

author gives the historical development which finally leads to the establishment of the identity of the enzymes pepsin and rennin, and suggests that curdling of milk is best explained by supposing that the curd is formed by the precipitation of a proteose of casein which is insoluble in acids and in water containing calcium salts. Cohnheim sadly but humanly remarks, "We meet here with one of the unfortunate cases in which science in stepping forward obliterates and renders useless the hard and skilful work of a whole generation of prominent men."

Of interest are the oxidative enzymes laccase and tyrosinase, which convert the aromatic cleavage products of protein into coloring matters which gradually become black. Laccase, of the lac tree, gives rise to oxyurushic acid which gives the brilliant black luster to the lacquer manufactured in Japan and China. Tyrosinase causes the production of coloring matter in the hemolymph of certain butterflies, it also attacks the proteins of the dead or dying leaves in the autumn and causes the brilliant coloring of the Indian summer; it is found in the ink-bag of the sepia; and to it may be ascribed the transformation of tyrosin into homogentisic acid in the human disease of alcaptonuria.

Written primarily for medical students, the above selections are merely an indication of the breadth of view from which the subject is surveyed.

The country should be grateful to Professor Cohnheim that, through the means of the Herter Lectureship Foundation, he has been able to add to its literature a treatise such as is "The Enzymes."

GRAHAM LUSK

SPECIAL ARTICLES

SYMPTOMATIC DEVELOPMENT OF CANCER

So little is apparently known of the external symptoms of internal cancer in its early stages that any contribution of attentive observation would seem useful. The following personal case is fairly paralleled by another which need not be described; and the parallelism would seem to give some weight to the inferences.

During my second expedition to Seriland in the autumn of 1895 my party had occasion to climb Sierra Seri, the culminating range of the region. After leaving the wagon camp the party moved on foot (with two pack animals) over some 10 miles of gently upsloping plain to the foothills, where the real climb began; the pace taken was rather rapid and I was somewhat but not excessively tired on reaching the foothills, where the pack horses were to be sent back. Within a few minutes after starting the climb I observed a condition novel in my experience—*i. e.*, inability to lift the feet (especially the left) more than a few inches above the level at which I stood. There was no pain, scarcely any discomfort—merely the inability to raise the feet without help from the hands. Assuming it a manifestation of exhaustion, I halted the party for a time and ate lunch; but, on resuming, the condition almost immediately returned. Greatly puzzled, I abandoned the climb and started back with the Indian in charge of the pack horses, finding no difficulty in going down-slope. Within fifteen minutes I was startled by a call from one of the remainder of the party making the climb, "El Gringo es muerto [The American is dead]." Even without explanation I knew this referred to W. D. Johnson, topographer of the expedition; and stimulated by the apparent tragedy I immediately turned to resume the climb to the point of the disaster—but despite the intense excitement, I had not climbed fifty steps before the former inability to lift the feet returned. So I remained in virtually helpless condition (sending my Indian up to the climbing party with specific inquiries) for perhaps half an hour; when the Indian returned with the gratifying intelligence that "El Gringo" had come to life and had gone on up the mountain—for it appeared that he had merely swooned under the stress of the long walk and the early stages of a stiff climb, and, recovering, had gone on with his accustomed persistence. This episode marked the first observed abnormality in locomotory powers which had been above the average.

The next noteworthy manifestation appeared during an expedition of 1900, when I frequently found myself unable to raise the left foot to the stirrup on mounting—indeed it became necessary generally to modify the attitude in mounting so as to permit giving a hitch upward to the left foot with the hand. Sometimes, too, on dismounting the left leg partially gave way; so that I acquired the habit of swinging out of the saddle in such a manner as to land on both feet. During subsequent months in office work I noticed an abnormal condition, though I failed at the time to associate it with that experienced in the field—*i. e.*, on rising after occupying my chair for a considerable time, either a sharp pain or a sensation of weakness was experienced in the left groin. This condition continued until the habit was acquired of rising with care and putting the weight at first wholly on the right foot.

In 1902 I noticed that the footfall sounds of my two feet as I walked the pavement were unlike; and I made considerable vain effort, sometimes with the help of friends, to find the reason for the asymmetry in movement indicated by the diversity in sound. This abnormality was not then associated with the abnormal conditions observed in field and office; but when within a year I noticed that the sole of the left shoe wore out twice as rapidly as that of the right I began to associate the several conditions, though without forming any idea as to cause.

In 1906 I suffered an epididymitis on the left; and in casting about for the cause of this attack my physician seemed so confident that it must be gonorrheal or syphilitic in origin (which I knew to be erroneous) that I gladly welcomed the occasion to have an expert blood examination made by a practitioner recently from a noted expert and school in London. The examination showed no trace of the infection suspected by the physician, but gained my confidence by detecting evidences of a typhoid fever through which I had passed some years previously; but it left the epididymitis totally unexplained.

