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## The General Truth

Some weeks ago I received the 1967 graduation number of The Dalhousie Medical Journal. It contained three well written essays, one by the outstanding scientist, Hans Selye. His was titled "If I Were Your Age" and in delightfully simple language he said how much he had enjoyed his career of basic research and discussed the qualities which would be found in research scientists. The most precious he believed to be "the power of original creative thought". He also pointed out how so few have this gift and how easily it "can be suppressed by excessive obligatory course work and routine technologic training". Selye is not the first to comment on this tragic side effect which can be the result of pressurized formal teaching when the student is required to absorb a maximum of knowledge with a minimum of criticism. As opposed to this, the original thinker, or intellectual rebel is likely to be a tough soul endowed with some common sense so his chances of survival are greater than might seem probable.

I read Selye's article many times for it seemed to me that he had omitted an important additional quality that the research scientist possesses which can sustain him and give a greater meaning to his career. I think the word is Truth. I believe that if a man is not concerned for Truth then he will find no pleasure in science nor can he claim to be a scientist.

How difficult is Truth, how relative, how rarely, if ever, absolute. Each research scientist must search for the absolute and make do with the relative. For a while he may even appear to have grasped the Holy Grail but time and his successors advance with glee to expose the illusion. Yet we must all have our faith. If we have no belief there is no purpose; and without this, so much seems of so little account. It has been said that if man knew his destiny, if it were known why we exist and understood the purpose of this life, there would be nothing left to strive for and indeed mankind might not survive the revelation. Yet, beneath it all and the very *vis a tergo*, is the desire to know. For myself, I cherish the thoughts that even at the present rate of acquiring knowledge there is enough unknown to keep us all thoroughly employed for a very, very long time to come and that when all is known to us we shall have evolved into something quite different from what we are now.

Nor can the bold researcher take refuge in the cautious advice of Cicero: -

"so near is falsehood to truth that a wise man would do well not to trust himself on the narrow edge."

Rather he must commit himself to his theory and be prepared to defend it. Nevertheless, the great scientist is apt to be a humble person without absolute belief or absolute conviction for he is well aware of the scarcity of absolute truth.

Selye differentiated between the "problem finders" and the "problem solvers" and made a plea for "the old fashioned holistic" approach. Indeed, it is remarkable how many famous men after reaching the stage in life when they can review the battlefield without aggression or rancour conclude that only a general or total approach will give the working truth. Not, mark you, the absolute, but one which in a sense is the middle path.

"Nothing too much" was one of the famous sayings written above the doors to the temple of The Oracle at Delphi. Beside it, we are told, was another: "Know Thyself". Neither of these dicta may in themselves be truth but they are certainly sound exhortations to those who would seek it.

The last time it was possible for one man to know everything then known was reckoned to be at the beginning of the reign of Elizabeth I of England. If this was a mild conceit then, it is a categorical impossibility today. And so, as always, man, being expedient, has specialized. But for medicine at least this is not new; Brian Inglis notes in his History of Medicine that about 440 B.C. -

"Herodotus described Egypt as overrun with specialists, each insisting on their exclusive rights to some part of the body - another characteristic symptom of decline."

A more homely version I received recently from a patient: "they have a whole bunch of specialists but no doctors". And so it would appear that for everyone the search for truth is not a satisfying end in itself. For some it can be like MacNeile Dixon's "categorical imperative" - by which he meant "the Law" - something to be banished "to an uninhabited island, where it can contemplate throughout eternity its own unapproachable perfection". We must also remember that truth is not always palatable, indeed, if directed at our own persons we might consider it a lie. Robert Burns must surely have had his tongue

in his cheek when asking that God give us the gift of seeing ourselves through the eyes of our friends, colleagues or enemies. I think it would be too much to bear.

While it is right and a great strength to the profession, to pursue research in every aspect of the subject, it would be tragic to forget that the purpose of it all is to help our fellow men. The elders of medicine preach this sermon frequently and at length but for the most part it falls on stony ground. The specialist can so easily confound us all with his special knowledge and his place in the order of medicine is beyond question. He is a referendum, a computer and a consultant. He is the result of careful training and painstaking labour but it cannot be expected that he would also have an holistic approach. To see things in relation to each other and to see them in proportion is a training in itself. Depth of knowledge has to be sacrificed for the breadth of it and the one cannot reasonably substitute for the other.

If Selye's plea for "the all-embracing view" is valid for research science then it is equally so for the practice of medicine. To acquire knowledge for its own sake may enchant the investigator but this can be a barren pursuit. Although theories may pyramid and ideas sprout, without application there is no test and without usage there is no proof.

I imagine that for the scientist there can be no greater reward than to find his work assimilated into practice. To me this would seem a vindication of his work and from this he must derive fulfilment. Perhaps he has even moved a little way in the quest for truth. □

Our Guest Editorial was contributed by Charles A. Robertson, M.B., Ch.B., Pietou, N. S.

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# Epidemiological Principles and Problems in Clinical Research Based on Hospitalized Patients

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Information derived from hospitals, either directly from patients or from their records and commonly referred to as a case series, is frequently used by clinical researchers. Two of the principle purposes of these investigations is to discover the frequency and distribution of the cases according to various characteristics and to identify attributes associated with the cases which may lead to a better understanding of the cause and prevention of disease or the value of various methods of treatment. These types of investigations thus employ the epidemiological method, for they involve populations, or groups of cases rather than individual patients, and in order to fulfil their purposes they should embody a comparison of those cases with a population at risk or a control group. The results of these studies which, of necessity, are usually carried out on a relatively small sample of cases are frequently and sometimes quite inappropriately generalized to the much larger population of cases from which the hospital sample was derived. The purpose of this paper is to discuss some of the epidemiological principles and problems involved in these studies.

Not all diseases or hospital systems are appropriate for studies of this nature. Table I lists some of the major factors to be considered in evaluating whether a particular disease or hospital system is appropriate for epidemiological studies. These then, constitute some of the major factors to be taken into account in the planning stage of the study.

1. **The condition should be diagnosed and treated conventionally in hospital.**

If one is planning to determine the total load of a particular disease in the community, by estimating the prevalence and incidence of the disease, then it is obvious that relatively few diseases are appropriately studied through hospital cases alone. In a study of epidemiology of fractured hips currently being conducted in the Department of Preventive Medicine at Dalhousie University, however, we feel that as these are conventionally admitted to hospitals we will be able to identify most cases in this manner and thus derive relatively accurate incidence rates, by age, sex and other characteristics. In the case of infectious hepatitis, however, it would be more appropriate to identify the cases through other sources.

On the other hand, if one is primarily interested in identifying certain demographic features which characterize the disease such as its age and sex distribution, or of identifying various attributes associated with the disease, then it is not necessary that one study all cases of diseases originating in the population. One can perform these studies, quite adequately, on the selected sample of the cases which are admitted to hospital, provided that one has some assurance that the sample of cases reaching the hospital is representative of all the cases of that disease in the population. We know, however, that many selective forces influence hospital admissions, such as age, socio-economic status, severity of the disease etc., and the magnitude of some of the selective forces is unknown.

TABLE I

## Factors to be considered in Evaluating the Appropriateness of the Disease and Hospital System

1. The condition should be diagnosed and treated conventionally in hospital.

Hospital cases are not all inclusive and tend to be selected according to

- (a) personal characteristics - age, sex, race, socio-economic status
- (b) severity of disease
- (c) associated conditions
- (d) administrative admission policies.

2. The disease should be defined adequately by uniform, objective criteria and determined by standard techniques.

Information obtained either directly from patients' histories or from hospital records is often incomplete and unstandardized. There is much diagnostic variability between physicians and between hospitals.

3. Adequate control groups should be clearly defined and available either in the hospital or in the community.
4. The hospital system should serve a defined population and there should be no significant migration of cases to hospitals outside this area. Cases referred into the area from other population groups should be identified and excluded from the study.

