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SPECIAL ARTICLE

Cause and Effect: The Fifth Alexander Gibson Memorial Lecture

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IT IS with mixed feelings that I rise to give the Fifth Alexander Gibson Memorial Lecture. Naturally I feel honoured for being chosen to follow such distinguished predecessors, but it is sad for me to consider that the reason for this occasion is the fact that a face, so familiar and dear to most of us, is absent.

When I was an undergraduate at Edinburgh, Alec Gibson was my best and closest friend. I can remember how I first noticed him in the class of physics, and I used to be staggered at the lightning speed with which he copied diagrams from the board to his notebook. Naturally he took the first medal in that class. As a matter of fact he took just about every medal and prize that could be taken. But I beat him once, in Schäfer's physiology class. Please don't think that I am boasting. There is always a reason for everything. In this instance my friend went to visit a rich relative in Pittsburgh, was taken into the country, developed typhoid fever, and was out of the physiology class until Christmas. So he only got the second medal.

Needless to say, when he graduated with first-class honours he was awarded the Ettles Scholarship for the most distinguished student during the five years of the undergraduate course. But even more noteworthy is the fact that during his Arts course, before he began the study of medicine, he won the Vans Dunlop Scholarship in Classics *and also* in Mathematics, although he was not allowed by the university rules to keep both. He also won the first medal in Saintsbury's English Literature class, and developed an abiding interest in words and good writing. He was exacting in his choice of English, and some of us might have had difficulty with our contributions to medical literature if he had been the editor of the journal to which we submitted our paper, for he did not suffer fools gladly. When he came to Winnipeg, Professor Allen in physics and Dr. Armes in chemistry used to take their papers to him before publication, because of his unusual combination of expert knowledge regarding physics and chemistry on the one hand, and English on the other. He was marked by all-round ability so uncommon in this day of specialization, for he was as good with his hands as with his brain. He could have been outstanding as an engineer, or as a professor of mathematics or of English. No wonder J. C. B. Grant and I, his fellow students, had no chance against him in the academic contest, unless aided by typhoid fever.

The one thing I taught him in our undergraduate days was rock climbing, and on Saturday afternoons we used to bicycle to the Salisbury Crags adjoining Arthur's Seat just outside Edinburgh, and climb those vertical cliffs with the safeguard of an alpine rope. Our greatest thrill was when we managed to do the climb called the Cracked Slabs. When we struggled to the top, Alec stood on his head in triumph.

When the result of the second-year examinations came out (Alec with first-class honours, I with none), we started out to bicycle south to the English Lake District, where we spent a heavenly two weeks, walking and climbing.

All this was a preparation for the evening of the day in 1908 on which the results of that purgatory of six weeks, the final examination, were published (with the same spread of honours as before), when Alec, I and four non-medical friends boarded the 10 p.m. train for Oban in the Western Highlands. We had never heard of sleeping cars, so we each rented a pillow for sixpence and slept soundly till 4 a.m., when we reached Oban on the twentieth of June. At 6 a.m. we were on the steamer sailing over the sea to Skye. As we lay on the deck in the glorious sunshine all thought of those terrible weeks faded from our memory. On landing in the evening there was a mere 10-mile walk to a crofter's cottage in Glen Brittle, carrying on our backs our baggage, together with a tent for sleeping, for a two weeks' climbing holiday in the Black Coolins.

Next morning was the 21st of June, the longest day of the year and my own birthday, and after a swim in the sea which was only 100 yards from our tent, we started on our first climb. Later in the day we stood on the summit of one of the Coolins and looked down:

> And God's own profound was above us,
> Around us the mountains, beneath us the sea.

Then another swim, supper in the cottage, and dreamless sleep in our tent.

This went on for two weeks, with some rather exciting experiences on the wild cliffs of the Coolins which I have not space to relate here. It is little wonder that Alec Gibson and I were the best and closest of friends.

Then internships and professional life separated us. He became an anatomist and later a surgeon,

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and I awoke one morning to find myself a psychiatrist who gradually picked up a smattering of pathology, because I had to do the autopsies and laboratory work in the mental hospitals in which I resided.

In 1913 Gibson was invited to accept the post of Professor of Anatomy at what was then the Manitoba Medical College, where he promptly became a brilliant success. He arrived in Winnipeg in the evening of the last day of the year. In the meantime I had managed to become the first pathologist to the Wolverhampton General Hospital.

