

CORRESPONDENCE

Definition of Cancer Research

SIR,—May I applaud the sentiment expressed in the article "What Price the Crusade for Cancer Research" (*Nature New Biology*, 230, 225; 1971) that "the pendulum of financial support should not be allowed to swing so far that cancer research becomes a synonym for the study of RNA viruses". On the other hand I am disturbed that the general theme appears to be merely that DNA viruses should also be studied. Perhaps no one is really advocating that the field should be so narrowly defined but it is evident that, because of so-called abuses, the range of projects supported by cancer research funds is to be severely restricted using relevancy as a basis for selection. As the *Nature* article implies, cancer research cannot succeed by virtue of its own advances alone: the more limited its outlook becomes, the more significant is this statement. A restrictive policy is, at best, acceptable only if adequate funds and facilities are available elsewhere so that all lines of research (and particularly those concerned with new concepts and fundamental issues) can still be accommodated. The present financial situation, however, is causing a general limitation on research: it is therefore essential to ensure that the studies supported by cancer research funds are those most likely to advance our comprehension of neoplasia and methods of treatment of the disease and hence that they are founded on correct concepts. It is therefore necessary, especially under present circumstances, to question the reasons behind, and the advisability of, the isolationist policy and the scientific grounds on which project selections may be made.

Abuse of funds arises primarily from the attitudes and motives of the clinicians and scientists concerned rather than the nature of their work. If it is an abuse to utilize or supply funds for fundamental studies or projects not directly associated with human tumours, then it is also an abuse to continue to pursue or support, say, a clinically orientated study which has failed to yield an effective means of therapy or is no longer likely to provide further and significant insight into the problem. Many studies based on conventional views are to continue despite the fact that they will probably do no more than amass relatively trivial facts and

may even cloud the real issues. The relevancy of a project is impossible to decide objectively (*cf* Poynter¹) as is its potential value, but surely it is better to attempt to apply the latter criterion if one must curtail projects. Again, novelty should be preferred to further variations on an outworn theme.

To my mind, anyone who proposes that the bulk of funds should be channelled into just a few lines of research is either displaying considerable (but unwarranted) faith or he is failing to acknowledge the complexity of the problem and the multifarious facets of the disease: for example, the many different forms in each of the many susceptible species; the extreme range in both the degree of malignancy and proliferation rates of tumour cells; the large number and variety of oncogenic agents (spontaneous initiation cannot be discounted); the fact that, in general, the individual properties of cancer cells (for example, glycolysis, respiration, proliferation rates, invasiveness) are not, in themselves, abnormal.

Failure to resolve a problem in the face of intensive and extensive research could indicate that the basic concepts are incorrect or that they are too rigid to allow a solution. It is possible that the malignant transformation reflects not one specific intracellular lesion but a change in the overall pattern of behaviour of the biochemical systems of the cell. Much of the research in this field appears to be based on the view that a genetic defect is involved (for example, a mutation, virome incorporation) although so far the evidence does not support this view. Theoretical considerations²⁻⁶ indicate that a given pattern of active genes or enzymes can be consistent with more than one stable metabolic state and hence it seems feasible that neoplasia is a result of transitions between conjugate states of this kind, probably affecting one or more biochemical sub-systems. In principle, such transitions could be induced by a variety of disturbances including, but not limited to, genetic changes. Reversal of a transition would not necessarily follow removal of the stimulus or be brought about by the processes of mitosis and cell division: hence the altered pattern of behaviour could be transmitted to daughter cells. Only if it were known that one particular type of agent alone induces all oncogenic transformations should attention be focused so dominantly on the properties of the agent:

since available evidence contradicts this kind of uniqueness, it would seem that we ought to concentrate attention on the response of the cell.

In addition to such considerations it is evident that we must understand the dynamics of cell biochemistry (normal or abnormal) if only to account for the cell proliferation features of this problem. Elsewhere⁷⁻⁹ I have briefly discussed, in general terms, the possible significance of cellular periodicities and suggested that the malignant transformation could reflect changes in the frequencies, phasings and so on of rhythmic biochemical variations (including supporting experimental data from a project now terminated as a result of a relevancy decision¹⁰⁻¹¹). Harington¹² has since considered a specific system in this light, *viz.* the Rapkin¹³ cycle involving thiol-disulphide rhythm, in relation to the cytokinetic aspects of malignancy. More recently, Sel'kov¹⁴ analysed the behaviour of the latter mathematically and decided that the thiol-disulphide system could exhibit two stable steady states each of which could be oscillatory. Transitions between these states might thus result in a change in the frequency of oscillation and hence altered proliferation rates. Moreover, Sel'kov points out that such a change, by virtue of the activation/inhibition action of thiols on various enzymes, could be expected to modify glycolysis, respiration etc., processes indicated by Warburg^{15,16}, Weinhouse¹⁷ and others as being concerned with the malignant transformation. I would like to take this view one stage further by pointing out that other cellular components (for example, metal ions) could, in principle, exhibit similar characteristics but be to some extent independent of the sulphhydryl system. If this is so, then the overall behaviour of all these systems and their pattern of interaction could play a major part in determining the properties (and hence the normality or abnormality) of cells.

