of approach in a journal addressed primarily to natural scientists. Students of applied economics have much to learn from the careful, painstaking, and patient researches of the natural scientists. We may fittingly conclude with some observations by Herbert Dingle, one of the most perceptive British historians of science, whose exhortations economists, especially those working in the sphere of underdeveloped countries, will do well to remember:

"We need to cultivate the restraint of Galileo, who left the world of angels and spirits until the time should come when it could be explored, and contented himself with such principles as he could extract with confidence from experience, though the resolution committed him to such trivialities as the timing of balls rolling down grooves. It is that self-control—the voluntary restriction to the task of extending knowledge outwards from the observed to the unobserved instead of imposing imagined universal principles inwards on the world of observation—that is the essential hallmark of the man of science, distinguishing him most fundamentally from the non-scientific philosopher" (*6*).

References and Notes

1. R. Nurkse, *Problems of Capital Formation in Under-Developed Countries* (Oxford Univ. Press, Oxford, England, 1953), pp. 4–5.
2. "A study prepared at the request of the Special Committee to Study the Foreign Aid Program, United States Senate, by the Center for International Studies, Massachusetts Institute of Technology" (Washington, D.C., 1957), p. 37.
3. The level of capital formation in underdeveloped countries is often understated, because of the exclusion from the statistics of agricultural capital formation by small farmers. This exclusion reflects either the practical difficulty of measuring capital formation in this type of activity or the tendency to equate capital formation with investment in large-scale or otherwise easily identifiable undertakings. (This latter tendency, in turn, may reflect the common but often mistaken view that peasant farmers are too poor, too hidebound by tradition, and too limited in foresight to save and invest productively.) The seriousness of this omission is clear from the development of peasant agricultural production for sale (both for local consumption and for export) in many underdeveloped countries; and this implies the development of large areas of peasant holdings under cash crops—that is, substantial direct investment in agriculture.
4. The importance of changes in the composition of capital may be illustrated by reference to the Industrial Revolution in England. T. S. Ashton, a distinguished British economic historian, writes of 18th-century England that ". . . the speeding up of production and distribution by the new machines and new means of transport made it possible to transmute circulating into fixed capital. The process is at the centre of what is called the industrial revolution." [*An Economic History of England: The Eighteenth Century* (Methuen, London, 1955), p. 112.]
5. A. O. Hirschman, *The Strategy of Economic Development* (Yale Univ. Press, New Haven, Conn., 1958), p. 32.
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Reoviruses

A new group of respiratory and enteric viruses formerly classified as ECHO type 10 is described.

Albert B. Sabin

The prototype (originally designated HE type 4 virus) of ECHO type 10 virus ("Lang" strain) (*1*) and four other closely related strains were first isolated and identified in this laboratory in 1954, from the stools of healthy children in Cincinnati (*2*) and Mexico (*3*). Subsequently, antigenically related strains were recovered from a spontaneous outbreak of rhinitis in chimpanzees (*4*), from a family outbreak of steatorrheic enteritis (*4*), from children with diarrhea (*5*), and from several outbreaks of illness in a nursery in Washington, D.C. (*6*). The sera of most human adults as well as of some monkeys, rabbits, and guinea pigs contain neutralizing antibodies, and antigenically related viruses have been recovered from monkeys (*7, 8*) and recently also from naturally infected calves (*9*).

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Differentiation from Other Viruses

The inclusion of this virus in the ECHO group was originally based on its origin from human stools, its optimal isolation in monkey-kidney tissue cultures, and the lack of pathogenicity of the initial strains for newborn mice, guinea pigs, rabbits, and monkeys. It was soon found (*10*), however, that the viruses of the ECHO 10 group were much larger (about 75 mμ) than the other ECHO viruses, the Coxsackie viruses, and the polioviruses in the group of enteroviruses that had been measured by filtration through gradocol membranes (about 18 mμ or smaller).

The cytopathogenic effect in monkey-kidney tissue cultures produced by strains of the ECHO 10 group was distinctive and different from that produced by all other enteroviruses. Furthermore, ECHO 10 virus was found to have a cytopathogenic effect in primary cultures from the kidneys of guinea pigs, cats, and dogs, and to a lesser extent from those of rabbits and calves, in which the other enteroviruses were without effect (*11*). Subsequent work also indicated that the prototype ECHO 10 virus was capable of yielding a variant that was pathogenic for newborn mice, with production of lesions in the brain, myocardium, and liver (*10, 12*), and that large doses of tissue-culture virus of some other strains exhibited a similar pathogenic effect on primary inoculation in newborn mice (*13*). It was also reported that low concentrations of periodate which were without effect on the receptors of human group O erythrocytes for the hemagglutinins of other ECHO viruses, as well as for those of influenza virus, completely destroyed the receptors for the ECHO 10 virus hemagglutinin (*14*).