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The fact that a false clinical picture of a disease can emerge from a study of hospital cases, which are selected so as not to be representative, was clearly illustrated by Morris in his study of ruptured ventricle in London, England.<sup>1</sup> On the basis of the 83 cases identified in all the London hospitals in the 2 years 1957-1958 the disease was believed to be more frequent in men, only slightly over half occurred in persons 70 years of age and over and 16% occurred while the patient was on anticoagulants. When Morris looked at the coroner's reports, however, he found another 345 cases which had never been admitted to hospital. These showed that the condition was not only far more common than previously supposed, but changed the clinical picture, for considering all the cases, it was now shown to be approximately equal in both sexes, 70% of the cases occurred in people 70 years of age and over and only 2% of the cases had been preceded by anticoagulants. It is hardly necessary to add that this false clinical picture created by the study of hospitalized cases alone has important implications in the teaching of the medical student as well.

**2. The disease should be defined adequately by uniform, objective criteria and determined by standard techniques.**

Hospital records are not primarily designed for research purposes but for the care of ill individuals. The information in the records was obtained by a variety of interviewers without the use of uniform interviewing techniques and interviewer bias may be a major problem for it is well known that the answer one gets depends to a large degree on the way the question is asked and who asks it. The physical findings and final diagnoses are made by many different physicians each with his individual diagnostic criteria. The laboratory tests are also subject to considerable variation both in performance and interpretation. In some cases the diagnoses are incomplete, listing only the primary diagnoses and not the additional or secondary diseases. It is thus essential that the disease under study be clearly defined and that specific criteria be drawn up which must be met before a case is included in the study. The charts may thus serve to simply identify potential cases which must then be further investigated and validated and only those cases included which meet the criteria which were laid down before hand.

In an attempt to circumvent some of the problems just discussed, in our study of fractured hips, we have defined a case as any fracture occurring at or above the greater trochanter, all cases are verified by observation of the X-ray film, and confirmed by the radiologists, and the cases are interviewed by one interviewer using a standardized and pre-tested questionnaire.

One further problem, if one intends to obtain the cases when they are admitted to hospital, as we

are, the simple method of selecting them from the hospital admission lists may not be valid. For example, we had to abandon this approach for we found that we were missing cases because of inaccurate admission diagnoses and one patient managed to be admitted without ever appearing on the admission list. We are therefore, now identifying cases by reviewing daily the X-ray reports in the Radiology Departments of the various hospitals. In any investigation a pilot study will often bring to light similar unforeseen problems, and result in modifications being incorporated in the final study.

**3. Adequate control groups should be clearly defined and available either in hospital or in the community.**

When one is interested in seeking out associations between two diseases, or between the cases under study and certain characteristics or attributes of possible etiological importance, one is required to use a control group. The finding among the cases of a higher frequency of individuals with another disease, or other characteristic under investigation as compared to the controls, would indicate that an association exists between the cases and the other disease or between the cases and the characteristic of interest.

The choice of a proper control group is difficult especially when doing hospital based studies. Ideally, both the cases and controls should be representative samples drawn from the same population. The control groups usually consist of patients with other diseases admitted to the same hospitals. For example, nearly all the retrospective studies indicating an association between lung cancer and cigarette smoking have been done in this way. However, there are certain problems encountered with this retrospective or case-control method which may seriously bias the study.

The most common problem may result from what is known as selection. Berkson<sup>2</sup> has shown the possibility of obtaining a false association between diseases or between a disease and a characteristic because of the different probabilities of admission to the hospital for individuals with the disease under study and for those with the other disease who constitute the control group. For example, if one is investigating coronary heart disease through hospitalized cases and comparing them with a control group consisting of patients with say, ulcerative colitis, one might find a positive association between coronary heart disease and diabetes which could be false because patients who have both coronary heart disease and diabetes are selected for admission, i.e. the presence of both diseases increases the probability of admission to hospital. In other words, the patients with coronary heart disease were not representative of all



cases but selected because of the presence of diabetes.

This potential bias can also work in the opposite direction. For example, from the first 7500 autopsies performed at the Johns Hopkins Hospital, Pearl<sup>2</sup> identified 816 persons with cancer and 816 control patients matched for age, sex, race and date of autopsy. In the cancer group, 6.6% showed active tuberculosis lesions while 16.3% of the controls showed these lesions. This negative association suggested an antagonism between Cancer and Tuberculosis and some cancer patients were actually treated with tuberculin. A recent examination of the original records revealed that the control group included a large number of persons who were admitted and died with Tuberculosis and thus necessarily had a higher prevalence of active lesions than the cancer patients. The control group thus gave a grossly biased estimate of the prevalence of tuberculosis lesions in the population. They were selected for admission because of the presence of Tuberculosis. Autopsy records are particularly subject to bias, of course, because those persons autopsied are selected not only for admission but selected again for autopsy.

If one is able to choose a control disease which has the same independent probability of causing the patient to be admitted as the disease under study then these biases may be avoided. However, as one cannot determine accurately the true probability of admission to hospital for any one disease, the use of a control group consisting of persons with a number of separate diseases is advisable. We should beware, however, of including among the control group those diseases which are etiologically related to the disease under study because we may thus miss a positive association when one actually exists. For example, patients with coronary heart disease would not constitute a suitable control group for a study of the relationship between bladder cancer and cigarette smoking because the investigator might well conclude that smoking is not related to either disease when in fact it appears to be related to both.

In choosing controls it is customary to match them with the cases according to certain factors. The general rule is to match for those factors known or strongly suspected to be related to the occurrence of the disease or to the frequency of the attribute under study. The age, sex, race and date of hospital admission are commonly used matching categories. When a factor is matched, however, it is eliminated as an independent study variable, and the control group can only be used for the study of other factors.

Two common procedures are used in matching. In one, the case and control subjects are selected in closely matched pairs. This tends to improve the clarity of the experimental situation and simplifies the statistical analysis. It is often used in performing clinical trials and each pair may be regarded as

forming a separate small experiment in its own right. In the second procedure, frequency matching, the subjects are not chosen in pairs but the two groups are selected so that the distribution of the subjects in the various categories, such as age and sex is approximately the same between the two groups. The point is, that the method of matching should be clearly defined for the type of analysis subsequently carried out depends on the matching procedure used.

To avoid some of the potential biases when hospital controls are used, controls are sometimes selected from the community. Often these are persons who reside in the same area as the hospitalized case and are similar in age, sex and race. Alternatively, a random sample of the general population may be selected. These methods are more difficult and expensive than choosing hospitalized controls but the resulting controls are presumably more representative of the population than hospital controls. However, this too has disadvantages in that the cases and controls are not comparable with regard to the accuracy of diagnostic data. For the cases, this is determined by examination and laboratory tests while in the controls this is usually determined by interview unless one is prepared to examine and test them as well.

#### 4. The hospital system should serve a defined population.

In order to develop prevalence or incidence rates it is essential to define the denominator of these rates, referred to as the population at risk. This is very difficult in some areas, because the catchment area, i.e. the population actually served by the hospitals, may not be accurately known. In this area the data from the hospital insurance commission has been very helpful and we know that the hospitals in Halifax City and County serve the vast majority of the people living in this area - very few are hospitalized outside this region. One can identify those coming in from outside the County and these then are eliminated from the numerator when one is deriving prevalence or incidence rates.

