

on this date showed a remarkable change from that of October 29, 1921: White corpuscles, 18,800. *Differential Count*: Polymorphonuclear neutrophiles, 48%; small mononuclear leucocytes, 20%; large mononuclear leucocytes, 3%; eosinophiles, 29%. Cells counted—300. Stain—Wright's. A great reduction in the percentage of eosinophiles.

November 7, 1921, a stool examined after a purge of magnesium sulphate had been given, showed but one ovum in thirty preparations, and this ovum was misshapen and somewhat broken up.

November 8, 1921, the seventeenth dose of 100 mgm. in 15 c.c. of sterile distilled water was given. A stool examined on this date for ova yielded negative results.

November 9, 1921, another stool was negative for ova.

November 10, 1921, the eighteenth dose of 100 mgm. was given as above.

November 14, 1921, the nineteenth, and November 16, the twentieth dose of 100 mgm. was given.

It will be seen from the foregoing that the patient received during the course of treatment 16.85 c.g.m. of the drug.

November 25, 1921, the blood picture showed the following: Red corpuscles, 5,320,000; white corpuscles, 9,800; hemoglobin, 89%. *Differential Count*: Polymorphonuclear neutrophiles, 50%; small mononuclear leucocytes, 29%; large mononuclear, leucocytes, 1%; transitionals, 1%; eosinophiles, 18%; basophiles, 1%. Cells counted—300. Stain—Wright's.

The blood had not yet fully cleared up, but such remarkable changes had taken place in it since October 29 and November 4, 1921, that we were led to believe it would become normal.

From November 8 to November 28, 1921, fourteen stools have been examined for ova. Half of this number were natural movements and half followed magnesium sulphate, as it was hoped that in such manner a more fair and true estimate of the condition could be appreciated. At least twenty preparations were made from different parts of each stool, but in no case were the ova of *Schistosoma mansoni* found.

The patient has steadily gained in weight and appearance. He has lost his languidness and is now wide awake and bright. His appetite has returned. His hoarseness has in a large part disappeared. The pain in the region of the gall-bladder and spleen, previously elicited by deep palpation, is no longer present. The signs noted in the chest during physical examination are no longer found.

During the month of December the patient remained under observation. His stools, sputa and urine were frequently studied, with negative results. The blood picture became normal, and upon January 1, 1922, he was discharged from the hospital feeling well in every way.

RECENT PROGRESS IN PHYSIOLOGY.

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THE CHANGE OF EMPHASIS.

DURING the past few years one can note a very distinct change in the subjects and methods of physiological research. The science has become more concerned with interpretation than with description. Fewer investigators are engaged in the study of complex coordinated systems, and more are seeking to discover the factors which affect the reactions of isolated cells or elementary tissues. It is as though we passed from observation of an automobile in working trim to an intensive collection of data regarding metals, oil, and gasoline. The new Physiology is less picturesque and more difficult than the old, but it appears to take us nearer to the fundamental properties of living matter. This shift in interest has made it necessary for those undertaking work in our laboratories to come with an equipment different from that which would formerly have sufficed. Detailed anatomical knowledge is rather less serviceable than it was to the masters of the classic period. General Physics and Chemistry now fail to provide the foundation and require to be supplemented by Physical Chemistry and Theoretical Electricity. Mathematics can no longer be shunned by the candidate. In short, the physiologist of the future will be less the naturalist making direct observations upon animals, and more the exact scientist dealing with tabulations and curves.

One feature of this change has been the obvious increase in the importance of Electro-physiology. Not many years ago this seemed a bizarre specialty remote from practical applications. Now it is seen that it promises to throw light on the most intimate mechanisms of stimulation and response. It must be remembered that changes of electrical potential are the only signs of life certainly to be recognized in nerves when disconnected from other tissues. The study of these rapid fluctuations by the ingenious methods now available is steadily making more clear the community of properties underlying the superficial diversity of cellular activities. It is by such technique that Forbes and Miller¹ have recently shown that ether cuts off the ascending nerve-impulses in the medulla. Crile had questioned the efficacy of ether to interrupt the afferent currents, and the latest contribution to the discussion is of the greatest practical interest.

PHYSIOLOGICAL REVIEWS.

It may not be superfluous to call attention to this new publication. The literature has become so voluminous that concise summaries covering special subjects are a necessity. *Physiological*

Reviews is a quarterly prepared for this purpose under the auspices of the American Physiological Society. It is now in its second year. Each volume is to contain about twenty articles written by men at home in their respective fields. Research workers will profit by the extensive bibliography, while a larger number of readers should be interested by the actual content of the reports.