Imagine my feelings when I received a letter from Alec dated June 9, 1914, a letter which I retain in my possession to this day. It starts as follows: "My dear Will, I received your very welcome letter about two weeks ago, and now hasten to reply to it. First of all, the Dean came to me yesterday, and asked if I knew anyone who would do for the post of the first Professor of Pathology in this university. I said I did, and asked the terms. Subjects to be taught—Pathology and Histology. Remuneration: Pathology, $3,000; Histology, $1,000. Total $4,000. Put that under your tongue. The authorities are writing to Osler at Oxford and Sims Woodhead at Cambridge, but I could help a whole lot here, I think. If you could see the sunshine we get here, it would almost persuade you. If you get the job I'll introduce you to a keen mountaineering man who goes to the Rockies every July. Man, it would be fine for us to be together again." Although I had never in my life given a lecture in pathology (or any other subject), or even demonstrated to one student, I got the job. Which just shows what pull can do—if you have the right man pulling the wire.

The First World War intervened, and by the time I got the notice of my appointment in Winnipeg I was in France with the R.A.M.C. When I was requisitioned to come to Winnipeg a year later, reading Mallory's Pathology on the boat in preparation for giving 100 lectures on the subject, Alec had left for overseas, where he did surgery with the R.A.M.C. After being torpedoed and sunk in the Mediterranean, and nearly dying of dysentery in India, he finally returned to Winnipeg, and at the end of the war he resigned from the Chair of Anatomy in order to devote himself to orthopedic surgery, a field in which, as might be expected, he rapidly acquired an international reputation, being later appointed to the Chair of Orthopedic Surgery in the university. The Dean asked him to suggest a successor in the Chair of Anatomy, and without hesitation he recommended his fellow student and mine at Edinburgh, J. C. Boileau Grant, who by that time was an accomplished anatomist, and with whose supreme ability and achievements all are familiar, some of the details of which were related in Sir Walter Mercer's First Alexander Gibson Memorial Lecture. I met John Grant when he arrived at the station, invited him to my house for dinner, where he met my wife's sister, Catriona, whom he promptly married. J.C.B. tells me of Alec, with whom he was closely associated during his early days in Winnipeg: "Any day at noontide you could learn from him all the news in the morning paper, world news, local news, the price of stocks, theatrical news, the bargains of the day as advertised. Nothing seemed to miss his eye." And the amazing thing was that he retained that power until the day he suddenly died in his office.

Such, in brief, is the story of the three Edinburgh students who came to Winnipeg to begin their university careers, and Grant and Boyd would never have been here had it not been for Alec Gibson.

But this memorial lecture must be something more than a biographical sketch of Alexander Gibson and his Edinburgh friends. As I have no special knowledge of orthopedic surgery, I shall direct my remarks to a subject of general interest to every scientist and to every doctor, namely the relation of cause to effect, especially when the effect happens to be what we call disease.

All reasoning about matters of fact, all physical science, depends on the relation between cause and effect. We must admit, however unwillingly, that we seldom or never really know the cause of anything. We merely note a constant association. The apple falls, and we say that it is caused by the action of gravity. But that is no adequate explanation, for we have not the remotest idea of how gravity acts on the apple. We say that the tubercle bacillus is the cause of tuberculosis. That is merely a way of saying that the bacillus is constantly associated with a certain type of lesion; it is no explanation of how the lesions are produced by the bacillus. The intrinsic properties of the tissues which render some animals and some persons susceptible to the infection and other persons immune are as yet unknown. In this sense the tuberculous reaction is just as mysterious as the neoplastic reaction. It will be noted that I am lumping (perhaps confusing) etiology and pathogenesis, including both under causation.

To attempt to define causation in relation to disease is an intellectual exercise as exasperating as any one can find. The Concise Oxford Dictionary, that masterpiece of exact description, defines a cause as "an antecedent invariably and unconditionally followed by a certain phenomenon". What, then, is the cause of diphtheria? Surely not the diphtheria bacillus, for the presence of that organism in the throat is certainly not "invariably and unconditionally" followed by development of the disease. An etiological factor in disease does not need to be constant. Malnutrition is an inconstant factor in the etiology of tuberculosis, but it may be an essential factor. It may of course be a result of tuberculosis. Finally, it may be neither, merely an associated condition. From these simple