It is, of course, important to recognize that cases going to one hospital may differ from patients going to another hospital. Thus, if one wishes to describe the disease according to various characteristics one may get a biased picture if one confines his study to only one hospital in the area. This is illustrated in Table II. These data were obtained from an examination of records in all the hospitals serving the population of Halifax County and refer to discharges from these hospitals in 1965. We know these data are incomplete and are only presented here to illustrate a point. It is apparent that selective forces have operated in such a way that the age and sex characteristics and site of fracture



TABLE II

**Fractures of the Femur Discharged from Hospitals within Halifax County in 1965**  
by Age, Sex, Site and Hospital

Age Groups	Victoria General		Halifax Infirmary		Camp Hill		All Hospitals	
	N	%	N	%	N	%	N	%
<45	12	21.8	—	0.0	—	0.0	12	15.2
45 - 64	10	18.2	1	5.0	1	25.0	12	15.2
65 +	33	60.0	19	95.0	3	75.0	55	69.6
All Ages	55	100.0	20	100.0	4	100.0	79	100.0

Sex	Victoria General		Halifax Infirmary		Camp Hill		All Hospitals	
	N	%	N	%	N	%	N	%
Male	14	25.5	1	5.0	4	100.0	19	24.1
Female	41	74.5	19	95.0	—	0.0	60	75.9
Both Sexes	55	100.0	20	100.0	4	100.0	79	100.0

Diagnosis	Victoria General		Halifax Infirmary		Camp Hill		All Hospitals	
	N	%	N	%	N	%	N	%
Head &/or Neck	21	38.2	9	45.0	1	25.0	31	39.2
Trochanter	21	38.2	9	45.0	3	75.0	33	41.8
Shaft	13	23.6	2	10.0	—	0.0	15	19.0
All Fractures	55	100.0	20	100.0	4	100.0	79	100.0

of persons with fractured femurs admitted to the Victoria General Hospital are quite different from those admitted to the other hospitals. Thus, generalization of the results obtained from the records at only one of these hospitals would be quite inappropriate and again lead to a false clinical picture. When the data from all the hospitals are pooled we get a more accurate picture of the age and sex distribution of fractured femurs originating within the population of Halifax County. We can then compare this with similar data derived from other population groups.

I would like to make just one other point. In some cases we may think we are getting all the cases, or at least a representative sample, through hospital records when in fact we are not. In Connecticut for example, 94% of the hospitals in the State agreed to report all cancer cases admitted to a control cancer registry. Yet of the 76,000 cases recorded from 1935 to 1951 almost 19,000 were first discovered by examination of death certificates. Most

of these had never received hospital care, and others had received it but were not reported.

Thus, hospital based studies are subject to many potential biases and while much can be learned from investigations carried in the retrospective manner we must be fully aware of their limitations and be very cautious in our interpretations. The results from these studies may, however, provide important clues leading to the development of hypotheses which can then be tested through prospective studies based on community population groups. □

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# Mechanism of Actions of Hormones

## PART II

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In Part I of this article (N. S. Med. Bull. Vol. XLVI, June 1967) some of the theories concerning the events which occur between hormones and their cellular receptor sites were reviewed. Attention was drawn to the connection between hormones and genetic regulation of cellular activity. The discussion of aldosterone which follows illustrates such a relationship.

### Mechanism of Action of Aldosterone

The effect of aldosterone on sodium transport has recently been investigated and is thought to be mediated through an action on the genetic control of protein synthesis. Aldosterone was discovered in the early 1950's and has subsequently been shown to be the most potent naturally-occurring salt-retaining steroid in man. The complexity of the mammalian kidney, however, made it difficult to study the molecular mechanisms of mineralocorticoid action; thus investigators sought a simpler tissue that would respond to aldosterone much as the renal tubule does. In the toad the urinary bladder is a reservoir of water which is reabsorbed under the action of vasopressin when water is in short supply. To carry out this function, the epithelial cells lining the bladder first pump salt from the urine into the blood to provide an osmotic force for the reabsorption of water. Crabbé in 1960 showed that aldosterone stimulated sodium transport across the toad bladder both *in vitro* and *in vivo*. Thus the toad bladder has some of the same transport characteristic as the mammalian distal renal tubule. An added convenience of the toad bladder is its bilobed structure which allows the use of one hemibladder as a control and the other as the hormone-treated system in simultaneous studies.

After endogenous hormones are washed out of exposed toad bladders by soaking in steroid-free solutions, added aldosterone produces striking and consistent changes in sodium transport. After a latent period of 60 to 90 minutes there is a steady rise in sodium transport over the subsequent 5 hours to a maximum rate that is 50 - 100 percent greater than base-line values. There are two possible explanations for the observed latent period, first; the steroid may penetrate the tissue

so slowly that it requires an hour or more to build up to threshold concentrations, or, secondly, the hormone may initiate a series of chemical reactions that culminate in the rise of the rate of sodium transport after an hour or so. The first hypothesis has been tested by studying the rate of accumulation of radioactive aldosterone in the bladder. This was found to occur rapidly, reaching maximal levels within 15 to 45 minutes, thus virtually excluding this mode of action. The second possibility was supported by the finding that a five minute exposure to aldosterone was enough to initiate mineralocorticoid effect, and that the removal of aldosterone during the latent period did not affect either the duration of the latent period or the magnitude of the increase in sodium transport. This suggested that once the steroid triggered the first chemical reaction in the cell, it started a sequence of events culminating in the rise in sodium transport. The next problem was to identify the nature of the chemical reactions triggered by aldosterone.

The first evidence that pointed to an interaction between the genetic material and aldosterone was obtained with the use of high-resolution autoradiographs. Toad bladders were incubated in solutions containing either tritiated aldosterone or tritiated progesterone. Aldosterone was shown to be selectively localized in the nuclei of the epithelial cells that are sodium transporters. In contrast, progesterone with no significant mineralocorticoid activity in the toad bladder was about evenly distributed between the nuclear and cytoplasmic areas. The finding that only the physiologically active steroid was concentrated in the nucleus suggested that the initial chemical reaction takes place in the nucleus and that its end result may be achieved by effects on protein synthesis.

A further approach to this problem was by the use of agents which block protein synthesis. The antibiotic actinomycin D blocks synthesis of messenger RNA. The addition of actinomycin to the medium prior to the exposure of toad bladders to aldosterone completely abolishes the response to the steroid. Puromycin, an inhibitor of ribosomal assembly of protein, similarly prevents



the effect of aldosterone. Fluorophenylalanine is a chemically modified form of the native amino acid phenylalanine. The protein-synthesis mechanism distinguishes poorly between these analogues and, as a result, fluorophenylalanine competes for incorporation with phenylalanine. If the new protein so formed is an enzyme that requires phenylalanine for full activity, the incorporation of the analogue will impair enzymatic activity. Thus, fluorophenylalanine acts by forming incompetent proteins rather than by blocking protein synthesis. In the toad bladder small concentrations of fluorophenylalanine significantly block sodium transport. Cycloheximide has been shown to interfere with the transfer of amino acids from the tRNA-amino acid complex to the ribosome. In very small concentrations cycloheximide is found to abolish the action of aldosterone on sodium transport, but has no effect on the control (steroid-free) hemibladder. (Fig. 1)

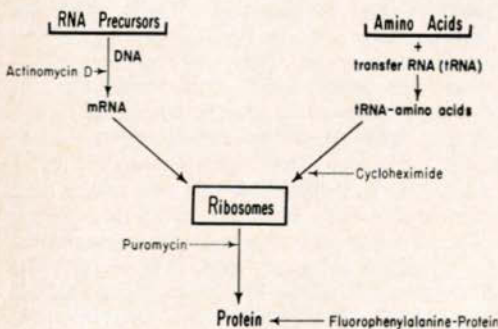


Figure 1. Inhibitions of protein synthesis.

Thus blockade of protein synthesis at four different sites with four different inhibitors impairs or eliminates the aldosterone-mediated increase in sodium transport. These results, therefore, support the concept that aldosterone reacts with a nuclear receptor to stimulate the formation of mRNA. The newly synthesized mRNA in turn directs the synthesis of proteins that participate in a rate-limiting step in the sodium transport mechanism.

Such results suggest that it should also be possible to detect an increase in the rate of RNA synthesis, measured by the rate of incorporation of radioactive precursors into RNA isolated from aldosterone-treated bladders, and that this increase should precede the onset of the effect on sodium transport. Experimental findings have confirmed these expectations.

To complete the story of aldosterone one must define the role of the steroid-induced proteins in the sodium transport mechanism. There are

three main steps in the process: (1) Passive diffusion of sodium across the mucosal face of the epithelial cell membrane into the interior of the cell, (2) Extrusion of the sodium from the interior of the cell by a sodium pump located in or near the inner face of the epithelial cell membrane, (3) Splitting of ATP into ADP and inorganic phosphate ( $P_i$ ) to provide energy for the sodium pump. (Fig. 2)

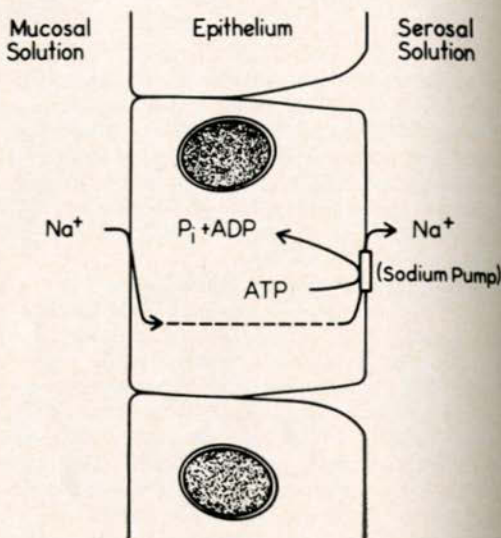


Figure 2. Phases of sodium transport by epithelial cells.

