

TABLE 1

| C57 strain mice  |  | Initial No. of mice | No. of sarcomas (at site of injection) |
|--|--|---------------------|--|
| <i>Materials tested</i>  |  |                     |  |
| Commercial cholesterol   |  | 43                  | 5                                      |
| 9 cholesterol-like compounds (cholesterylene, 7-dehydrocholesterol, etc.)            |  | 100                 | 0                                      |
| Cholesterol-rich fractions from mammalian (cattle) liver                             |  | 30                  | 0                                      |
| Commercial cholesterol + certain animal and vegetable oils                           |  | 60                  | 0                                      |
| " " + cod liver oil  |  | 10                  | 3                                      |
| " " + unsaponifiable fractions of human liver  |  | 20                  | 0                                      |
| " " + sesame oil   |  | 10                  | 1                                      |
| " " refluxed with KOH and alcohol  |  | 20                  | 0                                      |
| Unsaponifiable fraction of human bile and gall bladders (cholesterol content c. 90%) |  | 40                  | 1                                      |
| " " " cream (cow's milk) (cholesterol content c. 90%)                                |  | 10                  | 1                                      |
| " " " rat tumour tissue  |  | 15                  | 0                                      |
| Lard alone   |  | 10                  | 0                                      |
| Unsaponifiable fractions of human tissue (cholesterol content 90% and downwards)     |  | 227                 | 3                                      |
|  |  | 595                 | 14                                     |
| <i>Mixed stock mice</i>  |  |                     |  |
| Human liver, unsaponifiable fractions (cholesterol content 90% and downwards)        |  | 260                 | 3                                      |
| Unsaponifiable fraction of gall stones   |  | 10                  | 0                                      |
| <i>M.R.C. strain mice</i>  |  |                     |  |
| Commercial cholesterol   |  | 21                  | 2                                      |

The technique of testing was described in detail in the paper referred to above; in brief, the essential features were: (1) The material for test were dissolved in lard at 15 per cent concentration (except for the sesame oil experiment). (2) Injection in mice were made subcutaneously in the flank (0.1-0.4 c.c.) at fortnightly intervals; injections were suspended as long as a reservoir of material could be detected by touch. If groups of mice died early in the experiment, they were replaced so as to ensure that a satisfactory number of animals survived long enough in all tests.

The small number of solvent controls (10 mice) need cause no concern, for all the negative results with C57 mice (namely, 595 - 14 = 581) constitute the controls on the solvent (lard). More than 300 controls on lard have been carried out on mixed stock mice without producing a single sarcoma<sup>1,2</sup>. One must mention, however, that a closely allied species, the rat, behaves differently, for evidence is accumulating that it is liable to sarcoma production by the subcutaneous injection of a variety of fatty substances of animal and vegetable origin.

The latent periods for the different groups of tumours, that is, those produced by commercial cholesterol in lard only and those produced by the other preparations, show much overlap (Table 2).

TABLE 2. LATENT PERIOD OF TUMOURS IN TABLE 1 (MONTHS)

| Commercial cholesterol in lard | U.F.* of bile + lard | Commercial cholesterol + sesame oil | Commercial cholesterol + cod liver oil + lard | U.F. of human tissue fractions + lard | U.F. of cream + lard |
|--------------------------------|----------------------|-------------------------------------|---|---------------------------------------|----------------------|
| 11                             | 29                   | 14                                  | 20  | 18                                    | 13                   |
| 23                             |                      |                                     | 23  | 19                                    |                      |
| 18                             |                      |                                     | 25  | 19                                    |                      |
| 20                             |                      |                                     |   | 16                                    |                      |
| 22                             |                      |                                     |   | 12                                    |                      |
| 22                             |                      |                                     |   | 16                                    |                      |
| 23                             |                      |                                     |   |                                       |                      |

\* U.F. = unsaponifiable fraction.

