	Roekingham

REPORT OF D. MacKINTOSH,
MEDICAL OFFICER,
COUNTY ASYLUM, PUGWASH



A PLEA FOR REFORM

One feels a certain sympathy for the foreigner trying to learn English who, on reading the neon-lit sign "*Cavalcade — Pronounced Success*" committed suicide.

It was difficult enough to master the inconsistencies of the English language as used by the English, but it seems well-nigh impossible to integrate those introduced by our neighbours south of the border. I wish the Americans would really get down to reconstructing the language, instead of tackling it in the present half-hearted-manner. In some journals, the "Instruction to Authors" tells me to use Mr. Webster's Dictionary, which is fine — until I realize that apparently I must look up every word: how otherwise can I know when to substitute 'f' for 'ph' or to delete 'u' from 'ou' combinations.

I'm sure that no editor, American or otherwise, would accept the spelling 'fosforus', but 'sulfate' is all right; similarly, I can write 'stupor' but not 'stupendus'. Hasn't anyone the courage to declare that the kemikal simbol for fosforus is 'F' and that awl 'ou' kombinashuns shood be 'u' in feweher? Then, perhaps, I would be on the ant-eye-war path, discussing the habits of the fertile turtle.

E. H.

BRINGING HOME THE BACON

In a certain R.N. Hospital the Surgeon Rear-Admiral kept a piggery adjacent to his residence, supplying bacon to the Hospital and being supplied with swill from the wards. Great consternation one day: the Admiral's 340 lb breeding sow was missing. Immediately the guards at the main gate were alerted to prevent the escape of the sow. Knowing their Kings Regulations down to the last 't' the guards, of course, searched everyone going through the main gate. . . .

Contributed

To the Warden and Councillors of Cumberland.

I beg leave to submit the following report as Medical Officer of the County Hospital for Insane for the year ending December 31st, 1924.

In nineteen twenty four

I can say but little more

Than I said in fateful words in twenty three;

After which I made admission,

To appease some opposition,

That my words and facts did not all agree.

This admission or retraction,
Though a laudable transaction,
Was intended more to palliate than beg;
Ne'ertheless I just may mention,
In support of my contention,
That I really had to stand upon one leg.

As regards my present status,
If you honestly look at us,
Leaving out, of course, the ones that always yelp,
You'll find comparative contentment,
With a little mild resentment,
Among the inmates and the management and help.

Deaths

The death rate for the season,
No doubt for some good reason,
Which should not be forgotten or ignored;
Five women and three men
Make a total less than ten:
Either to be commended or deplored.

One death was from bronchitis,
And two were from carditis,
Two strokes from apoplexy did quick work,
One more was from retention,
The kind I will not mention
For fear that it might shoek your lady clerk.

One more was from paralysis,
Which after strict analysis,
Was spinal working upwards from below:
Two more were found quite dead
Lying quietly in bed,
But what the deuce they died of I don't know.

We are getting too congested:
And it cannot be contested
That something must be done to make more room.
Brick and labor, will be cheap
And workmen would just leap
If they thought that there was going to be a boom.

All of which is now submitted,
Nothing purposely omitted,
As my customary annual report:
But if you do not like it
You're at liberty to strike it
From the records, failing adequate support.

D. MACKINTOSH, M.D.,
Medical Officer.

Pugwash, N. S.
December 31st, 1924.



ORTHO-NOVUM SQ changes the picture with a sequential approach to treatment of the menopause.

Estrogen replacement alone in the early part of the cycle *plus* conception control.

Security: ORTHO-NOVUM SQ replaces the fear of pregnancy with the security that comes with virtually 100% contraceptive protection. Your patient doesn't have to live with the fear of starting a second family during menopause.

Assurance: The estrogen replacement in ORTHO-NOVUM SQ is sufficient to eliminate menopausal symptoms. There is no longer any reason why your patient should suffer through menopausal symptoms.

Confidence: Because ORTHO-NOVUM SQ is a sequential, it contains the progestin necessary to produce regular, well-controlled cycles. Your patient will not have to worry about irregular periods during menopause.



Ortho-Novum SQ*
Mestranol AND Mestranol WITH Norethindrone TABLETS

ORTHO PHARMACEUTICAL (CANADA) LTD.

