themselves. There is no significance in an observer of an object "knowing that it was moving"; what he should have known was that it was moving or not, according to his choice.

HERBERT DINGLE.

Imperial College,
London, S.W.7.
March 27.

Production of Tumours in Mice by Deoxycholic Acid

J. W. COOK[1] pointed out that the sterols and bile acids contain in their molecules condensed carbon-ring systems to which are attached a side-chain in such a position that a new 6-membered ring can be formed so as to give the 1 : 2-benzanthracene ring system without molecular rearrangement or group migration. The bile acids of the higher vertebrates are all mono-, di-, or tri-hydroxy derivatives of cholanic acid, which compound can be obtained *in vitro* from sterols by degradation, and the principal bile acids bear the names of lithocholic acid (3-hydroxy-cholanic acid), deoxycholic acid (3 : 12-dihydroxy-cholanic acid) and cholic acid (3 : 7 : 12-trihydroxy-cholanic acid). J. W. Cook and G. A. D. Haslewood in 1934[2] showed that, in the formation of dehydronor-cholene from deoxycholic acid by the procedure of Wieland, such a ring-closure to the 1 : 2-benzanthra-cene ring system had actually occurred. Dehydronor-cholene gave on dehydrogenation the benzanthracene hydrocarbon methylcholanthrene, which was found to be strongly carcinogenic. Afterwards, Fieser and Newman[3] showed that methylcholanthrene could be obtained also from cholic acid, which is the chief acid of human bile, and the parent hydrocarbon cholanthrene was synthesized by J. W. Cook, G. A. D. Haslewood and A. M. Robinson[4] and shown to be carcinogenic.

The discovery that a carcinogenic compound could be obtained from deoxycholic acid led us to test for possible action of this kind the acid itself, which was applied in solution in a mixture of alcohol and benzene to the skin of 20 mice in the ordinary way. An epithelioma at the site of application developed in a single mouse in 776 days. The experiment was repeated upon, in all, 80 mice, of which some lived more than 800 days, but no more tumours were obtained. Afterwards, deoxycholic acid was in-jected in sesame oil into the right flank of 10 mice of mixed stock, of which 5 lived for more than 6 months. Of these five, three developed at the site of injection spindle-celled tumours of the type usually produced by carcinogenic compounds and were killed on the 351st, 355th, and 367th days. The tumours were regarded as malignant on histological grounds, but did not grow when transplanted into other mice of mixed stock. These mice had received 15 injections containing in all 70 mgm. of deoxycholic acid in 300 days. This is, of course, a large amount, and the time required for the development of tumours is long. However, the experiment was repeated using 10 mice of the strain C_3H which, of eight strains examined by Andervont[5], is placed first in the order of suscepti-bility to subcutaneous tumours induced by carcino-genic hydrocarbons, and of these mice one has now developed a spindle-celled tumour in 155 days (that is, a period less by 200 days than that required by the stock mice) after receiving a total of 28 mgm. in the course of six injections. These results confirm those of Vittorio Ghiron[6], announced at the Third International Cancer Congress at Atlantic City in September 1939, who says "Desoxycholic acid elicited transplantable subcutaneous fibro-sarcomas in a high proportion of the mice and rats injected. This is believed to be the first experimental production of malignant growths with a compound that exists under some conditions in the human body". We have not found any more detailed publication by Ghiron of his results.

Occasionally, tumours are produced in mice by sesame oil alone (W. U. Gardner, personal communica-tion to Dr. Hieger) but we have obtained negative results with many compounds in this solvent, and we do not think that the incidence of tumours re-corded above could be attributed to it. We have no evidence that deoxycholic acid can be converted *in vivo* into methylcholanthrene, but at the same time the slow action and large amount required of the acid, and the superiority of injection over external application, are compatible with conversion into some more active compound. Shear[7] obtained negative results by injection of deoxycholic acid, and cholic acid, *sub cutem* in mice, but a single injection only, in glycerol, was given. We are carrying out further experiments with deoxycholic and cholic acids.

Several other investigations in progress here are concerned with the liver in relation to carcinogenesis. Thus Dr. L. D. Parsons[8] has described the increased flow of bile in some tumour-bearing mice, and the use of bile in preparing cell-free filtrates from tumours; Dr. Hieger has confirmed the discovery of Schabad[9] that some extracts of human livers will produce sarcomas in mice, and is preparing these results for publication; and J. W. Cook[10] has described compounds (2 : 2′-azonaphthalene and its transforma-tion product 2 : 2′-diamino-1 : 1′ dinaphthyl) which have a specific action in producing malignant tumours of the liver.

We are indebted to the British Empire Cancer Campaign for a grant which has supported this work.

J. W. COOK.
E. L. KENNAWAY.
N. M. KENNAWAY.

Chester Beatty Research Institute,
Royal Cancer Hospital (Free),
London, S.W.3. March 31.

[1] Cook, J. W., and Kennaway, E. L., *Chem. and Ind.*, **10**, 521 (1932).
[2] Cook, J. W., and Haslewood, G. A. D., *J. Chem. Soc.*, 428 (1934).
[3] Fieser, L. F., and Newman, M. S., *J. Amer. Chem. Soc.*, **57**, 961 (1935).
[4] Cook, J. W., Haslewood, G. A. D., and Robinson, A. M., *J. Chem. Soc.*, 667 (1935).
[5] Andervont, H. B., Public Health Reports, **53**, 1647 (1938).
[6] Ghiron, V., Summary of Communications, 3rd International Cancer Congress, p. 116 (1939).
[7] Shear, M. J., *Amer. J. Cancer*, **36**, 211 (1939).
[8] Parsons, L. D., NATURE, **144**, 75 (1939).
[9] Schabad, L., *C.R. Soc. Biol.*, **124**, 213 (1937).
[10] Cook, J. W., NATURE, **145**, 335 (1940).

Some Effects of Salicylate on Plant Viruses

DURING an investigation into the effects of various anions on the precipitation of the paracrystalline solid phase of tobacco mosaic virus nucleoprotein (*Marmor tabaci*, var. *vulgare*, Holmes) from its solution in water, the salicylate ion was found to behave differently from other anions. For each salt there was found a critical concentration at and above which the virus was precipitated from solution in the form of spontaneously birefringent microtactoids or fibres. The white precipitate of virus nucleoprotein