Based on these phases of action, sodium transport could be regulated in one of three ways, either (1) by facilitating the entry of sodium into the cell, or (2) by increasing the output of the sodium pump directly, i.e. by increasing the synthesis or activation of the sodium transport enzyme, or (3) by increasing the rate of synthesis of ATP and, as a result, driving the sodium pump at a faster rate.

Early experiments suggested that facilitation of the entry of sodium into the epithelial cell was the most likely mechanism, but more recent evidence indicates that the third mechanism - the increase of energy supply to the sodium pump - fitted the experimental data more closely. This inference was drawn from the response of starved bladders to substrates such as glucose or pyruvate whose metabolism is known to be linked to the production of ATP. When starved toad bladders are pretreated with aldosterone for three hours, the addition of the substrates produces a rise in the rate of sodium transport within 15 minutes. The time-course of the response is consistent with oxidative metabolism, suggesting that the response is dependent on the synthesis of ATP at the ex-



pense of substrate. A significant feature of the response to metabolic substrates after pre-treatment with aldosterone is the virtual elimination of the latent period, which is thought to be due to steroid induction of protein (in this case, enzyme) synthesis during the pre-treatment phase. Because of the absence of metabolic fuels owing to starvation conditions, the extra complement of enzymes can not generate any additional ATP and there is no increase in the rate of sodium transport. Upon addition of glucose or pyruvate, however, the additional enzymes made under the guidance of aldosterone rapidly metabolize the substrates without a latent period thereby providing more ATP for the sodium pump. If these inferences are correct the ATP content of epithelial cells should increase in the aldosterone-treated bladders, despite the fact that the increased rate of sodium transport requires the consumption of proportionately more ATP. If, on the other hand, aldosterone governs the rate of entry of sodium into the epithelial cells, more ATP would be consumed to pay for the cost of additional sodium transport. As a result ATP content should be decreased, or held at control levels by the compensatory response of the ATP-generating system. Recently, assays of toad bladder for ATP during aldosterone action showed a rise in ATP content which preceded the rise in rate of sodium transport and was maintained throughout the duration of this effect. Such findings are highly suggestive that aldosterone stimulates the formation of ATP to drive the existing sodium pump at a faster rate.

A summary of these findings is illustrated in Figure 3.

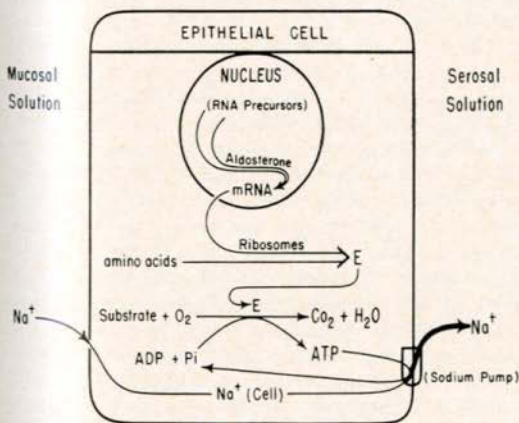


Figure 3. The role of aldosterone in sodium transport.

which indicates the theoretical pathway from gene activation to an increased rate of sodium transport. (1) Aldosterone stimulates DNA-directed synthesis of RNA from precursors by an unknown set of reactions. (2) The newly synthesized RNA acts as a messenger for the synthesis of protein enzymes from aminoacids by the ribosomes.

(3) The newly synthesized enzymes stimulate substrate oxidation and result in increased production of ATP from ADP and inorganic phosphate ( $P_i$ ). The increased supply of ATP drives the sodium pump at a faster rate.

Although the same basic mechanism of hormone-gene activity has been invoked to explain the action of several other steroid hormones, such a mechanism has been found to occur in such a clearly defined manner only in the case of aldosterone, the findings in other hormones having been much less consistent.

### Summary and Conclusions

In this paper an attempt has been made to provide a narrative, rather than chemical, review of some of the factors thought to be of importance in the investigation of the basic mechanisms of hormonal action. Certain common characteristics of hormones have been described together with some of the many factors which cause difficulties in the investigation of their cellular and sub-cellular actions. It has been suggested that hormones may act by activation of key enzymes, modification of cell membranes or intracellular structures, by provision of necessary chemical co-factors, and by alteration of genetic programming. The mechanism of action of aldosterone has been discussed.

It has been said that the flights of imagination of physiologists are part of the cumulative historical record. Neuman speaks of theories as vehicles for the design of experiments, and suggests that when they begin to show signs of breaking down, or when shiny new models become irresistible, they should be traded in without sentimentality. Discarded theories of the mechanism of action of hormones would fill a medium-sized used car lot. □

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# Sinusitis

ARTHUR G. SHANE\*

Halifax, N. S.

Every patient believes that it is his unquestionable right to have a nose that is always free and open, and that nothing should drain anywhere from any place at any time, and if it does, then he is considered to have sinus trouble, and everyone conveniently forgets about allergy, smoking, drinking, drugs, his home and work conditions and psychiatric adjustment. As students we heard a great deal about focal infection and the sinuses; tonsils and teeth were areas of great suspicion. It is possible for sinusitis to involve other tissues by bacteremia, or by liberation of an exotoxin in which tissues at a distance are sensitized and develop chronic changes. The sinuses also can effect the lungs by microdroplet infection.

## Physiology

The nose has two purposes, to assist in the sense of smell and to prepare the inspired air so that it will be well-received by the lungs, that is, the nose is an air-conditioning system. The nose itself is divided by a medial partition, the septum, and the two sets of turbinates with the meati between them. The septum and turbinates contain erectile vascular tissue and swell bodies which adjust to varying atmospheric conditions.

The sinuses are paired, air-filled cavities adjacent to the nose, consisting of the maxillary, ethmoid, frontal and sphenoid sinuses. These drain through openings into the meati. At birth, the maxillary and ethmoidal sinuses are present and filled with amniotic fluid. The frontal is not present until about 8 years of age and it may be absent in some people. The sphenoidal sinus starts to develop at 3 years of age and reaches full size at 13 to 14 years. The functions of the sinuses are:

- 1: To lighten, insulate and strengthen the bone structure of the skull.
- 2: To provide moisture for the process of olfaction.
- 3: To provide resonators for vocal production.

Proetz states that the sinuses form as the bones grow away from the cranium. The respiratory mucosa, a columnar, ciliated epithelium, is highly specialized and lines the nose from the anterior nares to the pulmonary area. The inspired air flows directly upwards in an arc, and at the level of the middle turbinate descends directly through the posterior choanae into the lungs. This is done with little or no turbulence-effect in the nose. The expired air

follows the same direction but is broken up into eddies and whirls in the nasal cavity and meati. The sinuses are emptied of air and moisture during inspiration and filled during expiration. The inspired air is cleaned, so that all dust and bacteria are removed, and brought to the right temperature, 98.6°C. It is also moistened and in achieving 75 to 80 percent saturation of the inspired air the nose gives off about one litre of fluid a day. This is all done in about four to five inches of nasal apparatus and within a matter of a quarter of a second. Humidification and air-cleaning or particle control is accomplished by the mucous blanket which rests upon the ciliated cells. This mucous carpet is renewed every 15 minutes. Ciliated movement is inherent in the columnar epithelial cell, and is not dependent on nerve impulses and may be propagated by acetylcholine. The movement may be stopped by drying, chilling, cigarette smoke and topical anaesthetics. This continual movement is essential to the maintenance of a clean respiratory tract. The cilia are numbered in the millions and their direction of movement is so co-ordinated that in the sinuses they all carry mucous to the ostium and from the anterior part of the nose to the pharynx. Any weight on the cilia stimulates them to beat.