Don Mills, Ontario

Devoted to research in family planning

*Trademark

Ortho-Novum SQ*

Mestranol • Mestranol • Norethindrone

COMPOSITION: The hormones used are familiar and well-proven. ORTHO-NOVUM SQ contains mestranol (ethinyl estradiol-3-methyl ether) and norethindrone (17 alpha-ethinyl-17-hydroxy-4-estren-3-one), the estrogen and progestin used in ORTHO-NOVUM* tablets for over ten years.

Each white tablet contains 0.08 mg mestranol. Each blue tablet contains 0.08 mg mestranol with 2 mg norethindrone.

INDICATIONS: The menopausal syndrome and sequential conception control.

DOSAGE AND ADMINISTRATION: For the first cycle only, have her take one white tablet a day starting on Day 5 of menstrual cycle followed by one blue tablet a day. At the end of the course of ORTHO NOVUM SQ, she stops the tablets for one week.

From now on, she simply completes each course of tablets, stopping at the end of each course for one week. The tablets should be started whether or not menstruation has occurred or is finished.

If spotting or bleeding should occur while taking ORTHO-NOVUM SQ, the tablets should be continued in the regular manner. It is not necessary to double the dosage.

CLINICAL EXPERIENCE: ORTHO-NOVUM SQ has proven highly effective in the control of conception and menopausal symptoms.

Almost all patients using ORTHO-NOVUM SQ tend to have a regular menstrual cycle with practically no change in amount of flow. Weight change is insignificant.

DURATION OF USE: As long as physician feels is desirable.

PRECAUTIONS AND CONTRAINDICATIONS: Although no causal relationship has been proven between the use of progestin-estrogen compounds and the development of thrombophlebitis, physicians should be cautious in prescribing ORTHO-NOVUM SQ. Tablets for patients with thromboembolic disease or a history of thrombophlebitis.

Patients with pre-existing fibroids, epilepsy, migraine, asthma or a history of psychic depression, should be carefully observed. Pre-treatment examination should include a Papanicolaou smear.

ORTHO-NOVUM SQ should not be taken: In the presence of malignant tumors of the breast or genital tract; In the presence of significant liver dysfunction or disease; In the presence of cardiac or renal disorders which might be adversely affected by some degree of fluid retention; During the period a mother is breast-feeding an infant.

PACKAGING: ORTHO-NOVUM SQ tablets are available in DIALPAK* Dispensers (one cycle of use).

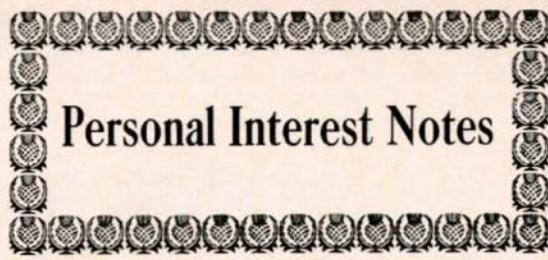
Detailed information available on request.

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ORTHO PHARMACEUTICAL (CANADA) LTD.
Don Mills, Ont.

MSMB 1969: 45: 87-8



Personal Interest Notes

Dr. J. Aquino — 3 daughters and one son won 14 first place prizes in the Halifax Music Festival in February.

Dr. Donald C. Brown — (Director of Residency Training in Family Practice) was special speaker at the Fredericton Hospital Staff luncheon meeting. Topic: "Trends in Teaching Family Practice".

House Calls by 'Chopper' — In what is believed to be a first for Canada, a private helicopter is being used by Drs Peter Goddard and Douglas Henshaw to visit patients in remote areas or to get to the hospital rapidly when traffic or weather conditions would make it difficult or impossible. Both stress that their intention is to use the aircraft to improve their own efficiency, and they do not intend to levy extra charges on their patients for the use of the helicopter.

Dr. Marvin Ramsay Clark (Kensington, P.E.I.) appointed Assistant Director of the Division of Continuing Medical Education, Dalhousie University.

Dr. C. L. Gosse was elected general campaign chairman of the Halifax-Dartmouth United Appeal Campaign for 1969.

Drs. F. Stewart and Otto H. Horrelt — The Senate of Dalhousie University approved the granting of the Diploma in Anaesthesia.