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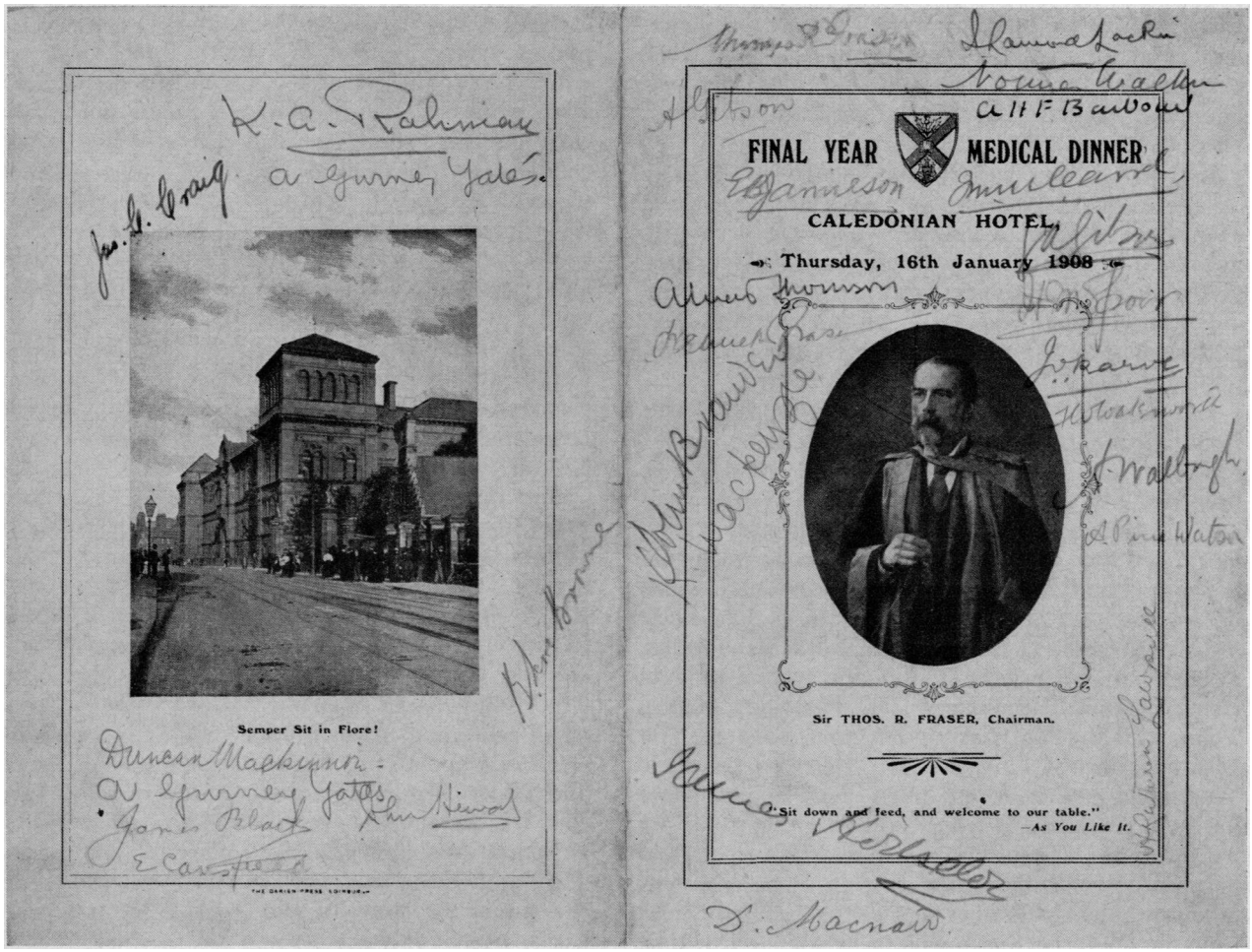
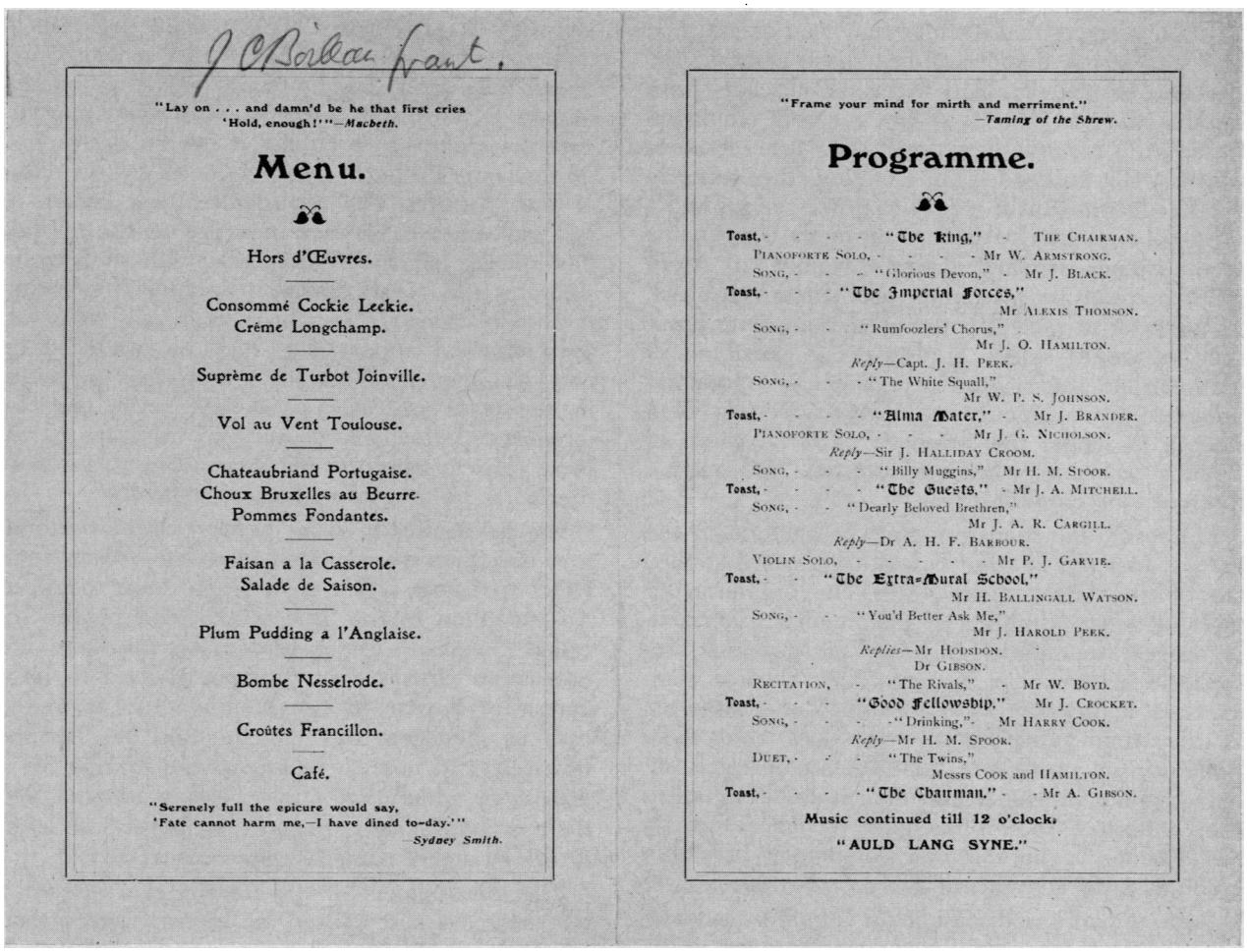


