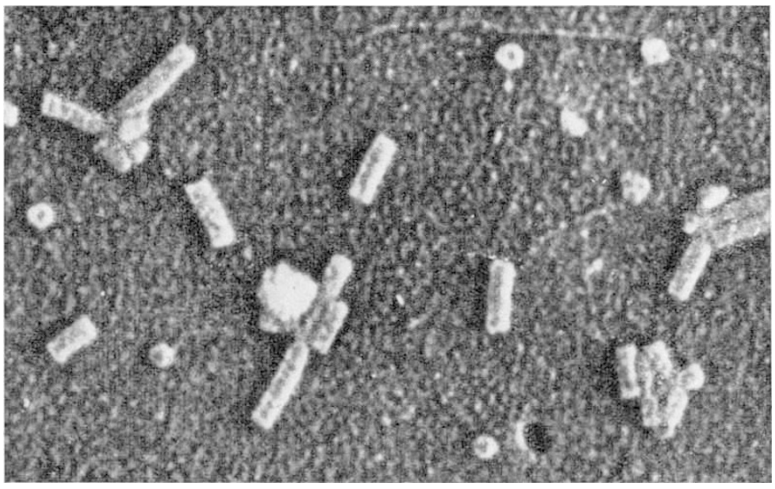

Fig. 3. Fragments of tobacco mosaic virus, filaments of ribonucleic acid and protein disks with a hole. × 150,000

prove by electrophoresis of a mixture of ribonucleic acid and tobacco mosaic virus.

A more detailed report of this work will be published in the *Zeitschrift für Naturforschung*.

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Cellular Control in Virus Infection

Marked changes may be produced by virus infection in a host cell when the amount of virus material is very small compared with the amount of host cell and when some of the host's synthetic activities are altered by the presence of the virus. Many authors refer to this control of the cell by the infecting particle; but experimental evidence is very scanty. In infection by coliphage T_2, Cohen[1] has shown that infected cells use an alternative metabolic pathway to a greater extent than do normal cells. No definite information is available in mammalian virus infections as to the presence of such metabolic alterations, nor the means by which such changes could be produced.

In mouse liver infected with ectromelia virus at initial infecting levels of about 1 *LD* 50 per liver cell, the infectious titre drops to less than 1 per cent of the initial level and then returns to the initial titre at about 11 hr. The titre remains stationary until about 22 hr., when an increase of some thirty-fold occurs. It was suggested recently[2] that the eclipse period was concerned with establishing control of the cell before multiplication occurred. Evidence which supports this suggestion has been obtained by studying the effect of this virus on regenerating liver. It was found that at the same stage of regeneration there was a lower mitosis-rate in livers of mice infected 12 hr. previously than in livers of uninfected mice. For example, in young mice examined 40 hr. after partial hepatectomy, an uninfected group had a mitosis-rate of $6{\cdot}7 \pm 0{\cdot}6$, whereas a group infected for 12 hr. had an average mitosis-rate of $1{\cdot}4 \pm 0{\cdot}3$. Mice infected for longer periods show a more marked effect, mitosis being rare after 20 hr. of infection. In the first 12 hr. of infection, we have been unable to detect any abnormality in morphology or composition of liver, or any alteration in oxygen uptake, fructose utilization, or lactic acid production. The infectivity titre shows no virus multiplication at this time, and stays unaltered until about 22 hr. Complement-fixing antigen rises to detectable level at 12–14 hr. and increases in roughly linear fashion. Results of preliminary experiments show that the deoxyribonucleic acid per nucleus is the same in infected and non-infected cells at the same period of regeneration.

The control of mitosis appears at an early stage of infection, and is established at the end of the eclipse period, which appears to be the onset of time of multiplication of virus material. The time sequence suggests that the effect on mitosis may be closely related to the essential primary effect of the virus on the cell. The lack of other changes found in the liver after 12 hr. of infection makes the phenomenon less likely to be a secondary change, though they provide no lead as to the biochemical basis.

A further indication of disturbance of normal control is found later in the growth-cycle. In intact livers studied 30–40 hr. after infection, there is an increase in the amount of cytoplasmic material far greater than can be accounted for by virus. There is an increase in the ratio of cytoplasmic to nuclear volume and in the amount of protein per liver, without any increase in the amount of deoxyribonucleic acid. There is no increase in the number of cells.

As a working hypothesis, we consider that the alteration in cellular economy necessary for virus production, first indicated by control of mitosis, leads to the production of more cytoplasm, and this abnormal form of growth is followed by damage to the cell. Cellular damage is regarded, however, as a by-product of, rather than a prerequisite for, virus multiplication.

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Nov. 24.

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A Mechanism for Citrate Dissimilation

Certain bacteria dissimilate citrate anaerobically to acetate and oxaloacetate[1–4]; the reaction is of particular interest since, unlike citrate biosynthesis, it is not dependent on coenzyme A[1,2]. We have partially purified extracts of *A. aerogenes* and have demonstrated the following properties of citridesmolase: (1) As the reaction proceeds, the enzyme is progressively inactivated and ceases to function with citrate in excess. The amount of citrate decomposed