Dr. D. W. Cudmore — will be installed as a fellow of the American College of Obstetrics and Gynaecology in April in Florida.

Dr. C. E. van Rooyen — has been appointed to the editorial board of the Journal of Infectious Diseases.

Dr. W. A. Ernst — Elected president of the active medical staff of the Halifax Children's Hospital. Other members of the medical executive: Dr. G. A. Gillis, B. S. Morton, J. A. R. Tibbles, R. B. Goldbloom, J. Ross.

In memory of the late Dr. C. M. Jones — an annual award has been established by the staff of the Halifax Infirmary.

Dr. I. E. Purkis — Elected president of the active medical staff of the Victoria General Hospital. Other members of the Executive: Drs. B. J. Steele, A. D. MacKeen, S. Hirsch, J. K. B. Purves, J. H. Charman, S. York, V. Ing, R. Yabsley.

Dr. A. L. Murphy — Became first full-time chairman of the University Grants Committee in January.

Dr. R. N. Anderson — Appointed chairman of the Medical Advisory Committee of the Nova Scotia Branch of the Canadian Heart Foundation.

Dr. R. M. Read, MDCM, has been appointed Assistant Professor of Ophthalmology at South Western Medical School at Dallas, Texas. He is a son of Dr. Horace E. Read, vice-president of Dalhousie and Mrs. Read.

Dr. Richard Shaw, medical geneticist, has been appointed assistant professor in the department of Paediatrics in the Faculty of Medicine. He will also lecture in the department of Preventive Medicine. A native of Redlands, California, Dr. Shaw has been assistant professor, Biology, at Wayne State U. Detroit.

Dr. W. T. Josenhans (Physiology) appeared before the select committee on taxation which met recently in Halifax. He spoke on the 'killers' — cigarettes, liquor, gasoline, and cars.

Dr. R. O. Jones (Psychiatry) gave the First Iago Galston Memorial Lecture, in the postgraduate faculty of the State of Connecticut, in New Haven, on April 8.

Dr. Allan Pyesmany of the Department of Pediatrics has received a research grant of \$20,000 from the Department of National Health and Welfare for the coming fiscal year. The research project involves determination of the incidence and titre of maternal antibodies to foetal antigens, and the possible role of these antibodies as a cause of abortion, congenital disease, and structural congenital anomalies.

Dr. Allan S. MacDonald of Dalhousie University's surgery department has received a \$36,000 Medical Research Council of Canada grant for research in transplanting of human organs.

A native of Antigonish, Dr. MacDonald will work at Halifax with Dr. S. G. Lannon, a member of the urology department at Victoria General Hospital and Dalhousie University.

As A Camsi Project, Dal Medical Students recently sought, sorted and shipped tons of badly-needed medical supplies to the Dominican Republic. The campaign was organized by Mike Antle, a second-year student, with the assistance of several major drug houses and the Saguenay Shipping Line. Seven other Canadian Medical Schools participated.

OBITUARIES:

Dr. J. Earle Hiltz, Dal./31., Superintendent, Kentville Sanatorium, died March 22, 1969 at the age of 60. Born in Truro, he attended Colchester Academy and Dalhousie University. He joined the staff of the sanatorium in 1935, and became assistant medical superintendent two years later. In 1946 he was transferred to Shelburne where he helped establish Roseway Hospital as a general hospital and treatment centre for tuberculosis. In 1947 he returned to the Provincial sanatorium as medical superintendent, where he remained until his death. To his wife and sister, we extend our deepest sympathy. An Appreciation for Dr. Hiltz appears on page 83.

Dr. Duncan MacMillan, M.L.A., Dal./28., died April 10, 1969. He was born in Lake Ainslie, Cape Breton, and received his early education there. He completed his high school education at Truro Academy before entering Dalhousie University. He practiced medicine in Sheet Harbour for over 40 years and was instrumental in the establishment of the Eastern Shore Memorial Hospital. Dr. MacMillan was first elected to the Legislature in 1956 where he served until his defeat in 1963. He was returned in the 1967 general election. He was well known as a community leader where the district high school was named in his honor. Our sympathy is expressed to his wife and family.

