5. When osteomyelitis complicates an operation on the frontal sinus it usually makes its appearance as a non-inflammatory oedema in the soft parts which cover the margin of the bony wound, and this sign is still more ominous if an area of oedema appears at some distance from the wound in the sinus. A coincident rise of temperature may be noted. If such a swelling be incised no pus escapes, but the wound does not heal and suppuration soon makes its appearance, while the oedema spreads still further.

The only treatment of any value in such case is to expose the frontal bone very freely and to remove its whole thickness involving a liberal area of healthy bone around the inflamed region. Delay and hesitation are unpardonable, while fomentations, incisions in the oedematous areas, or the administration of vaccines only betray the ignorance of the surgeon as to the grave condition of his patient.

6. As to the cause of the complication, my impression is that it is due to two details in faulty technique: (1) When the sinus is opened and the diploic spaces in the margin of the bony wound are exposed, infective material is introduced into them by curetting the walls of the sinus with a small sharp spoon. The diseased and pus-infected mucous membrane should be wiped away gently with small sterile swabs. (2) The lips of the wound in the soft parts should be left widely open and only the lightest packing placed in the sinus cavity. Since adopting these precautions I have experienced no anxiety in any of my cases.

It may not be out of place to state that opening an acute or chronic empyema of the frontal sinus by the intranasal method does not exclude the possibility of osteomyelitis of the frontal bone, for at least one case has already occurred, the details of which may be studied in the *Journal of Laryngology*, June, 1917, p. 186.

A NOTE ON THE ASSOCIATION OF HERPES ZOSTER WITH ARSENIC.

BY

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It is well known that arsenic administered in large quantity may have a harmful effect on the nervous system, both central and peripheral, and from time to time cases of herpes zoster have been recorded which have been ascribed to arsenic. Hutchinson was one of the first observers to point out this association.

Herpes zoster is looked upon commonly as being secondary to some change, either haemorrhage or inflammation, in the posterior root ganglia of the spinal nerves, but it has been recognized for a long time that the lesion is not confined to these ganglia. For instance, in some cases the cerebro-spinal fluid has been found to contain a well-marked lymphocytosis, pointing to involvement of the meninges, and in others the occurrence of Kernig's sign has suggested that the posterior roots have not escaped the inflammation.

Many cases of herpes zoster have been described which have been associated with, or followed by, a generalized vesicular eruption, and Dr. Parkes Weber¹ has recently summarized some of these. It has been suggested that herpes zoster is a modified and localized form of varicella, but the evidence of this is by no means conclusive. On many occasions the apparent connexion between these two diseases has been noted. There can be little doubt, however, that some of the cases were examples of a generalized shingles, but in others true herpes zoster appeared to have been produced from contact with a patient suffering from varicella, and vice versa.

The following case is of interest, as it relates both to the question of the association of arsenic with herpes zoster and also to the question of generalized herpes zoster:

A naval officer, aged 54, was seized during January, 1916, with an attack of multiple adenitis, together with paresis of the lower limbs and retention of urine. Except for the fact that he had spent twenty-three years in India there is nothing in his history which appears to have any bearing upon his illness.

He was a stout man of close on 15 st. in weight. On admission to Haslar on February 25th, 1916, he was found to

have almost complete paraplegia of the upper motor neurone type. The lymphatic glands in his cervical, pre-auricular, axillary, and inguinal regions were markedly enlarged and somewhat tender. There was no palpable enlargement of the spleen. The red cells were 4,500,000 and the white cells 3,000 per cubic millimetre. Of the latter, 50 per cent. were polymorphonuclears, and there were 2 per cent. of eosinophiles. The colour index was 0.77. His systolic blood pressure was 150 mm. of mercury. There were no visible haemorrhages. The Wassermann reaction of his serum was negative (Fildes). The cerebro-spinal fluid was not examined.

The connexion between the glandular enlargement and the paraplegia was not very evident, nor indeed was the nature of the adenitis. We were unable to obtain the consent of the patient to the removal of a gland. There was no evidence that the mediastinal glands were involved. Towards the end of March his general condition, other than that of the glands, had improved considerably. Treatment by liquor arsenicalis was commenced, and he continued with it until May 9th, 1916, when he went on convalescent leave.

On July 5th, 1916, he was readmitted, looking and feeling much better. He was able to walk quite well. The condition of the glands appeared to be about the same as when he was last seen. He told us that he had been taking the medicine throughout. On July 10th an eruption of herpes appeared on the right side of his abdomen. It assumed considerable dimensions, and covered roughly the area of skin corresponding to the eighth, ninth, and tenth dorsal segments of the cord. The eruption was not preceded by any pain but it was associated with pain when it was fully developed. By this date he had been taking 15 drops of Fowler's solution daily since March 23rd, a total of some 1,600 drops, or, roughly, 15 grains of arsenic. The eruption rapidly became generalized, vesicles appearing over the face, body, and limbs; the eyelids were considerably swollen. After a short time the eruption healed in the usual manner, and on July 28th the patient was discharged to his home. The condition of the glands was not materially altered. The temperature was normal throughout, except during the time when he was suffering from herpes.