Fig. 1.—The cover of the program for the Final Year Medical Dinner, University of Edinburgh, January 16, 1908.

examples it becomes evident how complex and difficult is the subject of the causation of disease. We can of course simplify it, as when we say: "I caught a cold sitting in a draft." But what is the answer to the question "Why did the patient die?" When I say "mitral stenosis", you counter by pointing out that he has had mitral stenosis for 20 years. The wonder is not that he died, but that he had lived so long.

Many instances will occur to the reader in which it is difficult, and sometimes impossible, to determine which of two conditions occurring in the same patient is cause and which is effect: for example, hypertension and the arteriolar sclerosis in the kidney which so often accompanies it. Much evidence can be brought forward in support of either of these views. Is coronary sclerosis the cause of the cardiac hypertrophy often found associated with it, or is the hypertrophy due to the hypertension common in the involutional age period and possibly a causal factor in the production of the coronary sclerosis? Is coronary thrombosis always the cause of the associated myocardial infarct, or in some cases may it not be the result of the infarction? These and other familiar examples indicate how involved and intriguing are some of the problems of causation.

With the development of the bacterial theory of disease it became evident, or seemed to become evident, that the cause of disease was predominantly external. It is hard to imagine a more fascinating story than the historical development of the concept of the bacterial origin of fermentation, putrefaction and infection, those three conditions apparently so diverse but in reality so intimately related. In 1680 Leeuwenhoek saw the spherical granules of yeast with his microscope. By the beginning of the 19th century yeast was known to be living. And yet in 1839 the great German chemist Liebig, supported by the even greater von Helmholtz, declared that germs were the *result* of fermentation and putrefaction, not its cause. Then Pasteur entered the field, and this simple French chemist, with equipment and accommodation which no self-respecting hospital resident would tolerate today, proved by conclusive experiment that fermentation was due to living microbial agents. The relation of fermentation to the putrefaction of dead bodies was then recognized, and the final proof by Pasteur and Lister that bacteria from outside are the essential cause of infection is known to everyone.



