CANCER AND CAUSATION*

BY

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It is surely a good sign that Mr. A. H. B. Kirkman⁵ should express the profound dissatisfaction of a large majority of the medical profession with the mass of contradiction and the confusion of ideas that represent the cancer problem, so-called. It is only natural that cancer research should believe that it understands the problem and is on the way to giving the solution, whereas biology, if asked, might disagree most emphatically. That biology has the final say in the matter ought not to surprise, for what is cancer if not a manifestation of life and, therefore, a strictly and entirely biological phenomenon, as inevitable and *natural* in certain conditions as embryonic development and physiological form and function in certain others? But biology shows little or no interest as yet, and we must shift for ourselves as best we can. This is my excuse for stating my opinions. I speak for myself, of course.

MALIGNANCY

As biology distinguishes between genesis of the organism and of every organ and tissue, and subsequent differentiation of the physiological characters of each, so should we distinguish between causation and birth of a cancer, and subsequent development of its proper characters. Of these malignancy is the most conspicuous and important for us. I have nothing to say of malignancy except this. It is clearly a physical sign and symptom of that form or upset of metabolism which is known as cancer, and in no sense of the word a "cause"; it is a problem of growth like that of all forms of physiological growth; and it is too much to expect that it will be solved before these by scientific methods. But all this is really of minor importance for the medical profession, for, prevent formation of cancer, and malignancy will automatically cease to trouble. Our most urgent concern is with causation.

CAUSATION IN THE LIVING ORGANISM

As we ask, so shall we be answered; and even the most scientific methods of observation and experiment scientifically used will not answer unscientific questions. We are, somewhat impatiently, clamouring to be told the "cause" of cancer, but forget that biology does not pretend to explain the "cause" of life. Are we not asking the wrong question, or, maybe, the right question in the wrong form? Do we not perhaps understand the principles of tumour formation better than we know?

Clearly our first concern is to understand the meaning of the word causation in the living organism. The *cause* of a phenomenon is, of course, the factor, or factors, necessary for its being. Now, every somatic character whatsoever ("physiological" and "pathological") is acquired as a *reaction* of the organism to a *stimulus*. Nothing happens without both: the stimulus and the reaction, I repeat. Both are equally necessary for the existence of the character, but not therefore for the form—the essential nature—of the character. This can be illustrated better by a homely example than by pages of philosophical argument: If I kick a log, I stub my foot; if I apply the same kick to a small child, he howls; if to a man bigger than myself, he knocks me down—or, should he be a bigger bully than I, runs away. Again, should I tender a coin instead of a kick, the response will be another in all, though still varying from case to case. This means that the same stimulus is followed by very different effects. The stimulus simply induces a response. But the form of the response or reaction is produced by the object stimulated: in scientific language, by the constitution—that is to say, the physico-chemical composition—of the organism. Not only will the same stimulus

induce different reactions in different individuals, but in the same individual at different times (provided his constitution be modified by interim reaction). And a moment's thought will show that *diverse stimuli will induce the same reaction*.

Perhaps the most important points are these: We cannot predict the form of the reaction except from previous knowledge of the organism; it is safe to kick a known coward, but not a stranger of equal bulk. Again, why diverse stimuli of totally different origin and composition induce the same reaction, whereas others, though closely related, do not, is indeed a mystery of life: mercifully it is no more the concern of cancer research than of biology, which, wisely, never asks the question "Why?" That they induce it is simply a matter of experience. How they induce it can only be explained, with present knowledge, with the not very satisfying statement that the organism reacts in the only way it can, the way it must, the way it is made. The biological sciences are in no better case.

CAUSATION OF CANCER

It follows of logical and biological necessity that the *cause* of cancer is a reaction of the organism to stimulation, and this regardless of whether the stimulus be always the same or whether it be one of many interchangeable stimuli, as it appears to us. As everywhere in biology, the "cause" is not so much the nature and composition of the stimulus or stimuli as the nature and composition of the reacting organism. When cancer is seen as a biological phenomenon, the principle of its causation is as clear and distinct as that of every other manifestation of life.

