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SIMPLICITY - THE KEY TO FRUITFUL MEDICAL RESEARCH

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ABSTRACT

Medical research is here divided into two broad categories. The great majority of research is "complex" and includes all studies of intricate body mechanisms. A minority of research is "simple" and deals mainly with direct relationships between human environmental or life-style factors and disease incidence (or with analogous studies on animals). In addition, it includes studies of simple body mechanisms. Examples are provided to demonstrate that most of our medical knowledge of practical benefit derives from simple research. This is particularly the case in the area of prevention.

INTRODUCTION

This century has seen stupendous advances in all areas of science and technology. These advances generally share two features: they generate a momentum of their own and are mostly considered intrinsically beneficial.

This phenomenon is manifested in medical research as much as anywhere else. The prevailing climate has therefore led medical researchers into evermore complex and sophisticated forms of investigation. Intellectually, this has been highly rewarding. Over recent decades a vast amount has been learnt concerning brain function, molecular genetics, endocrinology, carcinogenesis and so forth. However, the making of great strides in medical knowledge is altogether different from actually achieving success in the war on disease. This is seen in medicine's poor track record over the last 30 years with respect to most of the degenerative diseases (cancer, cardiovascular disease, arthritis, obesity and so forth).

COMPLEX AND SIMPLE RESEARCH

Medical research (using the term in its widest meaning) is here divided into two broad categories: complex and simple. The overwhelming majority of investigations come in the "complex" category and include virtually all studies of intricate body mechanisms.

"Simple" research is defined as direct observations of the effects of environmental and lifestyle factors on various parameters of health in humans and animals. This includes the following types of investigation:

(1) Human studies relating environmental or lifestyle factors to disease incidence (or to closely linked factors such as blood pressure or blood glucose level). The strategy employed may be epidemiology, prospective and retrospective studies or experimental intervention.

(2) Investigations similar to the above but using animal models of human disease.

(3) Certain studies of body mechanisms are included but only when they are clearly simple as, for instance, the effect of various foods on the pH of teeth plaque or of fibre on colon motility.

The rationale for the terms complex and simple lies both in the degree of complexity of the research itself and also in the interpretation of the data.

Which type of research has been of greater value? The successes of complex research have been largely confined to improving our understanding of body processes in health and disease. Relatively little of practical use has been learnt. On the other hand whereas only a small proportion of research conforms to the above definition of simplicity, it has contributed the large majority of that data directly relevant to the management of disease, particularly in the area of prevention. In reaching this conclusion the author has been greatly influenced by the writings of Cleave (1-3).

Many would argue that only by complex research into the intricate details of body functions can we gain an overall picture of disease processes and that only then can we succeed in combating disease. Such an argument has inherent flaws. In most cases body mechanisms are so complex that it will take many decades to comprehend them properly.

The problem may be likened to an underground cave system of such vastness that as soon as one tunnel is charted, two or three new ones are discovered. Thus complex research is

generally a very long-term (multi-decade) saga. Simple research, however, has on innumerable occasions produced useful data in the short-term.

Another problem with complex research is that even when all the information is finally assembled, to gain an overall picture of a disease process may necessitate integrating so much information as to be simply self-defeating (human arrogance will normally reject this argument).

Examples will now be presented of the superior value of simple research in producing information of practical use in medicine.

CANCER

Only a small fraction of cancer research has consisted of simple investigations into factors involved in cancer etiology (4). However, those investigations have contributed a large part of our useful knowledge.

For instance, findings from epidemiology suggest that a high fibre-low fat diet is of considerable value in the prevention of colon cancer (5-7). Experiments using animal models of the disease point in the same direction (5). Similarly, certain nutrients, particularly selenium (8-11) and β-carotene (12), are thought to be strongly anti-carcinogenic. Once again the evidence derives from a combination of human studies (epidemiology and case-control) and tests using animal models of cancer.

