widely scattered literature. It has been a difficult problem, therefore, to obtain representative material for an introductory course. This task is now greatly simplified by the present book, which is an outgrowth of a general course in limnology that has been given by the author for a number of years. The content of the book has been well and adequately selected and it is based chiefly on results obtained on American lakes and streams.

The subject-matter is fourfold in character, since it deals with the geology, physics, chemistry and biology of fresh waters. The geological part relates to the origin of lake basins, the dynamic action of the water on the shores and the great diversities in area, depth and elevation of lakes and in the character of their bottom deposits.

In the chapter dealing with the physical properties of lake waters, the annual cycle of temperature changes is discussed, together with the thermal stratification of the water, the heat budgets of lakes, the annual temperature changes in the bottom deposits and the penetration of solar radiation into different types of lake water. The quantity and quality of the radiation that reaches different depths are greatly affected by the color of the water.

The chemical discussion of lake waters includes a consideration of the dissolved gases, silica, phosphates, nitrates, calcium, magnesium and various other inorganic substances that are found in fresh waters. Also the organic matter that is present in the colloidal state or in true solution is discussed at some length.

Chapters VI and VII are devoted to a discussion of the effect of the physical and chemical conditions that obtain in lakes on the biota and to the various responses shown by aquatic plants and animals to the seasonal changes in these conditions.

The main part of the biological section (chapters VIII to XIV inclusive) deals with the various aquatic organisms and with the problem of the biological productivity of lakes; emphasis is placed on the latter and it includes the production of plankton as well as that of the bottom-dwelling animals and the large aquatic plants. The food value of this material is given consideration also.

The last three chapters relate to special types of water, such as ponds, bog lakes and streams. A good classified bibliography covering 54 pages completes the book.

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SPECIAL ARTICLES

CONCERNING ACTIVE IMMUNIZATION IN POLIOMYELITIS

THAT *Macacus* monkeys can be rendered actively immune to the virus of poliomyelitis has been known since 1910.[1] At that early date the important fact was also discovered that in process of the immunization, in which living virus was employed, a proportion of the treated monkeys, instead of becoming immune, always became paralyzed. The means employed in the treatment were to make successive injections of the virus beneath the skin; later the injections came to be made into the skin itself, which is still the method of choice in the monkey.[2] There is no essential difference in the double effects produced, except that skin injections seem to yield a higher degree of immunity.

Numerous and varied attempts have been made to modify the virus so as to preserve the immunizing properties and to remove the paralyzing action. Both physical and chemical means have been employed, but the results have not been satisfactory. Whenever the modifying agents inactivated the virus, no immunity followed the inoculations; when they reduced the activity, immunity would result, but paralysis also.[3] The effect of the physical and chemical agents seemed to be quantitative only; a dilution, not an attenuation, of the virus was produced. The virus recovered from the paralyzed monkeys injected with the chemically treated virus resembled in virulence the original virus strain before treatment was begun.

During the twenty-five-year period which has elapsed since the first experiments on immunization were made, certain virus strains have been passed through many *Macacus* monkeys. An effect of this passage was to enhance the virulence of some, but not of all the passed strains. It is noteworthy that the virus of poliomyelitis is strikingly unstable in its disease-producing or pathogenic properties; for reasons not understood specimens of high virulence will suddenly fall off in activity, after a time regaining the lost power while being preserved in glycerol.[4] On the other hand, some strains of virus possess enduringly weak activity; they are difficult to work with, because of the frequent failure to induce infec-

[1] S. Flexner and P. A. Lewis, *Jour. Am. Med. Assn.*, 54: 1780, 1910.

[2] W. L. Aycock and J. R. Kagan, *Jour. Immunol.*, 14: 85, 1927.

[3] F. W. Stewart and C. P. Rhoads, *Jour. Exp. Med.*, 49: 959, 1929.

[4] S. Flexner, P. F. Clark and H. L. Amoss, *Jour. Exp. Med.*, 19: 195, 1914.

tion in the monkey. Probably only the most highly susceptible animals respond to the weak strains when large doses are administered.