## Pathology

Most of the diseases affecting the nose and sinuses are due to changes in the epithelial layer; metaplasia may take place so that ciliated cells become squamous in character, the turbinates shrink and secretions dry and stagnate in the nose. The cells may also be changed to mucous-producing cells giving rise to a heavy, thick, mucous which remains because the ciliated cells are gone. The patients struggle to blow and remove this thickened mass. In patients with allergies the cells change to goblet cells and the submucosa swells leaving a thicker hypertrophic membrane with polypoidal tendencies. Sinus disease may be of bacterial origin with inflammation of the lining membrane. If odor is present, necrosis of the lining membrane may have taken place; if this is a particularly foul odor it is probably of dental origin: the last 2 to 3 molars may form part of the maxillary floor. Allergy may produce a thickened membrane, and infection may become superimposed and confuse the issue. Cysts or so-called polyps occur in chronic sinusitis and also in allergy states; in any acute upper-respiratory infection the

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sinuses are involved to a varying degree. Aero-sinusitis occurs due to vacuum-production during descent from a high altitude; the frontal sinuses are usually involved. The patient with a cold should probably not fly but, if he does, should use a mild vasoconstrictor. Trauma may also cause sinusitis.

### Symptoms and Signs of Sinus Infection

One must remember that an inflammatory process involving the mucous membrane of the nose may also involve any other part of the respiratory tract leading to associated problems such as sinusitis or a lobar pneumonia; with an upper respiratory tract infection ethmoiditis is most commonly followed by maxillary sinusitis. The acute frontal sinusitis one sees in children is usually the result of the child jumping into a swimming pool feet first and driving infected material up the nasofrontal duct into the frontal sinus.

One of the symptoms of sinus infection is nasal discharge, usually mucoidal and mucopurulent in character. This is accompanied by a variable degree of nasal swelling, there being more swelling in acute sinusitis than in a so-called chronic sinusitis. Head pain is present only when the ostium of the sinus is blocked by oedema and filled with mucous producing a build-up of pressure. Once the pressure is relieved the pain disappears: thus, pain and acute headache is more characteristic of acute sinusitis than of chronic sinusitis. In ethmoiditis head pain in the acute phase is situated between the eyes or in the temporal area; in maxillary sinusitis pain is on the ipsilateral side of the face or cheek and in the last 2 to 3 molars. The patient with frontal sinusitis complains of pain over the eye and with sphenoidal involvement the pain is situated deep in the head or in the occipital region. The patient with sinusitis also has a mild degree of fever and may feel ill.

### The diagnosis of Sinusitis

The diagnosis is made by inspection, palpation and percussion; as well as intranasal examination which may show swelling and injection of the middle turbinate and middle meatus; pus or a polyp may be seen in the middle meatus. The examination is repeated after shrinking the nose with a vasoconstrictor; I use 1 percent Otrivin. Post-nasal inspection is carried out in order to check for infection in the posterior group of sinuses, thickening of the mucous membrane of the vomer or of the posterior ends of the turbinates or to determine if there is mucopus in the superior meatus. One transilluminates the sinuses. X-ray studies are done. The suspected sinus may be lavaged. A culture can be taken from secretions obtained by suction.

### Treatment

Many cases of sinusitis coincident with coryza or an upper respiratory tract infection will resolve spontaneously. A diagnosis of sinusitis is frequently made after examining X-rays taken at this time; however, when these are repeated one month later

the clouding of the sinuses has disappeared. I would emphasize that vasoconstrictor drugs are fine during the acute phase which lasts for 3 to 4 days. One percent ephedrine or 0.25 percent neosynephrine are satisfactory for prolonged use because they are isotonic or only slightly acid in reaction. Nothing else need be added to the nose-drops because the infection is deep within the mucous membrane, and in addition one should remember that anything applied to the moving mucous blanket is wafted backward and arrives in the stomach in 10 to 15 minutes; there is also a danger of sensitization. I think the key word in the use of these potent vasoconstrictors is, 'temporary'. Instillation of nose-drops is by dropper with the head low and on the side, 'The Parkinson Position'.

When pus is present in the sinus, the old surgical dictum still holds true: if pus is present, let it out. The maxillary sinus can be irrigated through the inferior meatus or through its natural ostium. Irrigating a sinus once or twice may help by ridding it of the thickened secretions and allowing the cilia to keep it clean thereafter; the instillation of penicillin into the sinus is, in my opinion, of no value. The ethmoid and maxillary sinuses may be cleaned by the Proetz nasal displacement. Inserting a cannula into the frontal or sphenoid sinuses can be difficult and dangerous.

Surgery of the maxillary sinus involves one of two procedures. The more minor operation consists of the making of a window or intra-nasal antrostomy well-Luc procedure is indicated; this is done through the canine fossa with a similar counter-opening into the nose as described above. In children this is best avoided because of the possibility of getting into the secondary dentition. Surgery of the ethmoid, by removal of polypi or by an internal or external ethmoidectomy is usually reserved for chronic cases. Surgery of the frontal sinuses in the acute stage is limited to a small incision in the floor of the sinus, a trephine or drill-opening into the bone and insertion of a drainage tube through which irrigation can be carried out. This tube is left in place until pain and discharge has disappeared. For chronic frontal sinusitis the tendency is to use the osteoplastic-flap method of Goodale and Montgomery, carrying out complete obliteration, with straightening of the deviated septum at a later date. Surgery of the sphenoid sinus is rarely performed and treatment is usually confined to washing it out or removing its anterior wall.

Antibiotic therapy has greatly reduced the incidence of complications of sinusitis. Infection may spread directly by contiguity or along venous or lymph channels to the surrounding tissues and may involve the orbit, the meninges and brain or large venous sinuses. As long as the drainage and ventilation of a sinus is impaired, the probability of complications increases, and if the patient's resistance is low, infection may result. During the acute phase,



rest in bed, heat, Aspirins, Demerol, fluids, antibiotics, inhalation of medicated steam and use of a vaporizer are useful; local nasal decongestants should be used frequently. If the infection does not subside, then increased pain, tenderness and swelling over the area will develop. Among the complications which may follow are:

#### Orbital Cellulitis

Extension of infection from the ethmoids is common in children but not so common in adults. It generally presents as an early swelling in the area of the inner canthus above the internal ligament but presents below it in very young children, along with swelling of the periorbital contents, proptosis, chemosis and complete immobility of the globe. Treatment consists of incision and drainage.

#### Frontal Osteomyelitis

The frontal bone is diploetic in nature and infection from the sinuses enters into this system resulting in severe frontal pain, oedema, fever and chills, with possible extension to the dura and frontal lobe. The principles of treatment are essentially as mentioned above.

**Allergy** Plays an important role in the development of secondary infection of sinuses. Because of chronic cough and post-nasal drip as evidence of hypersecretion, as well as oedema, of the nasopulmonary membrane and loss of cilia, the normal drainage of sinuses is disrupted, secondary infection sets in and a vicious circle develops. One must therefore treat the primary cause, namely the allergy.

#### Sinusitis in Children

The most commonly involved sinuses are the ethmoid and maxillary. These may be affected by the acute exanthemata, by upper respiratory infections or by hypertrophied adenoids due to alternation in the ciliary streaming which predisposes to infection; there is also an allergic phenomenon in which allergy and infection complement and stimulate each other. Acute infections may present after the age of 6 months and then chiefly in the ethmoids. In chronic cases due to hypertrophied tonsils and adenoids the maxillary sinuses are most often affected. Children with this problem are mouth-breathers; they have large tonsils and adenoids, their noses are filled with mucus and they have a night-cough. Their X-rays show hazy sinuses. In these children removal of tonsils and adenoids will reverse the signs of sinusitis.

