rington, is much in evidence, and indeed the chief merit in the book is the broad, philosophical view of organization and integration which emanates from that influence. The minutely detailed account of the researches on stretch reflexes and other features of spinal cord physiology, which occupied the author during his years in Sherrington's laboratory, seems to involve over-emphasis of a specialized topic at the expense of other more fundamental matters, which suffer a corresponding neglect.

In a footnote (p. 73) is described how the author once espoused a chemical theory of central nerve function and disposed of rival electrical theories with arguments which, it may be noted, failed to consider the possibility of "reverberation," which was suggested in 1923 and for which a strong case has since been made by Lorente de Nó. The footnote goes on to explain how the author has now abandoned the chemical theory and with equal vigor espoused the electrical theory, just when cogent evidence for a chemical theory is becoming well-nigh overwhelming, without even a reference to experiments which have raised almost insuperable obstacles in the way of the electrical theory.[1] He prematurely accepts the evidence of Eccles, which seemed to rule out the synaptic action of acetylcholine, but which has since been convincingly answered by the work of Rosenblueth and Simeone.[2] In support of the electrical theory he makes dogmatic assertions concerning events in the cell membrane, including reiterated insistence on the unproved assumption that an antidromic impulse causes a discharge which sweeps through the entire nerve cell. This unfortunate bias reaches a climax on page 96, where he takes up the once ignored explanation of after-discharge by reverberating circuits and then states, "it seems unnecessary to discuss alternative hypotheses."

These adverse criticisms impress a reviewer to whom the basic questions appeal as standing at the portal of rational inquiry into the mechanism of conscious life. Not being qualified to pass expert judgment on the anatomical survey, which constitutes the greater part of the book, the reviewer is impressed with the quantity of material which is marshalled to provide an understanding of integration in the nervous system.

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SPECIAL ARTICLES

MICE AS CARRIERS OF PATHOGENIC PLEUROPNEUMONIA-LIKE MICROORGANISMS

Two distinct strains of filtrable pathogenic microorganisms of the pleuropneumonia group have recently been isolated from the brains of mice and shown to possess tissue affinities of such a nature that they can produce in mice two experimental diseases which bear some resemblance to certain phases of rheumatic fever and rheumatoid arthritis in man.[1] Strain A induces a transitory, migratory polyarthritis, multiplies in the brain and in mesothelial cells of the pleura, pericardium and peritoneum, and produces a typical exotoxin which gives rise to choreiform signs. Strain B produces no such toxin, but has an almost specific affinity for the joints in which it gives rise to a chronic, progressive, proliferative, ankylosing arthritis. These two strains are biologically and immunologically distinct from each other, from *Pleuropneumonia bovum* and from pleuropneumonia-like microorganisms that have been isolated from rats in pure culture or in association with *Streptobacillus moniliformis*.[2] These findings clearly suggested the necessity of determining whether or not similar microorganisms could be isolated from patients with rheumatic fever and rheumatoid arthritis, and following this indication, Swift and Brown[3] reported the isolation of pleuropneumonia-like microorganisms from acute rheumatic fever material.

The chief purpose of the present communication is to record certain experiences which indicate the inadvisability of using mice in attempting to isolate such microorganisms from human material. While studying exudates and tissues from patients with rheumatoid arthritis or rheumatic fever, it was found that inoculation of such material, normal synovial fluid or sterile broth into the eyes (vitreous) of mice, yielded positive pleuropneumonia-like cultures with great regularity. In a typical test, material under investigation was injected into both eyes of six 3-weeks-old mice; six days later the eyes were removed with separate, sterile instruments, immersed in anesthetic ether for one to two minutes (this was sufficient to bring about adequate sterilization of the exterior of the eye), incised, and streaked across 30 per cent. ascitic fluid agar. In most instances, innumerable, typical, microscopic, pleuropneumonia-like colonies appeared within two days. With the Rockefeller Institute Swiss stock, at least four or five mice out of each group of six yielded positive cultures from one or both eyes in ten different experiments. The colonies on solid medium resembled those of Strain A; after several transfers on fluid

[1] W. B. Cannon and A. Rosenblueth, *Amer. Jour. Physiol.*, 119: 221–235, 1937.

[1] A. B. Sabin, SCIENCE, 88: 575, 1938; *ibid.*, 89: 228, 1939.

[2] E. Klieneberger, *Jour. Hyg.*, 38: 458, 1938.

[2] A. Rosenblueth and F. A. Simeone, *Amer. Jour. Physiol.*, 1938, 122: 688–707, 1938; *ibid.*, 708–721.