Dr. Hugh Edgar Kelly, Dal./26, died April 11, 1969, at the age of 66 in Middleton where he had practiced medicine since 1928. Until recently he was chief of-staff of the Soldier's Memorial Hospital in Middleton. Dr. Kelly was born in Yarmouth where he received his early education. He graduated from Dalhousie Medical School in 1926. He is survived by his wife and two daughters, also a brother, to whom we extend our sympathy. □

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News Flashes

TO ALL PHYSICIANS

Re: PREGNANT Rh NEGATIVE PATIENTS

Rh Immune Globulin is available, free of charge, for use in Nova Scotia. It is supplied in phials of 1 ml. to be injected intramuscularly.

The Criteria, as determined by the Rh Committee, are as follows:

- 1) Rh negative gravida married to an Rh positive husband and baby is Rh positive.
- 2) Rh negative gravida who has aborted.
- 3) Rh negative gravida who suffers an ectopic pregnancy.
- 4) There must be *no* antibodies in the mother's blood at delivery, abortion, or at time of ectopic pregnancy.

The intra-muscular injection of the 1 ml. Immune Serum Globulin must be given *within 72 hours* of the delivery, abortion or ectopic pregnancy.

A repeat injection must be given after each succeeding pregnancy.

The distribution of the Immune Serum Globulin is through the Red Cross in Halifax. All hospitals in Nova Scotia stock the phials for use by the doctors on request.

It is now up to us to protect our patients by using the Immune Serum Globulin so that Rh disease becomes a thing of the past in Nova Scotia.

Rh Committee of
The Medical Society of Nova Scotia

FORTHCOMING MEETINGS

Dalhousie University is offering the following short courses:

A Day in General Practice	June 7
A Community Hospital Programme	
Edmunston, N.B.	June 10
Campbellton, N.B.	June 11
Grand Falls, N.B.	June 11

The Canadian Physiotherapy Association Annual Congress will be held at the Hotel Nova Scotian, Halifax, N. S. from June 8 - 13.

The Medical Society of Nova Scotia will hold their Annual Summer Meeting on June 25, 26 and 27, 1969 in Kentville, N.S.

102nd Annual Meeting of The Canadian Medical Association, 89th Annual Meeting of The Ontario Medical Association will be held in Toronto, Ontario on June 9-13, 1969.

Canadian Association of Physical Medicine and Rehabilitation, 17th Annual Meeting, August 21, 22, 23, 1969 to be held in Halifax, N. S. For information please write to Dr. W. O. Geisler, Secretary-Treasurer, 153 Lyndhurst Ave., Toronto 4, Ontario. The College of Family Physicians of Canada - Annual Assembly, Toronto, Ontario. Sept. 29 to Oct. 2, 1969.

The Second International Air Pollution Conference of the International Union of Air Pollution Prevention Associations will be held in Washington, D.C., from December 6th - 11th, 1970. The Program Committee invites submission of proposals to present papers at the Conference. Deadline January 31, 1970.

For more information on any of the above apply:
The Nova Scotia Medical Bulletin Office.

NOVA SCOTIA LACKS FACILITIES TO DEAL WITH YOUTH PROBLEMS

The MacKeen Royal Commission investigating the operation of Halifax County Hospital recently heard Dr. R. O. Jones, head of the Psychiatric Unit at the Victoria General Hospital state that there was a lack of facilities to care for adolescents with emotional problems. The drug problem which many adolescents are involved in today is a fact. He said "and indications are it will get progressively worse, not better".

Dr. P. Flynn, underlining the importance of screening potential staff members, described a 12 month on-the-job training program for new staff members taken on at the Hospital for Mental and Nervous Diseases, St. John's, Nfld.

Halifax Mail-Star.

FOETAL CHROMOSOME TESTING

It is reported in 'The Times' that Dr. Nadler, a genetic expert at Northwestern University, is examining foetal chromosomes from cells obtained by amniocentesis carried out early in pregnancy in women with a family history of genetic defects. Where the foetal chromosomes show that the baby will be born defective, he advocates therapeutic abortion. A subsequent pregnancy may show a normal foetus, and the pregnancy is then allowed to proceed to term. The report continues: "Widespread application of the technique could ultimately mean the elimination of many tragic and incurable conditions of genetic origin. . . . Chromosomal testing as a routine matter would require special laboratories and an army of specially trained biochemists".