Clearly, if such views are basically correct, then it is possible to hinder advances by concentrating effort on a few special oncogenic agents or on a few narrowly defined and conventional areas of research. The unenviable task of those dispensing funds is very great: the onus is on them to make the right decision and they therefore deserve to hear the varied opinions of more of those actively engaged with the resolution of this problem. I would thus like to suggest

that an open forum be made available in your journal for the expression of opinions from all parties concerned. Incorrect decisions made at this stage could lead to even more marked and warranted charges of abuse being made at some later date.

Yours faithfully,

D. A. GILBERT

Goodmayes,
Essex

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- ¹⁵ Warburg, O., *Metabolism of Tumours* (Constable Press, London, 1930).
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British Diary

Wednesday, June 2

Some Psychiatric Aspects of Murder (5.30 p.m.) Dr Denis Leigh, University of London, at the Institute of Psychiatry, Maudsley Hospital, De Crespigny Park, Denmark Hill, London SE5.

Friday, June 4

Duodenal Ulcer—a Continuing Challenge (11 a.m.) Mr C. Wastell, University of London, at the Royal Postgraduate Medical School, Hammersmith Hospital, Du Cane Road, London W12.

Monday, June 7

The Role of Church's Thesis in Intuitionistic Mathematics (5.30 p.m.) Dr C. Cellucci, British Society for the Philosophy of Science, in the Joint Staff Common Room, University College London, Gower Street, London WC1.

Reports and Publications

not included in the Monthly Books Supplement

Great Britain and Ireland

- The Exploitation of Biological Signals. By Professor B. McA. Sayers. (Inaugural Lecture, 27 January 1970.) Pp. 123-156. (London: Imperial College of Science and Technology, 1971.) 40p. [54]
- British Launderers' Research Association. Annual Report 1969/1970 (Jubilee 1920/1970). Pp. 32. (London: British Launderers' Research Association, Hill View Gardens, NW4, 1971.) [54]
- The Gardeners' Sunday Organization. Gardens to Visit. Pp. 64. (Dorking: Gardeners' Sunday, White Witches, Claygate Road, 1971.) 7½p. [54]
- Ministry of Agriculture, Fisheries and Food. Agricultural Chemicals Approved Scheme. Approved Products for Farmers and Growers 1971. Pp. 160. (Pinner, Middx.: Ministry of Agriculture, Fisheries and Food, 1971.) [64]
- British Standards Yearbook 1971, complete to 31 December 1970. Pp. xxxii+823. (London: British Standards Institution, 1971.) £1.50 net. [64]
- Discovery Reports, Vol. XXXV, pp. 179-198: On *Ithea magalhonica* (Apstein) (Tunicata: Salpidae) and *Ithea racovitzai* (Van Beneden). By F. Foxton. (London: Cambridge University Press, 1971.) £1.80. \$5. [64]
- The British Petroleum Company Limited. Annual Report and Accounts for 1970. Pp. 60. (London: B.P., 1971.) [74]
- University of Oxford. Seventh Annual Report of the Delegates of the Science Area for the year ending 31 July 1970. Pp. 133. 50p. Ashmolean Museum—Report of the Visitors 1970. Pp. 66+21 plates. 75p. (Oxford: The University, 1971.) [74]
- Chatham House, and PEP. European Series No. 76: Agricultural Policy and the Common Market. By John Marsh and Christopher Ritson. Pp. 199. (London: Chatham House, and PEP, 1971.) £1.25. [74]
- Royal Scottish Museum: A Catalogue of Fossil Vertebrates in the Royal Scottish Museum, Edinburgh. Part 1: Actinopterygii. By I. G. C. Henrichsen. Pp. ix+102. (Edinburgh: Royal Scottish Museum, 1970.) [74]
- Biobits and Doré-Smith Atomunits: Principles of Model Construction. By Ivor Smith, Margaret J. Smith and C. Frank Doré. Pp. 48. (London: Capital Biotechnical Developments, 1971.) 40p. [74]
- The Macaulay Institute for Soil Research. 1969-1970 Annual Report. (No. 40.) Pp. 80. (Craigiebuckler, Aberdeen: The Macaulay Institute for Soil Research, 1971.) [84]
- Potato Marketing Board. Sutton Bridge Experimental Station—Annual Review—1970. Pp. 32. (London: Potato Marketing Board, 1971.) [84]
- Rowett Research Institute. Annual Report of Studies in Animal Nutrition and Allied Sciences, Vol. 26, 1970. Pp. 117. (Bucksburn, Aberdeen: Rowett Research Institute, 1970.) 70p; \$1.70. [84]
- University of London. University College Annual Report, 1969/1970. Pp. 145. (London: University College London, 1971.) [84]
- Building Research Station Digest, No. 53: Project Network Analysis. Pp. 7. (London: HMSO, 1971.) 5p. [84]
- Unilever. Report and Accounts 1970. Pp. 48. (London: Unilever, Ltd., 1971.) [84]