To the best of my knowledge Morley Roberts⁶ was the first to illuminate pathology by applying the biological conception of causation to cancer fifteen years ago, when he says: "If it is then seen that there is no invariable single antecedent to malignancy, it must be admitted that there are many exciting 'causes,' of which x rays are but one. If such is the case, it follows logically that it is in the tissues concerned, their nature and relationship, that the true cause must be found." He thus shows cancer research how to take "a definite view of malignancy as a natural disorder and one only too likely to occur in such a construction as the mammalian body."⁶ He has developed this biological conception of cancer.⁷ Small wonder that five of those who see with him that the living body is really and truly alive should mark their appreciation of his insight.

ACCEPTED VIEWS

Cancer research, however, when not obsessed with the notion that cancer is "caused" by constitution alone (for example, a chromosomal mutation or malformation), persists in the vain—since philosophically unthinkable—idea that the composition of the stimulus accounts for the nature of the reaction and therefore the character. Naturally failing to "explain" how diverse stimuli "produce"—one effect, it too often hopes to find one "cause" behind—that is to say, instead of them all, conceived as a necessarily invisible "virus" for want of a better. Although no reasonable human being will deny that one or more forms of cancer may easily be induced by one or more ultramicroscopic living organisms, to extend the notion to all cancers is, with present knowledge, an offence against the principle of economy of hypothesis, based upon a logical fallacy.

KNOWN STIMULI

It is hard to get away from the fact that chemical compounds of diverse composition and origin, x rays and other forms of radiant energy without "chemical composition" at all, visible animal parasites, etc., are as surely followed by cancer as infancy by old age. Experimental pathology can claim with just pride that for tar cancer at all events it has demonstrated the steps in formation and subsequent development of a malignant tumour with the same degree of precision and complete-

* Received for publication February 14th, 1935.

ness and with the same method as embryology for the liver (see Deelman³). When allowance is made for differences in individual susceptibility—that is, constitution, reduced to a minimum in “pure strains”—pathology can assert, with experimental embryology, that the result of applying tar to the skin of a mouse “is just as definitely causally determined and predictable as the result of mixing two known reagents in a test-tube,” if I may quote Huxley and de Beer.⁴ Verily, the “cause” of tar cancer is as fully known and understood as the origin and development of the liver. Nay, better: for is not pathology immeasurably favoured above embryology, and cannot we see, smell, handle, weigh, and analyse the stimulus by the ton? And cannot we reproduce the cancer at will?

Moreover, we owe to Kennaway and his school² exact knowledge of the chemical composition of the “carcinogenic agent” in tar, and are thus able to think in terms of “exact” science. More important still, he¹ has quite recently told us the structure of another active compound obtained by simple chemical means from bile, thereby establishing “a direct relationship between the carcinogenic compounds and some normal constituents of the body,” and opening up vistas of endless possibilities.

CONCLUSION

Thanks to cancer research, our knowledge of stimuli that induce cancer, though very far from complete, is sound, more extensive than we are prepared to see, and increasing apace. Knowledge of the reaction, since unlooked for, is all to come. And knowledge of the changes

in physico-chemical composition of the organism, the very essence of cancer, is naturally no greater in pathology than in physiology, embryology, and biochemistry. All would be well if cancer, like an infection, were induced by a single stimulus, and few would suspect that they know and understand no more than by far the easier half of the “cause.” But cancer happens to be induced by diverse, interchangeable stimuli. Hence the confusion, when biological principles are ignored and we forget that we are alive. But to say with those who, knowing least, shout loudest, that cancer is veiled in mystery—mystery, mind you, deeper than that surrounding biology, every simple physiological reaction and every fully “explained” pathological lesion—is, frankly, to say the thing that is not.

SUMMARY

Cancer is a biological problem. Like every biological problem it is a philosophical problem too, not to be solved with a logical fallacy.