"Lay on . . . and damn'd be he that first cries
'Hold, enough!'"—*Macbeth.*

Menu.

Hors d'Œuvres.

Consommé Cockie Leekie.
Crême Longchamp.

Suprème de Turbot Joinville.

Vol au Vent Toulouse.

Chateaubriand Portugaise.
Choux Bruxelles au Beurre.
Pommes Fondantes.

Faisan a la Casserole.
Salade de Saison.

Plum Pudding a l'Anglaise.

Bombe Nesselrode.

Croûtes Francillon.

Café.

"Serenely full the epicure would say,
'Fate cannot harm me,—I have dined to-day.'"
Sydney Smith.

"Frame your mind for mirth and merriment."
—*Taming of the Shrew.*

Programme.

Toast, - - - - "The King," - THE CHAIRMAN.
PIANOFORTE SOLO, - - - - Mr W. ARMSTRONG.
SONG, - - - "Glorious Devon," - Mr J. BLACK.
Toast, - - "The Imperial Forces,"
Mr ALEXIS THOMSON.
SONG, - - "Rumfoozlers' Chorus,"
Mr J. O. HAMILTON.
Reply—Capt. J. H. PEEK.
SONG, - - - "The White Squall,"
Mr W. P. S. JOHNSON.
Toast, - - - "Alma Mater," - Mr J. BRANDER.
PIANOFORTE SOLO, - - - Mr J. G. NICHOLSON.
Reply—Sir J. HALLIDAY CROOM.
SONG, - - - "Billy Muggins," Mr H. M. SPOOR.
Toast, - - - "The Guests," - Mr J. A. MITCHELL.
SONG, - - "Dearly Beloved Brethren,"
Mr J. A. R. CARGILL.
Reply—Dr A. H. F. BARBOUR.
VIOLIN SOLO, - - - - - Mr P. J. GARVIE.
Toast, - - "The Extra-Mural School."
Mr H. BALLINGALL WATSON.
SONG, - - "You'd Better Ask Me,"
Mr J. HAROLD PEEK.
Replies—Mr HODSDON.
Dr GIBSON.
RECITATION, - "The Rivals," - Mr W. BOYD.
Toast, - - - "Good Fellowship," Mr J. CROCKET.
SONG, - - - "Drinking," - Mr HARRY COOK.
Reply—Mr H. M. SPOOR.
DUET, - - - "The Twins,"
Messrs COOK and HAMILTON.
Toast, - - - "The Chairman," - - Mr A. GIBSON.

Music continued till 12 o'clock.

"AULD LANG SYNE."

Fig. 2.—The menu and program.

But final proofs are not always readily accepted by our profession. In this respect the following passage from a book on "The Infectious Diseases", published in 1878, may be of interest. Under the heading "Conclusions as to the Bacterial Hypothesis" the writer makes this remarkable statement: "Is it not a fair inference, then, that the infectious diseases are caused by the bacterial germs, as now so largely claimed? In face of the negative character of all the testimony alleged in favour of such a theory, and the positive nature of that against it, the inference cannot be a fair one."

Causal agents of disease may be classified as exogenous and endogenous. The first external agent to be recognized was trauma. This recognition was easy, because effect followed cause at once or after a short interval. The onset of traumatic disease, however, may be insidious, and its origin correspondingly obscure and mysterious, not to be recognized by simple observation. The trained observer, and later the experimentalist, were needed gradually to reveal the underlying and hidden connection between traumatic cause and effect. An excellent example in the field of traumatic disease is afforded by subdural hemorrhage. A person sustains a comparatively trivial injury to the head, and weeks, possibly months later, when all recollection of the injury may have been lost, a train of mysterious cerebral symptoms develop which terminate in death. Only the observations of the pathologist in the postmortem room combined with the analysis of many such cases by the neurologist lead to the final conception that the large hematoma found under the dura is to be traced to the long-antecedent injury.

Pathology has progressed from behind forwards, or rather in the Chinese fashion of reading from right to left. First the symptoms of a disease were recognized and described, then the lesion responsible for the symptoms, and finally the causative agent which started the process. Thus *general paresis* was first recognized as characterized by delusions of grandeur, etc.; then atrophy of the frontal convolutions was noted; and finally the *Treponema pallidum* was discovered in these atrophic convolutions. The concept was first that of a mental disease, then a disease of the nervous system, and finally an infectious disease. But we still don't know how the Treponema wrecks the cerebral cortex, nor why in other patients it produces such an entirely different disease as tabes dorsalis.