#### Summary

Sinusitis is not as common as people suspect: out of a hundred patients who are told that they have sinus trouble, probably only two actually have sinusitis. The present-day literature does not contain significant articles on sinusitis. Sinusitis cannot be blamed for the many headaches and some of the discharges one sees today. The antibiotics have controlled the severe complications of sinusitis which were common a few years ago. □

**TOWARDS EARLIER DIAGNOSIS. A Family Doctor's Approach,** by Keith Hodgkin. E & S. Livingstone Ltd.; The Macmillan Company of Canada, Toronto.

This book should be particularly useful to those making the transition from hospital based medicine to family practice. It contains a great deal of information condensed in a concise and easily readable form. The author has kept very careful records of his cases over the years and by the use of statistics and accurate correlated observation gives the reader the benefit of a wide experience.

The book is well arranged and each system of the body is taken in turn with valuable pointers in diagnosis for most of the conditions met with in family practice. Misleading features and pitfalls are pointed out, an example being that diarrhoea does not exclude the diagnosis of acute appendicitis: he makes the interesting comment that 9% of the proven cases of appendicitis in his practice had this symptom. Under acute intestinal obstruction, eyebrows might be raised at the statement "attempts to reduce the hernia should be firm, not vigorous."

A novel feature of the book is the section entitled "Summary of the Author's Treatment and Prescribing Habits." This lists most of the common conditions met in practice and under the appropriate body systems suggests in one or two lines whether to treat or refer, and if not referred, his own treatment.

As medical textbooks go this is a rather unusual one but it is very practical and as a vademecum for those engaged in family practice it can be strongly recommended. □

W.E.P.

#### INSTRUCTIONS TO AUTHORS

Members and others wishing to contribute to *The Bulletin* are invited to submit their material to the Offices of The Medical Society, Public Health Clinic, Halifax, N. S. In general the rules laid down for the *Canadian Medical Association Journal* and published therein under the heading "Instructions to Contributors".

Material should preferably be typed on one side of paper 8/ x 11 inches, with wide margins. Carbon copies are not satisfactory. Any table, illustration etc. quoted from another published source must have the permission of both author and publisher.

Opinions expressed in articles appearing in *The Bulletin* do not represent the policy of The Medical Society of Nova Scotia unless specifically stated to do so.



# Correspondence

The Editor

Nova Scotia Medical Bulletin

Dear Sir

In World War I the training program of recruits included physical training, foot drill, musketry and bayonet exercises, and one saw some hundreds of recruits undergo this training without a single casualty.

This was achieved by advancing quickly the boys whose thinking coordination and reflexes had been conditioned by sports such as baseball and hockey.

The heavily muscled recruits from labor camps or farms if not so conditioned were put in special squads and with patience it was gratifying to see how their coordination and reactions improved, and they too made good soldiers.

Now we have a physical training syllabus in our schools and the picture has changed, and not for the better. It is not fair to blame it on the individual instructor, although one here and there is conspicuous for showing less judgment than his contemporaries.

The number of casualties, some of them quite severe injuries, in our physical training classes is inexcusable.

In our professional sports minded population great emphasis is put on winning teams and flashy performance; the result is that the pupils who are physically well developed and coordinated get the most attention and they could well get along without it, and those who really need the training are often side-lined or injured in attempting advanced work far beyond them.

One is almost forced to the conclusion that the training is being carried on for the benefit of the spectator rather than the pupil.

At the moment of writing a patient of mine is lying in hospital with a severe brain concussion received while attempting an exercise away beyond the individual's capacity, that should not have been permitted.

In conversation with doctors from different areas in the province one learns that this goes on in other districts.

One wonders what inspection and control is exercised and who is responsible.

If the medical profession in this province live up to their responsibilities they will make it their business to find out.

Yours truly,

H. A. Creighton, M.D.

"... the standardized senna was more effective than the control medication (mineral oil or magnesia) in overcoming puerperal constipation..."

# Senokot

## TABLETS

*for puerperal constipation*

1—Baldwin, W. F.: *Canad. Med. Ass. J.*  
89:566 (Sept.) 1963.

**Composition:** 1 Tablet contains an average of 187 mg. standardized senna concentrate equivalent.

**Dosage and Administration:** (Preferably at bedtime). Adults—2 Tablets daily; maximum—4 Tablets twice daily; with a glass of water or other liquid. Children above 60 lbs: one-half adult dosage. **Contraindication:** The "Acute Abdomen". **Supplied:** Bottles of 30, 100, 500 and 1,000. Full information in Vademecum or on request.



MEMBER  
PMAC

THE  
PURDUE FREDERICK  
COMPANY (CANADA) LTD.  
TORONTO, ONTARIO



# British Drug Houses announces new name, Bridine, for povidone-iodine products.



For many years now, B.D.H. has manufactured and sold Betadine Solution, Scrub and Aerosol Spray. As of July 1, 1967, the right to use this name as far as these products are concerned has been acquired by another Company and B.D.H. will now market the same povidone-iodine products under new names: BRIDINE SOLUTION, BRIDINE SURGICAL SCRUB, BRIDINE AEROSOL SPRAY

The only change in these products is the name. The same ingredients, the same process and the same know-how that has made these products the success they are, will be unaltered.

Your continued support of these products under the Bridine name will be appreciated.

B.D.H. the firm with experience in povidone-iodine.





A native of Belliveau Cove, Digby County, N. S. he returns each year to his native province, and has taken an active part in promoting the sport of tuna fishing. Last year he was captain of the Canadian Team at the International Tuna Tournament.

Doctor Kinde, a native of Kinde, Michigan, graduated from the University of Michigan, took public health training at Vanderbilt University, and was a Colonel with the United States Medical Army Corps from 1942 to 1946.

He is a member of the Association of American Medical Colleges, the American Medical Association, and Michigan State Medical Society; he is a Fellow of the American Public Health Association and the American College of Physicians, and a diplomate of the American Board of Preventive Medicine.

Doctor Kinde joined the Kellogg Foundation in 1938, and is the Director of the Foundation's Division of Medicine and Public Health.

The Kellogg Foundation, the prominent award granting agency which has in the past donated millions of dollars to universities in Canada and

the United States, awarded a grant of \$420,000 to Dalhousie in 1965, for the Medical School's new library, to be known as the W. K. Kellogg Health Sciences Library, which is located in the Sir Charles Tupper Medical Building.

The Sir Charles Tupper Medical Building,<sup>1,2</sup> conceived in 1964 to meet the need for expanded facilities for medical students and research, has been completed in record time for buildings of this complex nature. As the Centennial Project of the Province of Nova Scotia, the building fund has received a grant of \$2,500,000 from the Province, with a matching federal grant, and of more than eight million dollars from the Health Resources Fund, in addition to contributions from the W. K. Kellogg Foundation, Dalhousie University and the Alumni, as well as hundreds of individual donations.

The Medical Society of Nova Scotia would like to take this opportunity of congratulating Dalhousie University on the acquisition of a fine new building with which to open a new century of contributions to medical science. □

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## FORTY YEARS AGO

From The Nova Scotia Medical Bulletin, July 1927

The idea of presenting a report of the various activities of the Society for the year was so well received at last year's meeting, I felt I could not do better than to continue the practice this year.

We have had a successful year: our several activities have been maintained, our finances are in good shape, our relations amongst the branches have been harmonious and our interprovincial relations have been improved. The BULLETIN continues to flourish and appears to be filling a much felt need, and while it contains a few scientific articles, the main object is rather to keep our members informed of what is going on in the Society and to report matters of interest to the profession both in its relations to the community and amongst our medical friends.

**Local Societies:**—We have in Nova Scotia 428 registered and resident physicians available for membership in our Society, of which 255 are registered members (an increase of 22 over last year) and 11 honorary members; and 333 hold membership in our Branch Societies, of which there are 9, i.e. 77% are in the local societies, while only 60% are members of The Nova Scotia Medical Society, an increase of 15% in the past 4 years. Now, while this shows that the profession as a whole is taking more interest in the benefits of organization, it still leaves a large number who have not been sufficiently impressed with the increasing need for the largest possible

membership both for their own individual benefit and for that of the profession in the province. Here is a field where the various locals may do a lot of missionary service and I would earnestly commend it to the officers and executives of the different societies to make a survey of their non-members and endeavor to bring them into membership. For

“Full many a gem of purest ray serene

The dark unfathom'd caves of ocean bear:

Full many a flower is born to blush unseen

And waste its sweetness on the desert air.”