Of all the properties which distinguished the ECHO 10 group of viruses from the other members in the group of enteroviruses, its large size seemed most important. Since the size of many of the Coxsackie and ECHO viruses was not known, and since size was not

one of the original criteria for inclusion of a virus in this group, there was no firm basis for separating the ECHO 10 strains from this group until it could be shown that however else the various naturally occurring and tissue-culture-propagated members of the group of enteroviruses might vary, they had in common a certain small range of size. Gradocol-membrane filtration tests recently completed in this laboratory (*15*) showed that all other established types of Coxsackie A, Coxsackie B, and ECHO viruses have a size in the range of 18 mμ or less. On the other hand, further tests on five strains representing different antigenic variants of the ECHO 10 group all yielded similar results, with a size of about 72 mμ (membranes with an APD of 130 mμ permitted the virus to pass, while those with an APD of 120 or 110 mμ held it back completely). This marked difference in size between all the other enteroviruses and the various strains of ECHO type 10 provides a sufficient basis for removing ECHO type 10 from the group of enteroviruses.

Properties

Detailed studies carried out in association with H. J. Eggers and M. A. Koch in this laboratory on various properties of 11 different strains have provided the definitive information required for establishing these strains as members of a new group of viruses, for which I am proposing the name "reoviruses."

This name is intended to stress the association of this group of viruses with both the respiratory and the enteric tracts. Although other viruses (for example, the adenoviruses and some types of ECHO) are similarly associated with both the respiratory and enteric tracts, it is difficult to select any other property of this new group that by itself is not also shared with other viruses. The "reoviruses" are characterized by the following properties.

1) They are ether-resistant.

2) They are approximately 72 mμ in size, as determined by filtration through gradocol membranes.

3) They have a distinctive cytopathogenic effect in monkey-kidney tissue culture, in which the cells separate from the sheet, assuming a granular, degenerated appearance with intact nuclei; in stained, cover-slip preparations, cytoplasmic inclusions of varying size and shape, first reported by Malherbe and Harwin (*7*), were also found in this laboratory with five different strains representing the three distinct antigenic serotypes; the cytoplasmic inclusions (Fig. 1) are red after staining with hematoxylin and eosin and blue with Giemsa (*16*); according to Drouhet (*17*) the inclusions are Feulgen negative, they fail to stain red by the Unna-Papenheim method after treatment with ribonuclease, and they are negative for mucopolysaccharide.

4) The prototype "Lang" strain propagated in monkey-kidney cells also produces a cytopathogenic effect in kidney-tissue cultures from guinea pigs, swine, cats, dogs, and partly also in those from calves and rabbits (*11*).

5) All tested strains multiply in newborn mice, and some produce clinical signs of disease, with lesions in nerve cells (cytoplasmic inclusions in some cells), myocardium, and liver, but lesions are rare in the pancreas, brown fat, and voluntary, striated muscle (*13*); adult mice remain well, but the extent, if any, of virus multiplication in them has not been determined.

6) The prototype ("Lang") strain has been reported to multiply in chick embryos (*18*).

7) Occasional monkeys die after intracerebral inoculation, with lesions in the ependymal lining of the ventricles and in the choroid plexus.

8) The "chimpanzee rhinitis" strain produces a distinctive "common cold" syndrome on nasal instillation in sus-