When we ask for the proof that a bacterium is the cause of a given disease we find ourselves in

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need of every critical faculty that we possess. The first step is the demonstration of the germ in the affected tissues, coupled with its absence from healthy tissues. This was the method employed by Koch in his investigation of the cause of tuberculosis. He succeeded in staining the tubercle bacillus *in situ*. But if we try to prove the syphilitic nature of a gumma by demonstrating the Treponema in the tissues we shall almost certainly fail. More subtle methods for solving the problem are required. As a matter of fact, it is doubtful if absolute proof such as would satisfy a physicist is possible. All that can be said is that a gumma is frequently preceded by secondary and primary lesions of a disease in which the accepted bacterial cause of syphilis can usually be demonstrated. And what is the cause of sarcoidosis?

Moreover, the mere presence of bacteria in the tissues does not of itself constitute proof that they are of etiological significance. The organisms of typhoid fever, diphtheria, pneumonia, and meningococcal meningitis can lead a harmless saprophytic existence in carriers. They become commensals, a pleasant word meaning "one who eats at the same table". And why does *Salmonella typhimurium* produce a fatal disease in mice but only a minor intestinal infection in children, unless they inherit a mouse-like gene which results in the absence of an essential component of serum globulin with consequent loss of resistance?

Reproducing the disease in an animal by inoculation of infective material was a step of great value, but it must be admitted that some of the most important human diseases, such as typhoid and gonorrhea and leprosy, cannot readily be reproduced in laboratory animals, so that in these cases we have no direct means of determining the pathogenicity of the infecting organisms. Experiments on man, usually accidental, have helped in the matter.

In order to prove the causal relationship of a bacterium to a disease, isolation of the microorganism from the tissues is, of course, no longer necessary in every case. More indirect methods are available, such as the demonstration of specific immune bodies in the host's serum against the bacterium, e.g. agglutinins, precipitins, and fixation antibodies, not to mention the Wassermann reaction, which is not specific.

If it is sometimes difficult to prove conclusively the causal relationship of a bacterium to a disease, this difficulty becomes very much greater in the case of virus diseases. In addition to being ultramicroscopic in size, although now demonstrable by the electron microscope, a virus refuses to grow on non-living bacteriological media. It can therefore only be recognized by the effect it produces. This effect may be clinical or histological. Sometimes the clinical effect is unequivocal, as in the paralysis which follows inoculation with poliomyelitis virus; sometimes it is of the type in which certainty is extremely difficult, as in the case of influenza. Similarly, the histological change produced by a virus may be characteristic or indeterminate. Necrosis of a specific cell type may be pathognomonic, as exemplified by the destruction of the anterior horn cells produced by the virus of poliomyelitis. The peculiar features known as cell inclusions have been regarded as the tell-tale fingerprints left by a virus, and with such inclusions as the Negri bodies in rabies this is undoubtedly true. It is now recognized, however, that identical appearances may be produced by non-viral agencies. Thus the intranuclear inclusions in the liver in cases of yellow fever may be mimicked perfectly in severe and extensive burns. Proof of causality in the case of a virus may, therefore, be a matter of great difficulty.

We have already seen in the case of bacterial infection that we are accustomed to reason from effect to cause rather than from cause to effect. An exception to this rule is provided by the so-called "Orphan" group of viruses, for there are now more viruses than diseases. It used to be a matter of disease in search of a virus, as in the case of influenza, but the situation has become reversed, and now there are viruses looking for a disease by which they might become adopted, and their orphan state is recognized in the last letter of the strangely named ECHO viruses.

The development of the concept that disease is for the most part caused by external agents laid emphasis on the idea that the causal agent was of a positive character. The suggestion that disease might be due to a *deficiency* of some element necessary for the welfare of the body opened up an entirely new line of thought. Work was at first confined to the field of the vitamins, and it was learned that one vitamin is necessary for the health of the central nervous system, another for the epithelium of mucous membranes, a third for intercellular substance, and so on. In the course of time the idea of deficiency disease has widened, and it is now realized how potent as a causal agent of disease may be deficiency of various kinds, so much so that the modern classification of the anemias is largely on a deficiency basis. When I was a medical student in Edinburgh before graduating with Alec Gibson in 1908, I was taught that pernicious anemia was caused by hemolytic poisons produced by *Streptococcus hemolyticus* which lived in the small bowel. The germ only survived passage from the throat through the stomach in those who had no hydrochloric acid in the stomach. Hence the relation between pernicious anemia and achlorhydria. Simple, my dear Watson! If I had not repeated this nonsense in an examination, I would have failed and would not be here today. We were also told that arthritis was probably due to the absorption of toxins from the colon, and many a colon was removed—in London, not in Edinburgh.