The purpose of the present article is to indicate a few lines of work in which notable progress is being made. There are certain matters of such evident concern to the medical profession that they are not likely to be overlooked. It will be enough to mention two of these: the multiplied studies of the factors in rickets, and the endeavors of investigators at the University of Toronto to obtain in stable form the internal secretion of the pancreas, which is the regulator of carbohydrate metabolism. In these there is high promise of the therapeutic control of diabetes. Without dwelling upon matters so directly related to practice, we will turn to others less likely to be followed in detail by the busy physician.

"ALL OR NONE."

The "All or None Principle" continues to modify our traditional conceptions. Some ten years ago it won its way into our mode of picturing the contractions of skeletal muscle. We then ceased to think of the muscle-fibre as responding in different degrees to graded stimuli. The evidence marshalled by Lucas of Cambridge, England, compelled us to conceive of a slight muscle contraction as the maximal effort of a minority of the fibres, the majority remaining at rest. A little later Adrian showed that a nerve-impulse has the "All or None" character; it cannot reflect the intensity of the stimulus which gave rise to it.

The adjustment of our ideas to the doctrine of Lucas and Adrian has not been an easy matter, but it is gradually proceeding. Any who care to survey the problem may well read a recent paper by Forbes.² A few of the points made by him may be mentioned. If we accept the view that each muscle-fibre responds to stimulation in an "All or Nothing" fashion, and that the same principle holds for each fibre in a motor nerve, we must next ask how it is with the sensory apparatus. Have afferent fibres properties essentially different from those of efferent fibres? If they have not, what are we to think about the relation between stimulation and response on the sensory side? How shall we account for the seemingly smooth gradation of our sensations, and of measurable reflex actions?

Forbes tells us that the evidence will not permit us to think that sensory and motor fibres differ in any important respect. Assuming them to be much alike, we may still admit the following possibilities as we seek to explain how

increasing stimulation of receptive endings brings about increasing responses. First, stronger stimuli take effect on more numerous nerve-fibres. Second, very strong stimuli, though solitary, are capable of developing repeated nerve-impulses. Third, certain rhythms of stimulation favor the penetration of the gray matter by the resulting series of impulses; other rhythms are definitely unfavorable. It would not be profitable to follow the application of these guiding principles to the intricate mechanisms of the central nervous system. It is certain, however, that they will be employed in future analyses.

HIGH LEVEL NUTRITION.

Attention may be called to a protracted study in human nutrition reported by Gulick.³ It deals with over-feeding, and is thus complementary to previous investigations of the results of under-feeding, such as the elaborate one described in Publication 280 of the Carnegie Institution. Gulick made himself the subject of his experiments. By arbitrarily increasing the quantity of his food (without resorting to any artifices to make it more tempting) he carried his daily intake from about 2700 to about 4100 calories. In the course of many months he increased his weight by 10 kilograms, and attained to an equilibrium upon the new diet. Thus he added something like 50 per cent. to his ration, and operated his body with approximately 20 per cent. increase of mass.

These observations are on the whole consistent with the Carnegie findings. Benedict and his colleagues have shown that a man who sacrifices 12 per cent. of his original body-weight may do without some 40 per cent. of his former supply of calories. That is to say, he may maintain the new equilibrium, and still carry out the chief activities of his former program. Doubtless he conserves his muscular expenditures where he can. Summarizing the two studies, we may state that changes in weight are much smaller than changes in energy supply, whether one expands or contracts an allowance that has been habitual. One divergence between the results should be pointed out. Under-nutrition decisively cuts down the basal metabolism; during Gulick's period of excessive intake, this significant quantity remained practically unchanged.

THE PULMONARY EPITHELIUM.

As a rule, the accumulation of new data must be expected to add to the complexity of our conceptions. But now and then a welcome exception is noted: we find our interpretations simplified. Such an instance may be cited in connection with the physiology of respiration. Ten years ago the belief was strongly maintained by Haldane that the pulmonary epithelium can actively promote the movement of oxygen from the alveolar air to the blood. It was

taught that this secretory power came to be exercised at high altitudes and, in large measure, determined the success of acclimatization. An analogy was found in the well-known ability of the swim-bladder of the fish to secrete oxygen, albeit in an opposite way—from the blood to the lumen of the organ.