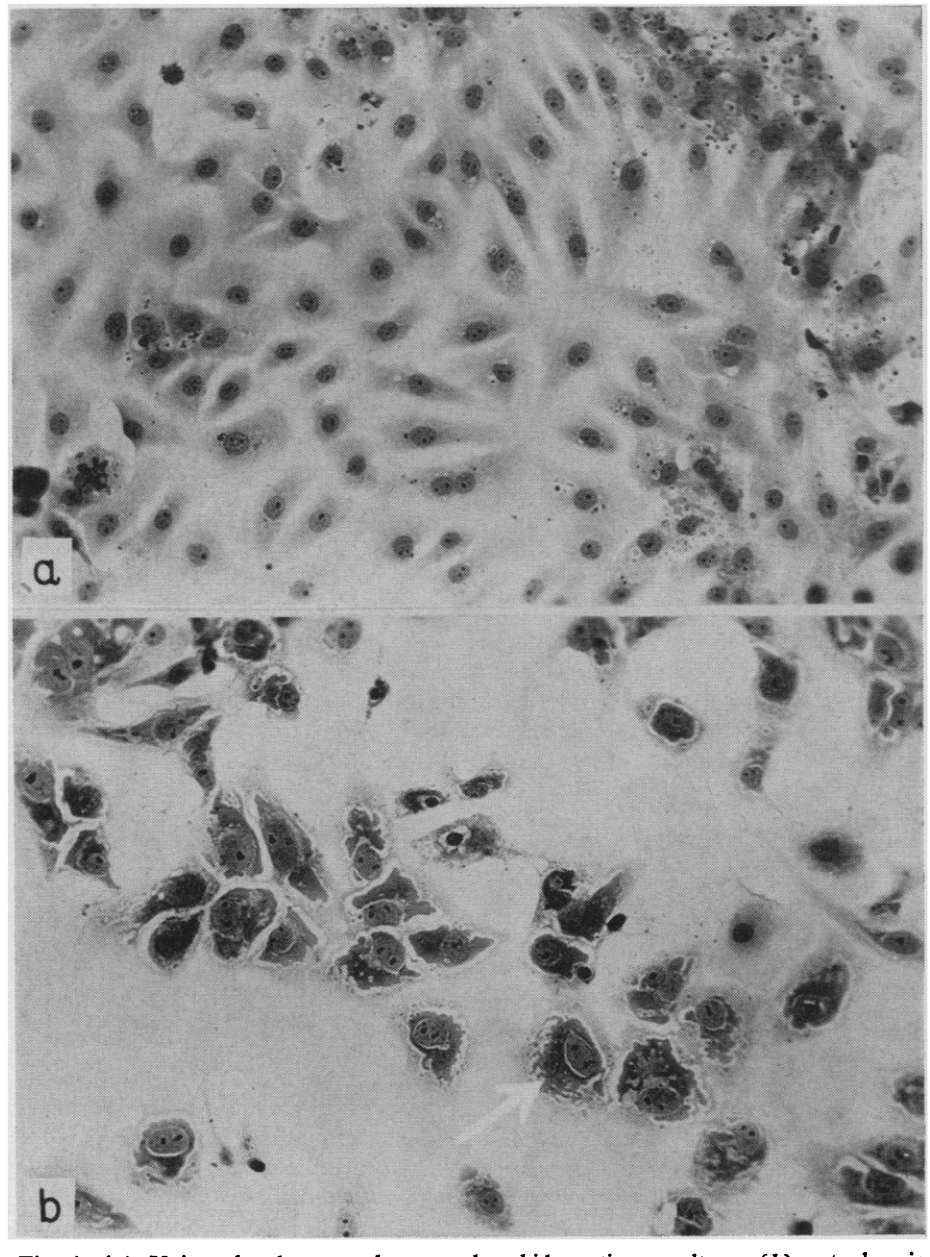

Fig. 1. (*a*) Uninoculated cynomolgus monkey kidney tissue culture; (*b*) cytoplasmic inclusions (arrow) in cells infected with reovirus.

ceptible chimpanzees, with virus multiplication both in the nasal passages and in the enteric tract (*19*).

9) All strains yield a hemagglutinin for human group O erythrocytes (*14, 20, 21*) but not for chicken, guinea-pig, sheep, or bovine erythrocytes (*14*); the erythrocyte receptors for this hemagglutinin are not affected by the receptor-destroying enzyme of *Vibrio cholerae* (RDE) (*20, 21*) but are destroyed by potassium periodate in concentrations as low as 1:1000 to 1:6000 (*14, 21*).

10) All strains possess a common complement-fixing antigen (*21*) but distinct antigenic differences are demonstrable by neutralization (*4, 5, 13*) and hemagglutination-inhibition tests (*21, 22*).

Distinct Antigenic Types

For the demonstration of antigenic differences by neutralization or hemagglutination-inhibition, antisera prepared in rabbits, especially in those without preexisting spontaneous antibody (*5, 13, 21*), or in guinea pigs and roosters (*22*), were found to be superior to those prepared by hyperimmunization of monkeys. By means of such tests (*13, 21, 22*), the available strains were clearly divisible into three distinct, but related, serotypes (Table 1).