In 1950 Doll and Hill (13) reported a survey among lung cancer patients in a search for possible causative factors. They discovered that the vast majority smoked cigarettes. Most useful research on lung cancer since that time has been little more than confirmation and extension of this finding. An extremely valuable development in recent years has come from simple studies of passive smoking (14).

In contrast to the above, complex research, such as gene regulation or the metabolism of the thousands of chemicals in tobacco smoke and their effects on the body, has been of minute value.

It was recently suggested that lung cancer is caused by radiation in tobacco smoke (15). Perhaps when this possibility is thoroughly explored and the exceedingly intricate interplay (as it will doubtless prove to be) between radiation, toxic chemicals and myriad other factors finally unravelled, then we can at last appreciate the biochemical (or biophysical) reasons that smoking causes cancer. What preventive

opportunities that far off success will herald, we cannot predict. In the meantime, of course, we can simply curtail active and passive smoking.

SMOKING AND CORONARY HEART DISEASE

In its relationship with smoking coronary heart disease (CHD) exactly parallels lung cancer. While cigarettes have been convincingly established as a risk factor in CHD, the etiology remains unknown. On the other hand in vitro work (eg studies of arterial metabolism) have provided little but suggestions for further experiments.

DIET AND CHD

The role of dietary factors in CHD has been intensively studied for several decades. Despite a colossal effort employing complex research the fact is that diet, blood lipid control, atherosclerosis, thrombosis and clinical CHD cannot yet be plausibly integrated.

I (16) have recently argued that the epidemiology of CHD is more closely related to refined carbohydrates than to dietary fat. The reinterpretation of data along these and similar lines is more likely to yield the required answers than further complex research.

ORAL CONTRACEPTIVES

The possible health hazards of oral contraceptives have been intensively investigated. Simple comparisons between users and non-users of the drug have provided the vast majority of the useful data (17). Complex research, meanwhile, has been of minor help.

OBESITY

The huge research effort into carbohydrate and lipid metabolism and their control has given us precious little of practical benefit in the prevention and management obesity. Conversely, the hypothesis of Cleave (1-3) concerning refined carbohydrates and the epidemiological evidence of Burkitt, Trowell and others (18) concerning a Western diet are of immense importance. Observations on the spontaneous obesity induced in rodents by a high fat diet (19) and by a "cafeteria" - type diet (20) have also been profitable.

LEAD POLLUTION

There are two approaches to the problem of lead and health. Virtually all useful information has come from examining relationships between environmental exposure, body lead burdens and toxic effects. Very little has been gained form detailed studies of the mechanisms by which these effects are induced.

WHEN SHOULD DISEASE MECHANISMS BE EXAMINED?

In the great majority of cases an attempt to unravel a disease mechanism is an immensely complex task. However, occasionally the reverse is true. Considerable success has been achieved in unravelling the etiology of osteoporosis, diverticular disease (2,21), tooth decay and peptic ulcers. This has been possible because the diseases themselves are sufficiently simple so that simple research suffices to understand them. In these cases examining disease mechanisms is fully warranted since it confirms that the correct causative agents have been identified. It may also help suggest how (other than by merely removing these agents) the disease might be prevented. The only reason these arguments do not apply to complex research is because the fruits of success almost invariably remain tantalisingly out of reach.

Of course, in advance of an investigation one can never be sure whether a disease problem will prove to be complex or simple. This merely emphasises the importance of devoting a certain fraction of research work towards disease mechanisms

PREVENTION VERSUS TREATMENT

The benefits of simple research pertain mainly to the prevention of disease rather than its treatment. On the other hand complex research is mainly of relevance as a means to develop improved treatments. In particular, most modern drug research is based largely on complex research. Its applicability is found almost entirely in the area of treatment, seldom in prophylaxis.

RESEARCH NEEDS

Based on the aforesaid arguments medical researchers should de-emphasize test tubes in favour of whole humans and animals.

A major problem with prospective studies is that insufficient sample size prevents the identification of factors strongly associated with uncommon diseases or weakly associated with common ones. This problem could and should be overcome by conducting prospective studies on a much larger scale than hitherto.

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