It has been difficult to credit the delicate endothelial cells of the lung with such a capacity, and it now appears that we are not obliged to make the assumption. Haldane had claimed that the tension of oxygen in the arterial blood of acclimatized subjects living at high altitudes might distinctly exceed the pressure of oxygen in the alveolar air. Such a state of affairs could hardly be explained without invoking a secretory process—an energetic transfer of oxygen to the blood. Careful experiments made last winter in the Peruvian highlands by British and American physiologists have failed to support the secretion hypothesis. Working at 14,000 feet, and using as subjects not only the members of their own group, but also the permanent residents, they found that the oxygen tension in the arterial blood was invariably below that in the alveolar air. Physical diffusion would therefore account for the passage of the gas into the blood.

If we are not permitted to include secretion of oxygen among the processes by means of which the organism maintains itself at high altitudes, we may still recognize the following factors as contributing to the adaptation. The number of corpuscles and the quantity of haemoglobin for a given volume of blood are both increased. The respiratory centre exhibits a modified activity, and by increasing the ventilation of the lungs, keeps the alveolar oxygen pressure nearer to the atmospheric than is the case at sea-level. Doubtless the vasomotor system gives efficient direction to the circulation. Surface relations between the air and the blood appear to be improved, and the permeability of the epithelium is probably increased.⁴

ALVAREZ ON THE ALIMENTARY CANAL.

An interesting monograph of the past year is the book by Alvarez.⁵ In it we have presented a body of evidence largely from original studies, emphasizing the autonomous capacities of the digestive tract. It is impossible in a brief abstract to do justice to the argument. The fundamental thesis is that the canal is normally characterized by a "metabolic gradient"—that the spontaneous rhythm of the musculature is progressively slowed as the successive segments are passed. In other words, we have here a condition comparable to that which we recognize in the heart. The auricle normally unloads to the ventricle, and acts as "pace-maker." We explain this by saying that the auricle has a superior rhythmicity; after it has executed a contraction it recovers, and is ready to repeat more promptly than is the case with the ventricle. In the same terms Alvarez would explain the

polarity of the intestine, and the usual advance of the peristaltic waves in a fixed direction.

He holds that reversal of peristalsis is a much more frequent occurrence than has commonly been assumed. It would be expected to set in if the irritability of any intestinal segment should be so intensified as to exceed that of the region next above. Such a change may conceivably result from inflammation. The contention is supported at length, and seems likely to modify long-accepted views. For several years Alvarez has maintained that the sensory symptoms of intestinal disorders are largely the result of mechanical conditions, and not of toxæmias. At this point he is supported by the recent work of Donaldson and his associates.⁶ These investigators, after personal trials involving no little discomfort, conclude that the ill feeling attending constipation is chiefly due to the mass of material distending the intestine, and to reflex disturbances therefrom, rather than to poisonous decomposition products.

DIFFERENTIATION OF MUSCLE.

One of the most revolutionary doctrines now before us is that which is advocated by Carey.⁷ He advances the opinion that the three contrasted types of contractile tissue found in the mammalian body owe their peculiarities to the use to which they have been subjected, rather than to any original characteristics. This is a dynamic theory of development. It suggests that smooth muscle, if persistently acted upon by a force alternately stretching it, and permitting it to contract, should acquire the nature and appearance of cardiac tissue. To test this possibility, Carey has patiently applied a distending pressure to the bladder of a young dog, injecting an antiseptic solution to fill the cavity of the organ, and then allowing it to empty itself. He reports that after a long course of these exercises the muscle cells from the bladder-wall have the microscopic aspect of cardiac elements. Such a finding, if confirmed, will be of the highest importance. It is certain to be rigorously examined.

REFERENCES.

- 1 Forbes and Miller: *Am. Jour. of Physiol.*, lxii, 1922, 113.
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- 3 Gulick: *Am. Jour. of Physiol.*, lx, 1922, 371.
- 4 Barcroft: *Lowell Institute Lectures*, 1922.
- 5 Alvarez: *The Mechanics of the Digestive Tract*. New York, Hoeber, 1922.
- 6 Donaldson: *J. A. M. A.*, lxxviii, 1922, 884.
- 7 Carey: *Am. Jour. of Physiol.*, lviii, 1921, 182.

TUBERCULOSIS OF ANKLE JOINT AND TARSUS.

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In the December 17, 1910, number of the *American Medical Association Journal*, Dr. James Warren Sever published an analytical study of the cases of tuberculosis of the ankle