Other Countries

- US Department of the Interior: Geological Survey. Professional Paper 306-D: Geology and Palaeontology of Canal Zone and Adjoining Parts of Panama—Description of Tertiary Mollusks (Gastropods: Eulimidae, Marginellidae to Helminthoglyptidae). By W. P. Woodring. Pp. iii+299-452+plates 46-66. \$2.25. Professional Paper 614-D: Pegmatitic Trachyandesite Plugs and Associated Volcanic Rocks in the Saline Range—Inyo Mountains Region, California. By Donald C. Ross. Pp. iii+29+1 plate. Professional Paper 642: Miocene Gastropods and Biostratigraphy of the Kern River Area, California. By W. O. Addicott. Pp. iv+174+21 plates. \$2.25. (Washington, DC: Government Printing Office, 1970.) [24]
- The Federal Government and Research Museums and Libraries of the Future. By H. William Koch. Pp. 10. (New York: American Institute of Physics, 1971.) [54]
- National Science Foundation. Federal Funds for Research Development and Other Scientific Activities, Fiscal Years 1969, 1970, and 1971. (Surveys of Science Resources Series, NSF 70-38, Vol. XIX.) Pp. x+264. (Washington, DC: Government Printing Office, 1971.) \$2. [54]
- Information Processing Letters, Vol. 1, No. 1, February 1971. Pp. 1-34. Published bi-monthly. Subscription price per volume Hfl. 90; \$25. (Amsterdam: North-Holland Publishing Company, 1971.) [54]
- International Union for Conservation of Nature and Natural Resources. IUCN Eleventh Technical Meeting, New Delhi, India, 25/28 November 1969. Papers and Proceedings, Vol. 5. Sixth Session: Landscape Planning Commission. 'Creative Conservation in an Agrarian Economy. Pp. 97. (Morges, Switzerland: International Union for Conservation of Nature and Natural Resources, 1971.) [54]
- Cimbebasia. Ser. A, Vol. 1, No. 7: Report on a Small Collection of Fishes from the Kunene River Mouth. By Mary-Louise Penrith. Pp. 165-176. Ser. A, Vol. 1, No. 8: Some Decapod Crustacea from Northern South West Africa, including a New Species of *Hippolyte*. By Brian Kensley. Pp. 177-188. Ser. A, Vol. 1, No. 9: The Constitution of the Intertidal Fauna of Rocky Shores of South West Africa, Part 1. Lüderitzbucht. By M. L. Penrith and B. F. Kensley. Pp. 189-240. Ser. A, Vol. 1, No. 10: The Constitution of the Fauna of Rocky Intertidal Shores of South West Africa. Part 2. Rocky Point. By Mary-Louise Penrith and Brian Kensley. Pp. 241-268. (Windhoek, SWA: State Museum, 1970.) [54]
- US Department of the Interior: Geological Survey. Bulletin 1322: Stripping-Coal Resources of the United States—January 1, 1970. By Paul Averitt. Pp. iv+34. \$0.25. Bulletin 1324-A: Changes in Stratigraphic Nomenclature by the US Geological Survey, 1969. Pp. iii+41. \$0.30. (Washington, DC: Government Printing Office, 1970.) [54]
- Smithsonian Contributions to Zoology, No. 80: Freshwater Triclad (Turbellaria) of North America. IV: The Polyparyngeal Species of Phagocata. By Roman Kenk. Pp. 17. \$0.30. No. 86: A Revision of the Genus *Zenoria* Mulsant (Coleoptera: Coccinellidae). By Robert D. Gordon. Pp. 22. \$0.35. (Washington, DC: Smithsonian Institution Press, 1970 and 1971. For sale by US Government Printing Office.) [54]
- Carnegie Institution of Washington. Year Book 69, 1969-1970. Pp. x+767. (Washington, DC: Carnegie Institution of Washington, 1971.) [54]
- Annals of the New York Academy of Sciences. Vol. 171, Article 3: Metabolism and Biological Functions of Polyamines. Edited by Edward J. Herbst and U. Bachrach. Pp. 691-1009. (New York: New York Academy of Sciences, 1970.) \$26.50. [64]
- US Department of the Interior: Geological Survey. Water-Supply Paper 1965: Quality of Surface Waters of the United States, 1965. Parts 9-11: Colorado River Basin to Pacific Slope Basins in California. Pp. xiv+678. (Washington, DC: Government Printing Office, 1970.) \$3. [64]
- The Dental Care Program of the Los Angeles Hotel-Restaurant Employer—Union Welfare Fund—Summary Report of an Evaluation. By Jay W. Friedman. Pp. 46. (Bethesda, Md.: Dental Economics Section, Division of Dental Health, Bureau of Health Manpower Education, 9000 Rockville Pike, 1971.) [64]

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