Table 1. Homotypic and heterotypic hemagglutination-inhibition antibody titers of three types of reovirus rabbit antisera. The rabbit sera were adsorbed with human group O erythocytes and with kaolin prior to their use in hemagglutination-inhibition tests.

Virus		Antiserum			
Type	Strain	Lang (type 1)	D 5 (type 2)	Dearing (type 3)	Abney (type 3)
1	Lang	*2560*	40	10	80
2	D 5	10	*1280*	20	20
3	Dearing	40	40;160	*2560*	2560
3	Abney	160	160	5120	*5120*

For type 1, the prototype is the original ECHO 10, "Lang," strain; three other strains recovered from healthy children in Cincinnati ("Cocrel") and Mexico (CHHE 127 and 276), a simian virus (SV-12) (*8, 22*), and 22 strains isolated by Rosen *et al.* (*6*) during a 1957 winter outbreak in a Washington, D.C., nursery were also identified as type 1.

For type 2, the D 5 (Jones) strain derived from a child with diarrhea (*5*) is the prototype; other strains belonging to this type are those derived from an epidemic of rhinitis in chimpanzees (*4, 13, 19, 21, 22*), a strain (SV-59) (*8*) recovered from the lung of a monkey which died of pneumonia (*13, 22*), a strain ("Amy") recovered from a child with steatorrheic enteritis (*4, 13, 21*), a strain recovered from a healthy child in Mexico, and two strains recovered in a Washington, D.C., nursery by Rosen (*22*).

For the type 3 prototype we (*13, 21*) have selected the "Dearing" strain derived from a child with diarrhea (*5*), and one other strain (BVA 6) in our collection, derived from a healthy child in Mexico, belonged to this type. Rosen (*22*) independently discovered a third type and has used the "Abney" strain, which was isolated from a child with a febrile upper-respiratory infection and was representative of 12 strains recovered from children in a Washington, D.C., nursery, as the prototype of type 3. We (*13, 21*) have found that our two type 3 strains and the "Abney" strain are serologically identical. Rosen and Abinanti (*9*) recovered four type 3 strains from naturally infected cattle.

Conclusion

The reoviruses, a new group of cytopathogenic viruses made up of the former ECHO type 10 virus and of others antigenically related to it, are distinct in their properties from all other known viruses. The optimum medium for their isolation is monkey-kidney tissue culture. They have been recovered from human beings, chimpanzees, monkeys, and calves, and serologic data suggest that guinea pigs, rabbits, dogs, and cats may also be naturally infected. Their size of approximately 72 mμ, as measured by gradocol membrane filtration, is somewhat smaller than that of the myxoviruses, the adenoviruses, and the CCA (chimpanzee coryza agent) or RS (respiratory syncytial) virus (*23*) and distinctly larger than the enteroviruses. The reoviruses are ether-resistant, like the adenoviruses, with which they share an affinity for both the respiratory and the enteric tracts, and unlike the myxoviruses and the RS virus, which have an affinity predominantly for the respiratory tract and are readily destroyed by ether. The cytoplasmic inclusion produced by the reoviruses is distinctive. The great sensitivity of the reovirus, human group O hemagglutinin to destruction by periodate and its resistance to RDE is another distinctive property. The capacity of all reoviruses to multiply in newborn mice, with the production, by large doses of some strains, of clinical manifestations and lesions in the brain, myocardium, liver, and pancreas similar to those produced by the Coxsackie B viruses, at first suggested a possible relationship to this group of viruses (*10, 12*), but many other properties, most particularly their large size, clearly distinguish the reoviruses from the Coxsackie viruses (*24*). The association of various reoviruses with respiratory and enteric illness in human beings, chimpanzees, and monkeys points to the necessity of including the reoviruses in any systematic study of the complex viral etiology of respiratory and enteric diseases of human beings. The capacity of reoviruses to produce lesions in the brain, liver, and myocardium of newborn mice also points to the need for considering them as a potential cause of similar lesions in reovirus infections of newborn children (*25*).

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24. The committee on enteroviruses of the National Foundation considered the data presented in this article and unanimously voted to remove the ECHO type 10 virus from the group of enteroviruses.
25. The personal studies reported in this article were aided by grants from the National Foundation.