The passion for general theories to explain disease has persisted from the time of Galen. As Sir George Pickering put it in his Harveian Oration to the Royal College of Physicians of London last October: "When I was a student and house physician it was focal sepsis . . . . Later came the psychosomatic era, then diseases of adaptation, now auto-immunity." The list of diseases is the same: only the cause changes, as does its treatment, though not necessarily its efficiency.

A simple but rather intriguing example of *multiple* causal factors was brought to my notice by my friend Professor Kreyberg of Oslo, who was in the Russo-Finnish war of 1939. During the intense cold of January and February the airmen suffered from frozen faces. A couple of months later, when the weather was considerably milder, the lesions of frost-bite became more, rather than less, severe. This was because to the effect of the cold was now added the actinic action of sunlight, the combination of factors being sufficient to result in the stasis which is the essential basis of frost-bite.

It seems probable that in the future more and more stress will be laid on the duality or multiplicity of factors in the causation of disease. Bacterial and virus infection, vitamin deficiency, and mineral deficiency may be combined in various ways at which we are only now beginning to guess. To break one link in the chain of causal factors may mean therapeutic success, but it does not mean that there are not other links in the chain. Thus, splenectomy may cure the clinical picture of hemolytic jaundice, relieving the patient of all his symptoms, yet undue fragility of the red cells still remains, which can be blamed on spherocytosis of those cells, but we now realize that the basic defect is a genetic one involving the intracellular phosphorylation of adenosine triphosphate. Similarly, removal of the thyroid may work wonders in a patient with Graves' disease, but that does not justify the conclusion that dysfunction of the thyroid is the basic factor in the production of that disease.

We can control diabetes by appropriate therapy with remarkable success, but we still do not know the cause of diabetes. Pancreatectomy or merely destruction of the islets will induce the onset of diabetes, but in the maturity-onset type of the disease beta-cell granulation may be well developed and the supply of free insulin may be adequate to the needs of the body. We know that diabetes mellitus can be produced by anterior pituitary, adrenocortical and thyroid hormones. It was Joslin who called heredity "the basis of diabetes", but we do not really know which organ is the seat of the primary gene change, whether in the pancreas or elsewhere. Diabetes may be present from birth as a prediabetic state in the form of an inherently defective carbohydrate mechanism which can be triggered in a variety of ways. What better example could we have of the truth that there is no necessary relation between knowledge of therapy and knowledge of cause?

The possibility of multiple factors is of special interest and importance in the disease which first directed my attention to the subject of causality, namely cancer. Many causes of cancer are already known; so many, indeed, that the result has been confusion. We say that we know the cause of inflammation, namely an irritant. Well, we know the cause of cancer, namely a carcinogen. Cancer in the animal is identical with cancer in man, and experimental cancer can be produced by the application of tar and a host of synthetic products, by the injection of an ovarian hormone, by filterable viruses, by exposure to x-rays and radium, and by yet other methods. How then can we speak or even think of *the* cause of cancer? A filterable agent is the cause of the Rous sarcoma; continued administration of ovarian hormone may cause carcinoma of the breast; and prolonged mechanical irritation of stratified squamous epithelium may result in the development of epidermoid carcinoma. It is easy to understand how an ovarian hormone might act as a causal agent in the production of breast carcinoma. It is more difficult to understand how it could be responsible for such a tumour as osteogenic sarcoma. Yet in one strain of mice 80% of the females die with osteogenic sarcoma, but less than 20% of the males are similarly affected. The injection of estrin in males of this strain increases the tumour incidence up to that of the females.

The reference to one particular strain of animal in which an exogenous factor is operative in the production of cancer introduces the idea that there is also an intrinsic factor to be considered, one bound up with the cellular or humoral constitution of the patient. If 100 mice are tarred, not every one will develop cancer. Selective breeding, in other words heredity, will affect the result to a marked degree. This is equally true of spontaneous cancer in animals. The susceptibility is not merely for or against cancer, but for one particular kind of cancer, in one particular organ, a susceptibility which is transmitted in the genes of the chromosomes from one generation to another. And why does methylcholanthrene produce cancer when implanted in the brain of one mouse, but when removed later and implanted in the brain of another mouse it may fail to do so, yet when the same crystals from the brain of the second animal are introduced into that of a third mouse, cancer may again develop? Here we encounter individual resistance to cancer, as in the case of the smoker who consumes countless thousands of cigarettes in the course of a long lifetime, yet never meets the end he so justly deserves. And what have we to say regarding the demonstration by Zimmerman and his colleagues that the implantation of methylcholanthrene in the brain of mice which subsequently develop a neoplasm is accompanied by

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the appearance in the cytoplasm of great numbers of virus-like particles, which vanish as neoplasia develops? And to which of the various agents I have mentioned do we attribute the increase in frequency of carcinoma of the pancreas, and the drop in the death rate of carcinoma of the stomach to less than half in the past 30 years? There must be a reason, and if we knew that reason we might be able to do something about it, but unfortunately it remains an enigma.