News Flashes

PROPHYLAXIS AGAINST HAEMORRHAGIC DISEASE OF THE NEWBORN

Recommendations of the Committee on Neonatal Mortality concerning the administration of Vitamin K to all newly born babies.

Hemorrhagic Disease of the Newborn can be defined as a hemorrhagic disorder of the first few days of life, caused by a deficiency of Vitamin K characterized by a deficiency of prothrombin and proconvertin and probably other factors. This condition is the major cause of bleeding in this age period. The incidence of this condition varies widely, but the usually cited incidence in full term infants who do not receive Vitamin K (and whose mothers do not receive Vitamin K during labor) is 1 in 400. Well controlled studies have shown a decreased incidence of this condition when Vitamin K is used.

Administration of the drug to the mother is not satisfactory because it is almost impossible to specify a particular dose that will be both effective and safe for the newborn infant. Large doses up to 50 mgs may have to be used to be effective, and at this level a serious effect on the baby may occur, leading to hemolytic anemia, hyperbilirubinemia, kernicterus, and death.

For reasons mentioned above, it is recommended that Vitamin K prophylaxis be administered to the infant after birth rather than prenatally through administration to the mother.

In view of the above, it is therefore recommended that all Hospitals in the Province of Nova Scotia adopt the simple routine procedure of administering Vitamin K to all newborn infants. A single parenteral dose of 0.5 to 1.0 mgs or an oral dose of 1.0 to 2.0 mgs of Vitamin K₁ (Aqua Mephyton) is probably adequate for prophylaxis. The synthetic Vitamin K analogues (Hykinone, Synkayvite) in a dose of 1.25 to 2.5 mgs I.M. are also effective for prophylaxis. However, the Vitamin K₁ preparation is to be preferred because it has a greater margin of safety and also its action is somewhat faster.

References

- (1) *Vitamin K Compounds and the Water Soluble Analogues*. Pediatrics, Vol. XXVIII, No. 3, September 1961.
- (2) *Standards and Recommendations, Hospital Care of Newborn Infants*. American Academy of Pediatrics, page 46.

DOCTORS SPONSOR MEDICAL STUDENT

A Truro man is three years closer to his dreamed for medical degree and it's all thanks to the Colchester East Hants Medical Scholarship Trust Fund.

The student, who his benefactors prefer not to name, was employed in a paramedical branch of a large institution but had his heart set on someday entering into practice as a qualified physician. But the financial commitments inherent in supporting and raising a family mitigated against his hopes until a number of Truro area doctors spear-headed by Henry R. L. Martenstyn, M.D., set up the scholarship fund on January 1, 1968. Since that time, and even retroactively, the fund has provided \$100 per month during the school year to help defray the expenses of the student and his family.

Members of the Colchester East Hants branch of the Medical Society are now increasing the amount of money in the fund and if their current drive for funds is successful, they plan to assist another deserving student in September.

An Education For Your Son

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For Information Write to
the Headmaster,

C. H. BONNYCASTLE, B.A., LL.D.
ROTHESAY, New Brunswick

News Flashes

A STERILE DISPOSABLE ASPIRATING TUBE

A disposable aspirating tube individually packed sterile in special peelable envelope is now available for collecting cell washings and sputum samples during bronchoscopy. Supplied in two sizes, 8.5 cc and 20 cc, they are available from Davis and Geek of Canada.

PHYSICIAN WANTED

Doctor required for group practice in West Coast City of 15,000, starting July, 1969. Hospital has good facilities with new, modern 150-bed hospital being constructed. Starting salary \$1400 with partnership in one year if both parties agreeable. Clinic well equipped. Compulsory post graduate course annually at Clinic expense. Jet service twice daily to Vancouver. Schooling to grade XIII. Beautiful scenery, mild climate, varied sports activities, good fishing and skiing. If seriously interested, write or phone collect for complete details.

Apply to Greene Clinic, 122 Second Avenue West, Prince Rupert. Phone 604-624-9121.