I cannot put this too strongly; for if we look about and take notice of many things that are happening near home and in some of our neighboring localities, the need, for the greatest co-operation in our own Societies as well as our fullest support to the Canadian Medical Association is very apparent, and as the idea of community service continues to grow, and it is growing rapidly, the medical profession should be in a position to render the greatest possible assistance in this field and direct its activities in matters that pertain to personal and public health. This is not a matter of selfish interest, for if we do not live up to our obligations in our community life, the public will draw its inspiration from other sources; and we know that the proper moulding of public opinion is much more satisfactory work than attempting to reform what has gotten away to a wrong beginning. □



# Maritime Medical Care Incorporated

The Annual Meeting of the Board of Directors, Maritime Medical Care Inc., took place on April 19, 1967. Immediately following this the first meeting of the new Board of Directors was held.

## Board of Directors M.M.C. Inc., 1967-68

Director	Branch Medical Society Represented	Appointment Expiring
Dr. H. B. Whitman	Pictou County Medical Society	1969
Dr. B. L. Reid	Halifax Medical Society	1968
Dr. R. A. Burden	Cumberland Medical Society	1968
Dr. G. W. Turner	Valley Medical Society	1968
Dr. T. B. Murphy	Antigonish-Guysborough Medical Society	1968
Dr. H. F. Sutherland	Cape Breton Medical Society	1968
Dr. F. G. Bell	Lunenburg-Queens Medical Society	1968
Dr. C. K. Fuller	Western Nova Scotia Medical Society	1968
Dr. P. R. Little	Colchester-East Hants Medical Society	1969
Dr. A. M. Lawley	Inverness-Victoria Medical Society	1969
Dr. P. S. Mathur	Eastern Shore Medical Society	1969
Dr. T. Mears	Shelburne Medical Society	1969
Dr. A. N. Lamplugh	Dartmouth Medical Society	1969
Dr. A. Gaum	Cape Breton Medical Society	1969
Dr. J. McD. Corston	Halifax Medical Society	1969
Dr. M. F. Fitzgerald	Pictou County Medical Society	1968

## Lay Members

Mr. David Zive	Halifax	1968
Mr. J. A. Walker, Q.C.	Halifax	1969
Mr. J. N. Foster	Halifax	1969
Mr. V. N. Thorpe, Q.C.	Kentville	1969

## The Board of Directors elected -

Dr. H. B. Whitman - Westville - President  
 Dr. B. L. Reid - Halifax - Vice-President

## The Executive Elected are the Officers and -

Dr. F. G. Bell	Liverpool
Dr. P. R. Little	Truro
Dr. H. F. Sutherland	Sydney
Dr. G. W. Turner	Windsor
Mr. J. A. Walker, Q.C.	Halifax
Mr. J. N. Foster	Halifax

# Annual Report of the President

## Gentlemen:

As President of M.M.C. I am pleased to welcome you to this, our Corporation's eighteenth Annual Meeting. As Directors you have played an important part in piloting the Corporation through another busy year. In the next few minutes I would like to highlight the achievements of the year and also point out some areas which will require the Board's attention in 1967.

Perhaps I should start by pointing out that since the last Annual Meeting the Board of Directors has

met on five occasions, the Executive Committee three times, the Finance Committee eight times and the newly formed Special Medicare Committee on six occasions. I am pleased to note from the minutes that all meetings have been well attended, which speaks well for the interest shown by the Directors in the various duties they have assumed.

## Financial

During the year 1966 our income from subscriptions rose to \$5,424,872 from the 1965 level of \$4,894,392, an increase of \$530,480. Payments for



benefits during the same period rose from \$4,156,692 in 1965 to \$4,982,870 in 1966 or from 84.9% to 91.8% when paid benefits are expressed as a percentage of subscription income. Our income from investments showed improvement during the year by rising from \$134,967 in 1965 to \$165,049 in 1966, a gain of \$30,082.

With regard to the cost of administration, I reported last year that costs had more or less stabilized at 11.7% of revenue in 1965 when compared with 11.6% in 1964. This year it is my pleasure to report for the first time in several years a marked decline in this ratio from 11.7% to 10.7%. This I feel is quite commendable when we bear in mind that the volume and variety of services provided increased over the previous year.

I would like to comment in more detail on the financial status of our Medical Care programs as opposed to our overall operating position during the year. Looking at the audited statement one might gain the impression that the increased percentage of the Fee Schedule paid to physicians since the last quarter of 1965 as well as the benefits added since that time have not proved to be as costly as was first anticipated. This of course is not correct as a study of our Annual Cost by Coverage Report will quickly show. In 1965 the combined subscription income from our Group and Non-Group Comprehensive and Health Security plans exceeded the cost of claims by \$21,889 whereas our 1966 experience shows the cost of claims exceeding subscription income by \$282,496, a difference of \$304,385. This drain on Corporation reserves by the Medical Care plans was planned and will no doubt continue in 1967, however the new Board should watch this rate of depletion very closely once the revised Schedule of Fees (soon to be introduced) has been approved by the Board as the basis for payment of M.M.C. benefits.

With respect to our ancillary plans I am pleased to note that both the Supplementary Hospital Plan and our Extended Health Benefit Plan show surpluses again this year, totalling about \$24,000.

#### Enrolment (see table below)

It is interesting to observe that in spite of all the talk of Medicare enrolment in our Medical Care programs has continued to grow at average rate of 1,000 persons per month.

Our Sales Department was also successful in improving our enrolment under the para-medical programs, with our Supplementary Hospital Plan now approaching 46,000 members and over 23,000 members covered on our Extended Health Benefit Plan.

Over 198 new groups were enrolled this year and a very high proportion (143) purchased one or both of our para-medical plans in addition to coverage for physicians' services.

#### Amendment to Act of Incorporation

I am pleased to report that the amendment to our Act of Incorporation was approved by the Legislature on March 22, 1967. As you are no doubt aware the amendment, which has the approval of our sponsors, will give M.M.C. greater versatility in the field of health insurance. We will now be permitted to offer para-medical programs separate from as well as along with our basic medical plans. It will also permit the Corporation to enter into arrangements with other Health Associations, which could include the acceptance by such associations of certain underwriting risks for insured services provided by its members in much the same manner as the medical profession has done over the years. Without such amendment M.M.C. might have found it extremely difficult to operate successfully after Medicare.

#### Medicare

A considerable amount of time has been spent on various projects associated with the proposed Medicare plan for Nova Scotia. Our administrative staff has completed many reports and has met frequently with members of the Medical Care Insurance Advisory Commission and their consultants in carrying out your wishes to assist the Commission in every way possible. Our Office Manager, Mr. Waller, has been loaned to the Commission as its full-time Executive Secretary and adviser, and I am pleased to report that the Commission are high in their praise of his contribution to their deliberations.

#### Statement of Enrolment by Plan at December 31, 1966

##### Showing Gain or (Loss) over 1965

	No. Contracts	Gain Over 1965	No. Persons	Gain Over 1965
Group Comprehensive	48,401	3,081	141,296	8,508
Non-Group Comprehensive	11,700	1,475	33,596	3,740
Health Security	986	(28)	3,253	(58)
Seniors' Health Plan	10,307	32	13,593	(93)
<b>Total Medical Care Plan Enrolment</b>	<b>71,394</b>	<b>4,560</b>	<b>191,684</b>	<b>12,097</b>



We have also been working closely with and providing information and assistance to the Physicians' Services Insurance Committee of The Medical Society of Nova Scotia in their representations to the Medical Care Insurance Advisory Commission. The Corporation's grant of \$5,000 to the Medical Society of Nova Scotia to help defray part of the cost of maintaining the P.S.I. Committee was, I feel, a justifiable expenditure and one which was appreciated by the Society. The groundwork laid by our Special Committee this past year will form a firm base from which we hope to negotiate an acceptable "agency" role for M.M.C. in the province's proposed Medicare plan. Formal negotiations on the feasibility of such an arrangement have begun and we are hopeful that general agreement can be reached at an early date in order that detailed planning may begin without further delay. There is a great deal to be done if we are to provide an efficient administrative force of a size capable of handling Medicare by its anticipated effective date of July 1, 1968.