About this time I made a trip through the Sierra Nevada region, largely in company with Gifford Pinchot, then Chief Forester, and J. A. Holmes, now Director of Mines; and in the course of the trip was much embarrassed by inability to climb or to ascend slopes of more than moderate degree—the trouble lying in the same inability to lift the feet first observed in Seriland.

In the autumn of 1909 while in field work in Washington state I noticed uncertainty in coordination of the control and movement of the left foot, especially in passing over slippery rocks or logs; and on one occasion suffered an accident of some severity due to a needless slip of the left foot. About this time also I noticed a slight bladder difficulty which continued increasingly for over a year—when treatment began for enlarged prostate. After preliminary examination and treatment of the conventional sort, prostatectomy was prescribed, and in April, 1911, I underwent the operation—which revealed a cancerous condition in which the carcinomatous tissue was of an exceptionally hard type, and too extended for complete extirpation. Recovery was tedious and complicated, and within a few weeks after leaving the hospital an epididymitis on the right developed—this time with little doubt in my mind as to the cause. The symptom of weakness and pain in the left groin also recurred with increased intensity, and a hitching gait was developed. The bladder never became completely normal; and in January, 1912, the lower intestine evidently became affected, producing assimilative difficulties of growing gravity.

In April, 1912—a year after the operation—a condition gradually developed on the tendons of the left knee similar to that first observed in the groin—the twinge of pain on sudden movement, inability to exercise full control, etc. The general burden on the system attending the abnormal development was noticed (without realization of the cause) about 1904, and increasingly thereafter.

Any significance this record may have lies

merely in bringing out the association between a series of obscure and puzzling symptoms developed in the course of several years, which finally seem to have found explanation in the cancerous growth revealed well toward the end of the series.

W J MCGEE¹

REVERSIBLE CHANGES IN PERMEABILITY PRODUCED
BY ELECTROLYTES

ACCORDING to one opinion permeability is a relatively fixed property of the cell and is altered only as the result of injury: the alteration is then irreversible.

Another view assumes that there are reversible changes in permeability which involve no injury and which may form a normal part of the activities of the cell. If such changes occur it is clear that they may control the course of metabolism. That permeability may be altered in this manner is suggested by a number of facts,¹ but their interpretation is too doubtful to place this view on a firm basis. It is highly important that its truth or falsity be established by rigorous proof. Such proof seems to be afforded by a series of experiments, some of which are described below.

The method pursued in these experiments has been described in a previous paper.² It consists in cutting disks of living tissue from fronds of the common kelp (*Laminaria*) and measuring their electrical conductivity in various solutions. Under the conditions of these experiments an increase or decrease of conductivity denotes a corresponding increase or decrease of permeability.

Upon transferring the living tissue from sea water to pure sodium chloride of the same conductivity (and at the same temperature) an immediate increase of conductivity was observed. The conductivity continued to increase at a regular rate for about two hours. At the end of this time the conductivity of the tissue was equal to that of the same

amount of sea water. At this point it remained stationary even when the tissue was replaced in sea water. This signifies that the tissue was dead.

In this case we are dealing with an irreversible change in permeability. It is natural to ask whether this change is not, up to a certain point, reversible. In order to test this, fresh living tissue was transferred from sea water to sodium chloride of the same conductivity (and at the same temperature); readings were then taken at intervals of two minutes. In the course of five minutes the resistance had fallen from 1,000 ohms to 850 ohms.³ The tissue was then replaced in sea water and readings were taken at intervals of five minutes. In the course of five minutes the resistance rose to normal and remained unaltered until the following day, when the experiment was discontinued. This experiment was repeated many times under different conditions and with a variety of salts. The results were similar throughout.

In order to make certain that no injury resulted from the treatment with sodium chloride an experiment was performed to ascertain the effect of repeated treatments on the same lot of tissue. In one experiment the tissue was treated with sodium chloride until the resistance dropped from 1,020 ohms to 890 ohms and was then replaced in sea water, after which the resistance rose to 1,020 ohms; this was repeated daily on the same lot of tissue for fifteen days. On the tenth day the tissue began to show a falling off in resistance, which continued to the fifteenth day, when the experiment was discontinued. As this falling off was also shown by the control, which was kept in sea water throughout the experiment, it was not due to the sodium chloride, but to other causes.

The objection may be made that in this experiment the increase in conductivity was due to an increase in the number of sodium ions and that these may normally penetrate the cell more easily than the other ions of the sea water: it might therefore be unnecessary

³ All the figures in this paper refer to readings taken at 18° C.

¹ Dr. McGee died on September 5, 1912.—*Editor*.

² For a recent summary see Höber, "Physikalische Chemie der Zelle und Gewebe," Kap. 7 und 10, Dritte Auflage, 1911.

³ SCIENCE, N. S., XXXV., p. 112, 1912.