An interesting sideline in the study of causation is the history of the discoveries which later proved to be wrong. The single example of yellow fever must suffice for purposes of this discussion. Leaving out the innumerable theories, we may note that in 1913 Seidelin published a paper illustrated by the most convincing colour plates showing that the disease was caused by a protozoal parasite—a piroplasma resembling the malaria parasite. Large numbers of the red blood cells contained minute bodies, which appear to have been merely artefacts. In 1915 Noguchi declared that the disease was due to a spirochete, a pardonable mistake, as the clinicians misled him by wrongly diagnosing as yellow fever cases which in reality were examples of Weil's disease. It was only in 1927 that the true cause of the disease was shown to be a filterable virus.

So far I have not referred to sex, for which I must apologize. What part does sex play in diseases? Why are thromboangiitis obliterans and polyarteritis nodosa so much commoner in the male, while disseminated lupus and Takayashu's disease or young female aortitis are so much commoner in women? I do not know. But surely this must involve cause and effect. We know the what, but not the why.

And genes: Not so long ago we never heard of them in relation to disease. Now they are used to explain everything that is not blamed on allergy or autoimmunity.

And finally, we should not neglect to consider the doctor as a causal agent. In fear of the public we seek refuge in another mystic word, iatrogenic, trusting that the patient will not consult a medical dictionary and find that "iatros" is Greek for physician and "genetic" means produced by. Unfortunately what is powerful for good may also be potent for evil, as is so agonizingly evident in the case of radiation therapy.

Although so much of the endeavour of scientific medicine is directed to the discovery of causes, and such discovery is necessary for the true understanding of a disease, it is of course true that there is no necessary connection between knowledge of the cause and ability either to cure or prevent disease. If Jenner had waited for the discovery of the cause of smallpox, or Pasteur for the cause of rabies, before applying the principle of protective vaccination, theirs would not be the great names they are in medicine. The cause of tuberculosis was discovered in 1882, but we had to wait till 1944 for effective treatment. Knowledge of the cause of malignant disease will not necessarily prove a weapon in the war against the scourge, although I would like to know why cancer is so common in the stomach and colon, yet so rare in the adjoining duodenum and ileum. This does not lessen the truth of the statement that knowledge of causation is one of the most valuable prerequisites for the mastery of disease. Without that knowledge the most grotesque mistakes are possible, as we can see from even very recent medical history. Perhaps those who follow us will look back on our ideas of the causation of atherosclerosis, eclampsia, chronic arthritis, and malignant disease with even greater astonishment.

I have probably succeeded in confusing you as much as I myself am confused, but I trust that I have made it clear that there is no more challenging problem in medical science than the intriguing but perplexing subject of causality. Finding out the "what" in disease is not too hard, but when we come to the "why"—ah, there's the rub. If only we could have listened to Alexander Gibson discussing this problem, which would have appealed to him by reason of its combination of the philosophical with the practical, how much more we would have learned!

40 Arjay Crescent,
Willowdale, Ont.

PAGES OUT OF THE PAST: FROM THE JOURNAL OF FIFTY YEARS AGO

A VERY SAD SIGHT

Last Sunday I managed to walk to Furnes. It had been shelled the day before and there was no telling at what moment the Germans might begin again. The town was not altogether deserted, though on the road there we passed refugees in various kinds of delapidated vehicles and little carts drawn by dogs. It is extraordinary that so many of the poor inhabitants stay there when they might easily flee away, and should do so. In the little shop where we got some post cards, the woman told us that she just escaped down into the cellar when the shells began to fall. We saw bags of straw and sand, placed in front of the cellar windows all along the streets as a protection against the flying metal or fragments of stone. Happily the fine buildings in the "Grand-Place" seem to have been untouched. But nearly all the windows in the town are broken and some of the houses completely ruined. It was all a very sad sight.—T. A. Malloch, *Canad. Med. Ass. J.*, 5: 357, 1915.