insufficient evidence to warrant a clinical investigation of the efficacy of 'Viractin' in acute respiratory disease in man.

The 'Viractin' used was kindly provided by Dr. L. W. Byers, Department of Psychiatry and Neurology, Tulane University School of Medicine, New Orleans, Louisiana.

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¹ Leach, B. E., Hackman, P. E., and Byers, L. W., *Nature*, **204**, 788 (1964).

² *Lancet*, **6**, 36 (1965).

³ Buckland, F. E., and Tyrrell, D. A. J., *J. Hyg. Camb.*, **62**, 365 (1964).

⁴ Buckland, F. E., Bynoe, M. L., and Tyrrell, D. A. J., *J. Hyg. Camb.*, **63**, 327 (1965).

⁵ Hoorn, B., and Tyrrell, D. A. J., *Brit. J. Exp. Path.*, **46**, 109 (1965).

THE data presented by Drs. Walker and Tyrrell on their tissue culture and animal investigations of 'Viractin' confirm that this substance has no significant *in vitro* activity by the test systems used. Our similar results were reported in the first publication on this subject¹. We have another publication in the press giving further data on 'Viractin' in tissue cultures infected with adenovirus².

I realize that the preponderance of opinion is such that animal studies must precede clinical trials. This may be thought of more as an ethical rather than a scientific matter. It clearly involves a feeling that efficacy must be proved in some animal species or tissue culture before it can be investigated in man. It is my contention that this is not necessarily true, and this has been demonstrated with 'Viractin' to a limited extent in that the *in vitro* tests have been negative, but the clinical investigations have demonstrated a sufficient degree of efficacy to warrant further investigations. We are continuing our efforts to extend the preliminary investigations reported earlier.

Litchfield³ points out some of the limitations in our thinking about the correlations of findings between laboratory animals and man. He also feels that the net result of depending on tests in laboratory animals to find compounds for the treatment of diseases in man is that

relatively few effective and safe drugs will emerge. Could it be that our screening programmes are not altogether effective?

Looking back over the past fifty years or so it is difficult not to be impressed with the distinct possibility that a number of drugs which are useful and are being used daily would probably have never reached a clinical trial by to-day's standard. Digitalis, without prior knowledge of its pharmacological properties, would probably have been discarded because it had a variety of toxic effects on the heart and a slight overdosage of it would produce fatal cardiac arrest. I would predict that to-day it would never have progressed to the stage of clinical trials. Another very useful drug, quinine, might not have been tested clinically because of its extreme toxicity to dogs. The foregoing are but two examples of valuable drugs that came to use first by observations in man.

I wish to mention one antibiotic which is being used clinically that did not show any significant activity in animals. This is cycloserine; it did not have *in vitro* activity against most bacteria, but was active against *Mycobacterium tuberculosis*. When cycloserine was tested in guinea-pigs infected with experimental tuberculosis, it was inactive. In man it is effective against a wide variety of bacterial infections and is also one of the effective agents against tuberculosis. The reason for the lack of activity in animals is that D-alanine is a specific antagonist for cycloserine, and man does not have this metabolite⁴.

It would seem to me that the foregoing illustrations point to the fact that we may be depending too much on our screening methods to select drugs for clinical trials. This may be the case with 'Viractin' since the limited clinical tests have shown that it holds promise as an effective prophylactic agent for upper respiration infections.

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¹ Leach, B. E., Hackman, P. E., and Byers, L. W., *Nature*, **204**, 788 (1964).

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⁴ Hoepflich, P. D., *J. Biol. Chem.*, **240**, 1654 (1965).

HERPES VIRUS SPECIFIED RIBONUCLEIC ACIDS

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IN general, when a virus particle successfully infects a host cell, the viral genome first initiates synthesis of new nucleic acids, some of which then programme or induce qualitative or quantitative changes in the synthesis of proteins. The metabolism of the cell thus undergoes a sequence of changes which lead to the production of progeny virus particles. As a result, the host cell is usually destroyed.

While most present-day knowledge of this situation is derived from extensive investigations of infection of bacterial cells by T-even bacteriophage¹⁻³, recent work indicates that mammalian cells respond to virus infection in an analogous fashion. Thus, in the case of HeLa cells infected with vaccinia virus, the normal patterns of syn-

thesis of RNA specified by the cell genome is gradually destroyed, while new messenger-RNA functional in the synthesis of virus-specified protein is concomitantly transcribed from the viral genome in the cytoplasm^{4,5}.

The present article describes the changes in RNA synthesis induced by herpes simplex virus, which grows in the nucleus of the infected mammalian cell.

Earlier investigations with BHK 21 cells infected with herpes simplex virus established⁶ the time course of certain virus-induced events, in particular the appearance of herpes DNA, virus-specific protein and mature virus particles. It was also observed that the activities of DNA nucleotidyltransferase (EC 2.7.7.7) and deoxyribonuclease (EC 3.1.4.5) increase markedly after infection⁷. We have recently obtained evidence which suggests that these increased activities are due to virus-specified enzymes⁸.

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