### Physician Relations

Our relations with individual Participating Physicians and the Medical Society continue to be excellent. Our Participating Physician membership now stands at 999 compared with 979 reported last year. With the publication this year of a Specialist Register by the Provincial Medical Board, it is now possible for M.M.C. to accept such registration as the basis for entering into a Participating Specialist Agreement with any Specialist in the province.

Last year for the first time the Board of Directors held one of its regular meetings in conjunction with the Annual Summer Meeting of The Medical Society of Nova Scotia. This I feel was a highly successful undertaking for it created a greater awareness of the close relationship which exists between the Society and Plan. It is my hope that future Boards of Directors will give serious consideration to repeating this arrangement should a similar invitation be forthcoming from our Sponsors.

As a service to Participating Physicians, our Medical Director has begun a series of regional seminars for Medical Secretaries and other office assistants. Five such seminars have been held so far and they have proved helpful to the Plan as well as the participants.

In our capacity as agents for the Medical Society in the administration of the provincial medical plan for certain recipients of Welfare benefits, we were pleased to provide information and assistance to the Society in its negotiations for a new rate of reimbursement effective April 1, 1966, and for the acceptance of additional categories under the plan effective September 1. This plan began the year with a monthly enrolment of 9,700 and rose to 17,000

by year end, with every indication that in excess of 20,000 persons will be covered by the end of the current year.

Your General Manager, Medical Director and President continue to attend as many Branch Society meetings as possible during the year and are most appreciative of the excellent reception received and interest shown at all meetings.

### Benefit Changes

Since our last Annual Meeting the Corporation has continued to broaden its spectrum of benefits to physicians and subscribers. The remaining items on the negotiated list of fees have been eliminated and payment for all benefits is now based on the published Schedule of Fees. The removal of limits on continuing and directive care in hospital by Specialists, broader Psychiatric services, the addition of routine physical examinations after twelve months membership without medical attention, extension of obstetrical benefits to single contracts and dependents of subscribers, and payment for intra-group consultations, are but a few of these improvements. These extensions have been made in keeping with the Corporation's desire to meet the goal set by our sponsors of providing as comprehensive a range of benefits as possible.

### T.C.M.P. Activities

Our Plan's Commissioners, Dr. Bell and Mr. Brannan, have represented the Corporation at two T.C.M.P. meetings this year with the majority of national activity centering around Medicare and Federal Bill C-227. We are indeed grateful to the T.C.M.P. national office for its representations in Ottawa on behalf of doctor-sponsored plans and their use as fiscal agents under Medicare. In this respect M.M.C. and its relations with the Nova Scotia Medical Care Insurance Advisory Commission was cited frequently at Ottawa as an example of how an agency arrangement could function. Our Plan was also privileged to act as host for the T.C.M.P. Office Practice Committee meeting held in October.

### Conclusion

In conclusion I would like to thank all of you for your co-operation and assistance during the year. In particular I would like to acknowledge the services of Dr. R. L. Aikens, Halifax and Dr. Watson Sodero of Sydney, who are retiring from the Board, this being their last meeting.

On your behalf I would also like to extend our thanks to the M.M.C. staff for the faithful and efficient manner in which they have carried out their duties in 1966.

Respectfully submitted,

H. B. Whitman, M.D.,  
President.



# Auditors' Report

We have examined the balance sheet of Maritime Medical Care Incorporated as of December 31, 1966 and the statement of income and expenditure and general reserve for the year ended on that date and have obtained all the information and explanations we have required. Our examination included a general review of the accounting procedures and such tests of accounting records and other supporting evidence as we considered necessary in the circumstances, including verification of bank balances and investments.

In our opinion, and according to the best of our information and the explanations given to us and as shown by the books of the corporation, the accompanying balance sheet and statement of income and expenditure and general reserve, together with the notes thereto, are properly drawn up so as to exhibit a true and correct view of the state of the affairs of the corporation at December 31, 1966 and the results of its operations for the year ended on that date, in accordance with generally accepted accounting principles applied on a basis consistent with that of the preceding year.

PEAT, MARWICK, MITCHELL & Co.  
Chartered Accountants

Halifax, N. S.  
April 6, 1967

## BALANCE SHEET

December 31, 1966 (with comparative figures for 1965)

### ASSETS

	1966	1965
Cash on hand and on deposit	\$ 356,482	\$ 313,390
Accounts receivable	175,652	27,257
Prepaid expense	618	475
Accrued interest on investments	42,062	38,000
Investments, at cost:		
General funds	2,973,752	2,658,355
Restricted funds	41,761	41,761
Quoted market value		
December 31, 1966	\$2,872,663	
December 31, 1965	\$2,629,056	
Inventory of supplies, at cost	14,322	11,429
Furniture and office equipment, at cost	79,144	76,697
Less accumulated depreciation	45,412	39,294
Net furniture and office equipment	33,732	37,403
	\$3,638,381	\$3,128,070

### LIABILITIES

	1966	1965
Cheques issued, but not presented for payment	\$ 369,602	\$ 203,498
Subscribers' claims payable	949,476	759,731
Unpresented subscribers' claims, estimated	331,851	196,735
Accounts payable	13,753	12,009
Trust funds - Province of Nova Scotia Welfare Plan	126,612	69,737
Subscriptions received in advance	127,976	154,814
Payable re railway contract, estimated (note 1)	158,063	113,499
Total liabilities	2,077,333	1,510,023
Restricted funds:		
Contingency reserve, re railway contracts	41,761	41,761
Retained by the Corporation:		
For stabilization of payments to physicians	359,276	416,275
Reserve for decline in market value of investments	100,000	30,000
Reserve for Employee Retention Plan	235,000	235,000
General reserve, per statement attached	825,011	895,011
Total retained	1,519,287	1,576,286
	\$3,638,381	\$3,128,070



**Statement of Income and Expenditure and General Reserve**

**Year ended December 31, 1966**  
(with comparative figures for 1965)

	1966	1965
Subscription income	\$5,424,872	\$4,894,392
Expenditure:		
Medical care for subscribers		
Current year medical claims paid or provided for	4,982,870	4,156,692
Add:		
Medical claims paid re prior years in excess of amount provided	84,236	( 26,963)
Administration costs, Schedule "1"	5,067,106	4,129,729
	581,491	572,115
Total expenditure	5,648,597	4,701,844
Operating deficit (income)	223,725	( 192,548)
Net income:		
Income from investments	165,049	134,967
Sundry	1,677	1,998
	166,726	136,965
Net deficit (income) for the year	56,999	( 329,513)
Appropriation from:		
Reserve for stabilization of payments to physicians	56,999	—
	—	( 329,513)
Appropriation to:		
Reserve for stabilization of payments to physicians	—	47,464
Reserve for decline in market value of investments	70,000	15,000
Contingency reserve, re railway contract	—	1,349
Adjustment of amount receivable re mutualization of 1961-1962 railway contract	—	39,380
	70,000	103,193
Balance appropriated to General Reserve	( 70,000)	226,320
Amount of General Reserve at beginning of the year	895,011	903,691
	825,011	1,130,011
Transferred to Reserve for Employee Retention Plan	—	235,000
	\$ 825,011	\$ 895,011

**Notes to Financial Statements**

**December 31, 1966**

- Effective January 1, 1965 the Corporation entered into a two year contract, in conjunction with similar medical service plans in Canada, to provide medical coverage for the employees of Canada's railways. The contract provides that at its termination the experience of the participating plans will be reviewed in order to determine the net gain or loss from the contract. The experience of each plan is then related to the experience of the group as a whole, and then appropriate financial adjustments are made among the plans. Based on the experience of the Corporation on this contract, it is estimated that at December 31, 1966 a refund by the Corporation to the participating plans of approximately \$158,063 will be required.
- Under the terms of the agreement between the Corporation and the participating physicians, the Corporation may, after the expiration of a twelve month period, cancel any unpaid balances outstanding on approved claims. The Board of Directors has passed the necessary resolution to cancel all such unpaid amounts to December 31, 1965. □