[3] H. F. Swift and T. M. Brown, SCIENCE, 89: 271, 1939.

medium the cultures were found to be agglutinated in high titre by anti-A serum and to produce a neurotoxin which was completely neutralized by the "A" strain antitoxin. Further studies revealed that these microorganisms were inhabitants of the external surface of the eye, from which they could be cultured with great regularity, and frequently in large numbers unassociated with any bacterial colonies. It was apparent that as a result of the intraocular injection some of these microorganisms were carried into the eye, where they multiplied in the course of a few days. Similar studies carried out with mice of the Rockefeller Institute albino stock and of another Swiss strain (Freed) originating from the Institute stock but bred elsewhere for the past six to seven years, revealed the same condition, but the carrier rate was lower; it was thus possible to encounter groups of six mice from which these microorganisms could not be obtained, while in other groups of six, either all or a varying number yielded positive cultures of the same type. Evidence was also obtained that these microorganisms inhabit the mucosa of the nose and accessory sinuses from which they may be carried into the lungs in the course of nasal instillation under anesthesia.[4] It may be of interest to note here that in one test in which six mice were given nasal instillations under ether anesthesia and intraocular injections of pericardial fluid from a patient who succumbed to acute rheumatic carditis, three different types of pleuropneumonia-like microorganisms were isolated: a Type A from the eyes, a Type B from the lungs of one mouse, and a new type (to be called "C") which produced arthritis in mice but no toxin and was immunologically distinct from all the others studied. Two pleuropneumonia-like strains producing pneumonia in mice (isolated by Dr. Dienes in the course of passaging two human rheumatic heart muscle suspensions through the lungs of mice) were submitted to me for study[5]; they were found to be immunologically identical with Strain A and to produce neurotoxin in cultures which was neutralized by "A" antitoxin. Of three cultures isolated by Drs. Swift and Brown from pneumonic lungs of mice inoculated with rheumatic fever material, one was found to be a Type A, one a Type B and the third the same as the newly isolated Type C.

It is apparent, therefore, that the presence or absence of pleuropneumonia-like microorganisms in rheumatic fever and rheumatoid arthritis exudates and tissues will have to be established primarily by cultural methods, and not by passage through mice or other animals.

[4] This finding suggests that viruses, such as that of influenza, which are passaged by nasal instillation in mice, should be cultured periodically to determine whether or not they have been contaminated by microorganisms of the pleuropneumonia group.

[5] Dr. L. Dienes informs me that he was able to isolate a similar strain by passaging normal mouse lung.

Using a large variety of solid and fluid media and "passaging blindly" six or more times, I have been unable thus far to grow pleuropneumonia-like microorganisms from thirteen rheumatoid arthritic exudates (twelve patients), four rheumatoid subcutaneous nodules (three patients), rheumatoid synovial tissue (two patients), acute rheumatic blood, pleural fluid, pericardial fluid and heart muscle (two patients),[6] but many more cultivation experiments will have to be performed with suitable specimens before a final decision can be reached.

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THE PREPARATION OF PITUITARY GROWTH HORMONE FREE FROM LACTOGENIC AND THYROTROPIC HORMONES

THE knowledge that the anterior hypophyseal growth hormone is comparatively stable to alkali led us to assume that this protein would be free from disulfide linkages (–S–S–) and therefore resistant to cysteine reduction. Therefore a 5 per cent. solution of growth hormone in its purest form[1] was treated with double the amount of cysteine at pH 8.0. The reduction which resulted caused a precipitation of one half the total protein, whereas the supernatant contained most of the growth hormone when tested in normal plateaued female rats. (Table 1.)

TABLE 1

RETENTION OF GROWTH HORMONE POTENCY AFTER TREATMENT OF ANTERIOR HYPOPHYSEAL EXTRACTS $DAP35_2$ AND $DAP74_1$ WITH CYSTEINE

Preparation	Daily dose of total protein	Daily dose of soluble protein	Number of rats per group	Grams grain per rat*
	mg	mg		
$DAP35_2$ Untreated	1	1	9	39
$DAP35_2$ Cysteine treated	1	0.43	6	39
$DAP74_1$ Untreated	1	1	12	51
$DAP74_1$ Cysteine treated	1	1	5	43

* Average gain of normal plateaued female rats by 17 daily injections over a period of 20 days.

We tested the above-mentioned cysteine-treated growth hormone for its lactogenic and thyrotropic activity. Up to the very high levels tested, these hormones were found to be absent.[2] (Table 2.)

[6] I am deeply indebted to Dr. Edward F. Hartung, of the New York Post-Graduate Hospital, for supplying most of these specimens.

[1] Prepared by modification of the method published by Evans, Uyei, Bartz and Simpson (*Endocrinology*, 22: 483, 1938).

[2] As regards gonadotropic hormones: the follicle-stimulating hormone was known to be nearly completely absent from the untreated solutions, so tests for this substance were not considered necessary; inactivation of ICSH did