The total production of sarcomas in mice at the site of injection by substances of biological origin is given in Table 3, which represents the chief results of experiments in progress in this Institute up to the time of writing<sup>1,2,3</sup>.

TABLE 3

| Material   | Total sarcomas |
|--|----------------|
| 1. Unsaponifiable fraction of cow's milk (experiments of Prof. E. L. Kennaway)   | 1              |
| 2. Unsaponifiable fraction of cream (cow's milk)   | 1              |
| 3. Commercial cholesterol  | 11             |
| 4. Unsaponifiable fraction of human tissues (liver, lung, kidney, muscle) and bile from cancerous and non-cancerous subjects | 31             |
| Ether extract (that is, saponifiable) of human cancerous liver   | 2              |
| 6. Ether extract (that is, saponifiable) of mouse mammary tissue   | 1              |

The foregoing data now suggest three possibilities: (1) That cholesterol is, in fact, a slow carcinogen, particularly in the presence of other facilitating lipids, and in the absence of inhibiting factors.

(2) That commercial cholesterol (cholesterol content high but uncertain, of the order of 98 per cent perhaps) contains a small amount of an unknown but potent carcinogen; and that cholesterol-rich fractions from human tissues (liver, lung, kidney and muscle), from cow cream, from cattle brain and spinal cord, and from human bile all contain, in addition to cholesterol, the unknown carcinogen.

(3) The operation of unknown factors (for example, important variations of susceptibility of the experimental mice).

This work was supported by grants-in-aid from the British Empire Cancer Campaign, the International Cancer Research Fund, the Anna Fuller Fund and the Jane Coffin Childs Memorial Fund for Medical Research.

*Note added in proof.* At the time of writing there are still a few surviving mice in the experiments described in the tables. Thus the total of tumours shown is a minimum figure and may have to be slightly raised when all the mice are dead.

<sup>1</sup> Hieger, I., *Cancer Res.*, **6**, 657 (1946).  
<sup>2</sup> Hieger, I., *Amer. J. Cancer*, **39**, 496 (1940).  
<sup>3</sup> Hieger, I., *Science*, **93**, 262 (1941).

## FORTHCOMING EVENTS

Wednesday, August 27—Wednesday, September 3  
 BRITISH ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE (at Dundee).—109th Annual Meeting.

Wednesday, August 27  
 In the Caird Hall, City Square, Dundee, at 8.30 p.m.—Sir Henry Dale, O.M., F.R.S.: "Science in War and Peace" (Presidential Address).

## APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the dates mentioned:

ASSISTANT PHYSICISTS (2) in the Radiotherapy Service, and an INSTRUMENT MAKER.—The Secretary, South Wales and Monmouthshire Joint Cancer Committee, County Hall, Newport, Mon. (August 30).

PRINCIPAL OF THE IPSWICH SCHOOL OF TECHNOLOGY.—The Chief Education Officer, 17 Tower Street, Ipswich (August 30).

LECTURER IN PHYSICS, and a LECTURER IN CHEMISTRY.—The Clerk to the Governors, South-East Essex Technical College, Longbridge Road, Dagenham (August 30).

RESPONSIBLE LECTURER IN PHYSIOLOGY (Senior Assistant)—The Principal, Chelsea Polytechnic, Manresa Road, London, S.W.3 (August 30).

UNIVERSITY LECTURER IN MATHEMATICS, with special qualifications in Statistics.—The Secretary, Appointments Committee of the Faculty of Mathematics, Trinity College, Cambridge (August 30).

ASSISTANT MASTERS in H.M. Dockyard Schools (one each at Portsmouth and Chatham)—The Director, Education Department, Admiralty, London, S.W.1 (August 30).

LIBRARIAN, and an ASSISTANT LIBRARIAN, at the Coventry Technical College.—The Director of Education, Council House, Coventry (August 30).

SENIOR ASSISTANT IN ELECTRICAL ENGINEERING in the Bournemouth Municipal College.—The Education Officer, Town Hall, Bournemouth (August 30).