The statement has been made that the Rockefeller Institute passage "mixed virus" has gained in virulence for monkeys and declined in activity for human beings.[5] There is no experimental evidence supporting this statement. Indeed, aside from the unexplained and temporary fluctuations in activity, referred to above, this strain has remained remarkably constant; probably for this reason it has been sought by investigators in all parts of the world. The assumption that adaptation of the virus to monkeys is accomplished at the expense of diminution of pathogenic power for man is not only to go beyond existing knowledge, but is negatived by the observed effects when original human virus is employed directly for the immunization of monkeys.[6]

The term "human virus" simply means that portions of the spinal cord from fatal cases of poliomyelitis are used for the inoculation of monkeys, without having been passed through monkeys previously. This material can be preserved in glycerol, as can the monkey passage virus. When the human virus is injected successively into the skin of *Macacus* monkeys, it produces active immunity in the greater number, but paralysis in a proportion of the inoculated animals, just as the passage strains do. The same is true of early passage strains which have not had time to become specially adapted to the monkey.

Now, the human virus must have passed an indeterminate number of times through human beings in the course of the epidemics of poliomyelitis which have occurred as natural phenomena for scores of years. And yet, this virus has retained the property of both immunizing some monkeys and paralyzing others on repeated small injections. Probably the more refractory become immune, and the more susceptible paralyzed; no way is known of identifying the two varieties of animals prior to inoculation, just as there is no known method of selecting the small proportion of children falling victims to poliomyelitis during epidemics, from the large proportion passing through the outbreaks unattacked.

The experimental studies on which the statement of the effects of human strains and early monkey passage strains of the virus is based were carried out during the 1931 epidemic of poliomyelitis in New York State.[7]

[5] J. A. Kolmer and A. M. Rule, *Am. Jour. Med. Sci.*, 188: 510, 1934; J. A. Kolmer, G. F. Klugh, Jr., and A. M. Rule, *Jour. Am. Med. Assn.*, 104: 456, 1935; J. A. Kolmer, *Ann. Institut Pasteur*, 55: 365, 1935.

[6] S. Flexner, *Jour. Am. Med. Assn.*, 99: 1244, 1932.

[7] The data relating to this subject will appear in a paper to be published in the *Journal of Experimental Medicine*.

The observations on which the preceding statement is based may be summed up as follows:

(1) No adequate evidence has been presented showing that through the action of physical and chemical agents the virus of poliomyelitis may be attenuated so as to preserve its immunizing properties, while being deprived of its potential paralyzing power.

(2) The available evidence indicates that virus exposed to injurious physical and chemical agents is either inactivated (destroyed) or merely reduced in concentration. When the virus is actually destroyed, it no longer possesses immunizing power; when it is reduced in concentration, it immunizes certain animals and may paralyze others. The proof that the treated active virus has not been attenuated is provided by the recovery of fully active virus from the paralyzed animals.

(3) No evidence exists showing that passage of virus through monkeys removes its power to infect and produce paralysis in man. On the contrary, we possess convincing observations which show that an indeterminate number of passages of virus through human beings does not deprive it of its potential paralyzing effect when injected into monkeys.

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THE ERGOT ALKALOIDS. SYNTHESIS OF 4-CARBOLINE CARBONIC ACIDS

A PROVISIONAL structure for lysergic acid (3-propenyl-4-methyl-3, 4-dihydro-4-carboline-5-carbonic acid) has been suggested,[1] based on the interpretation of analytical data, of its properties and of the substances obtained from it by alkali fusion. Such a structure, if correct, would therefore place this acid in close relationship to the *harmala* group of alkaloids. Parallel with the continuation of the study of its degradation by different procedures, we have been attempting to check the validity of such a structure by synthesis.

The first steps in the synthesis have been readily realized by an extension of the method used by Tatsui[2] and by Akabori and Saito[3] in which tetrahydroharman was produced by the condensation of tryptamine with acetaldehyde. By the substitution of tryptophane[4] itself for tryptamine in this reaction we have found that a number of 3-substituted tetrahydrocarboline-5-carbonic acids have become readily acces-

[1] W. A. Jacobs and L. C. Craig, *Jour. Biol. Chem.*, 111: 455, 1935.

[2] G. Tatsui, *Chem. Centralbl.*, II: 668, 1928.

[3] S. Akabori and K. Saito, *Ber. chem. Ges.*, 63: 2245, 1930.

[4] W. O. Kermack, W. H. Perkin, Jr., and R. Robinson, *Jour. Chem. Soc.*, 119: 1616, 1921.