REFERENCES

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- ⁴ Huxley and de Beer: *The Elements of Experimental Embryology*, Cambridge, 1934.
- ⁵ Kirkman: *British Medical Journal*, February 2nd, 1935, p. 230.
- ⁶ Roberts, Morley: *Warfare in the Human Body*, London, 1920.
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VOLUNTARY BLOOD DONORS ASSOCIATION

REUNION DINNER

The second annual dinner of the Voluntary Blood Donors Association took place in London on March 21st, when two hundred members and their friends assembled under the chairmanship of Lord Horder.

Lieutenant-General Sir Harold Fawcus read greetings from the patron, the Duke of York, and the president, Sir Arthur Stanley. Mr. Geoffrey Keynes, in proposing “The Service,” recalled his experiences of blood transfusion in the war, when he was among the first to take advantage of the new technique. Applying it to a number of men in what was known as the “moribund tent” at the casualty clearing station, he was astonished to find how many lives were saved. Some difficulty was experienced in finding donors until fourteen days’ leave was attached to this service, whereupon “the whole British Army volunteered.”

Mr. P. L. Oliver, head of the British Red Cross Transfusion Service, was also reminiscent. The service began in November, 1921, on the request of the secretary of King’s College Hospital for a blood donor, and it had grown until, in 1934, the number of calls in London was 3,855, and already in 1935, although not three months had passed, there had been over a thousand calls. In a recent week the number of calls had averaged fifteen a day. The number of donors on the roll was 1,881, and, including in the computation the new recruits, each of them had given on the average seven transfusions. One donor had given fifty-six transfusions, and had been the means of saving forty lives. Mr. Oliver urged that in future every patient entering the hospital for whom there was the slightest possibility of this service being required should be grouped as a matter of routine, in the same way as temperature and pulse rate were taken. That would save these many midnight calls for a universal donor on the ground that there had not been opportunity to group the patient. The suggestion had, indeed, been made that everybody should be grouped at birth, the grouping being tattooed on some inconspicuous part of the body. It should certainly be made a regulation at the infant welfare centres throughout the country that every expectant mother should be grouped, and, if possible, the husband or a relative should also be grouped in view of an emergency.

The toast of “The Visitors” was proposed by Mr. D. P. Kennedy, deputy chairman of the association, and responded to by Professor J. W. Eyre; and Dr. A. M. A. Moore proposed “The Ladies,” a toast acknowledged by Sister Linstead, the first donor of the service. Dr. H. F. Brewer, medical officer of the service, mentioned a recent observation of 300 cases which had shown that, provided the donor did not serve more than once in three months, no harmful result occurred. About 20 per cent. of the donors had told him they had improved in health as a result of the service. An important step forward was the placing on the market of efficient grouping serums at a cheap rate. In reply to the toast of his health, which was proposed by Dr. R. G. Canti, Lord Horder praised this highly altruistic public service. He had made a calculation that, supposing the average amount of blood given by the donors at each transfusion to be 15 oz., no fewer than 323 gallons had been given during the past year. He thanked the donors for a service which had been done to medicine as well as to the patients concerned.

ERADICATION OF THE BED-BUG

At the request of the Ministry of Health the Medical Research Council has undertaken to promote further investigations into the health problem caused by the infestation of houses by the bed-bug, and has appointed the following special committee to advise and assist in this work:

Professor J. C. G. Ledingham, F.R.S., director of the Lister Institute, chairman; Professor P. A. Buxton, London School of Hygiene and Tropical Medicine; Mr. C. S. Elton, University of Oxford; Mr. C. R. Kerwood, Ministry of Health; Dr. John Macmillan, medical officer of health, Woolwich; Dr. G. W. Monier-Williams, Ministry of Health; Professor J. W. Munro, Imperial College of Science; Dr. P. G. Stock, Ministry of Health; Dr. R. E. Stradling, Director of Building Research; Mr. A. W. McKenny Hughes, British Museum (Natural History), secretary.

On the recommendation of this committee grants have been made by the council for research under the direction of Professor Buxton into the natural history of the bed-bug, with reference to the conditions of its viability, and for research under the direction of Professor Munro into chemical methods for its destruction.