FOR SALE

Apeco Super Stat Copier
Gomeco suction Anesthesia portable table
American Castle Sterilizer
Three Surgical Lights
Three examination tables
Ultra - Violet Infra Red Lamp
Electric Cast-cutter (Stryker with suction unit)
Two foot stools
Kiddes-Robbins Tourniquet
E.N.T. Chair
Surgical instrument side table
I.V. Pole Hyfereator
Surgical instrument cabinet
Wall cabinet
Allen-Welch Portable head light with portable battery
Other Medical office equipment

Contact Dr. J. K. Sanghi
R.R. No. 1
Kentville, Nova Scotia
Tel: 902 678-7448

MEDICAL PLACEMENT SERVICE

The first of its kind in Canada, a new medical placement service will commence operations in Toronto this month. Serving both generalists and specialist, it will liaise with clinics, hospitals, government agencies, municipalities, industries and practices which may be in need of its services.

Medical Placement Services Limited is designed to find the right man for the right role, and their operations will be conducted on a high ethical plane. They will seek doctors in Canada, the U.S. and from abroad through advertising and direct mail. They will supply physicians with detailed data regarding geography, climate, economic, social cultural and recreational facilities of centres where positions are available, as well as an outline of existing medical and hospital facilities.

Doctors clinics or medical institutions seeking medical assistance will be provided with a detailed report regarding the applicants qualifications, and other relevant information.

The offices of Medical Placement Services Ltd., are located at I Medical Place, Toronto.

ON PRODUCING A GENIUS

Associated Press reports the findings of a survey of 16,000 seven-year-old children in Aberdeen, conducted by Sir Dugald Baird, professor emeritus of obstetrics and gynaecology at Aberdeen University. His main findings: the best guarantee of intelligence is to be the first child born to a woman over 35. The worst prospect is to be the fifth or subsequent child born to a mother under 30.

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The Nova Scotia Medical Bulletin.

News Flashes

10 STEPS TO SAFE DRIVING

The following are the 10 most important things safe drivers do to AVOID accidents and PROTECT themselves and their passengers against injury:

1. Keep both hands firmly on the wheel - at 10 and two o'clock - and both eyes on the road.
2. Never tailgate - allow at least one vehicle length for every ten miles per hour of speed - use the Timed Interval Formula.
3. On wet, snowy or icy roads, reduce speed well below posted speed limits, depending on the severity of conditions.
4. Always signal intentions - turns, lane changes, passing.
5. Curves require special attention - slow down before entering, then apply power to wheels. Be alert for oncoming cars; they often cross the center line.
6. Never pass on hills or curves. On straight-aways pass only when positive the way is clear.
7. DON'T drive after heavy drinking. After moderate drinking, allow one hour for each ounce of alcohol consumed, before driving.
8. Keep the car in good operating condition, especially brakes, tires, steering and front end suspension, front and rear lights, mirrors, turn signals, wipers, muffler and exhaust pipe.
9. Always fasten safety belts and lock car doors.
10. Drive defensively; be ready for the unexpected; know what to do to avoid an accident; react in time.

"Observance of these 10 steps by drivers," says the Canada Safety Council, "will cut down by 90 per cent their chances of being involved in car crashes".

EXPENSIVE PROSTHESES 'FOR THE BIRDS'

It is reported in the Halifax Mail-Star that at the Annual Meeting of the Canadian Cancer Society a patient who had undergone radical mastectomy complained that expensive plastic prostheses were uncomfortable in summer and would harden in winter. With changing temperature she just couldn't rely on it staying in place. The answer to the problem had been suggested to her by Dr. Filbee, a radiotherapist, who advised that she fill a linen shape with bird seed. This had proved so successful that she has been making breast forms of bird seed for many other patients. They are used with cross-your-heart bras only.

FIFTIETH ANNIVERSARY

Congratulations to the Department of Health and Welfare for fifty years of service to the people of Canada, through Public Health Programs, Outpost Nursing, support for community Welfare programs, and in many, many other ways.

BRIEFS

A young theologian named Fiddle Refused to accept his degree: "For", he said, "It's enough to be called Fiddle Without being Fiddle, D.D."

* * * *

Four year old Bobby was stroking his cat before the fire in perfect content. The cat, also happy, began to purr loudly. Bobby seized her by the tail and dragged her away from the fire, and when his mother scolded him for hurting pussy, said "I've got to get her away from the fire, mother, she's beginning to boil".

Health Rays

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