REFERENCE.

¹ *British Journal of Dermatology*, March, 1916.

The Croonian Lectures

ON

ADAPTATION AND DISEASE.

DELIVERED AT THE ROYAL COLLEGE OF PHYSICIANS,
LONDON, JUNE 26TH, 1917.

BY J. G. ADAMI, M.D., F.R.S.,
TEMPORARY LIEUT.-COLONEL C.A.M.C.

LECTURE IV.

THE PHYSICO-CHEMICAL BASIS OF IMMUNITY AND
EVOLUTION.

(Abstract.)

In the previous lectures it had been shown that the studies upon pathogenic bacteria and upon immunity proved conclusively the existence of direct adaptation of a definite order, both in the lowest and in the highest forms of life. To the academic biologist such a suggestion of a direct action of external agencies as a prime cause of variation is as shocking and improper as would be the suggestion of a risqué story to some dear, modest elderly maiden lady. And yet it is along these lines that medical research is surely leading us.

Believing that we are in the right, where is it that the biologists have gone wrong? It was suggested that the

Photograph taken to show enlargement of glands and healing herpes on July 26th, 1916. A few of the generalized vesicles can be seen.

biologists, from the morphological trend of their studies, have perforce conjured up separate individual particles or structures, each the bearer of an individual property or group of properties. Their conceptions have perforce been in the terms of specific atomies. In his Pangenesis hypothesis Charles Darwin evolved such a conception, and in his great sanity cast it aside. Weismann rioted in such, with his *ids*, *idants*, and determinants, all figments of the imagination. The same tendency is shown and carried forward in full vigour by the modern Mendelians. It is because he cannot picture in his mind an atomy or structure suddenly making a first appearance in the germ cell, after the manner of Venus rising from the sea foam, that Professor Bateson finds it impossible to imagine the positive acquirement of new properties by the individual or the race. He found himself in the predicament of the late King George of glorious memory and muddled, who could not imagine how the apple got into the dumpling.

Suppose we start instead from known facts and known phenomena, and upon these endeavour to build up our idea of the nature of the germ cell and of the organic basis of heredity. First, as to the constitution of living matter—we know that whatever form of life we investigate, animal or plant, mammoth or microbe, whatever form we analyse, or whatever tissue, leaving out of account water and certain vehicular salts to which no specific vital functions can be attributed, just one order of highly complex compounds is common to and to be isolated from all, and these are the proteins. This universal presence in itself indicates that they are intimately associated with vital functions. When isolated chemically they are inert; in other words, living matter contains proteinogenous, rather than protein substances. A large portion of the lecture was taken up with a study of the chemistry of the proteins in relationship to metabolism; the huge size of the protein molecule, close to the limits of visibility under the highest power of the microscope; its great molecular weight; the impossibility of gaining identical analyses of two samples of the same protein, even if, like haemoglobin, crystallizable; the structure of these molecules; their dissociation into smaller complexes, the peptones; their further dissociation into amino acids; the synthesis of the polypeptids. The protein molecule may, therefore, be represented as a ring or chain of linked peptone molecules, each having its ring of glycocoll nuclei with swinging side-chains. In the much simpler bodies with which the organic chemist is in the main concerned, bodies like the carbohydrates or the benzol derivatives, we know how the transfer of a given radicle from the *alpha* to the *delta* position, for example, upon a ring, may bring about a profound change in the chemical and physical properties of the compound. When two carbon atoms are united together there are, or may be, six free affinities, and when these are satisfied by six different univalent groups, twelve different isomeric arrangements are possible. What must be the possibilities in a protein like haemoglobin, with 700 and more carbon atoms in the complex? and haemoglobin is simple compared with the nucleo-proteins.

If the biophores, or molecules of living matter, be at least proteinogenous, obviously it is not necessary to demand a separate determinant, a separate molecule for each specific property; it is simpler to regard properties inherent in the biophores as an expression of the constitution of the same, of the mode of linkage of the various nuclei, their number and the nature of their side-chains. This conception is within the bounds of physical possibility; Weismann's *ids* and *idants* certainly are not.

Accepting this conception of the chemical constitution of the essential living matter as a working hypothesis, we know that in conjugation the one element of the germ cells contributed in approximately equal portions by both parents to the zygote, or fertilized ovum, is the nuclear chromatin, and as heritage of properties may come equally from either parent, in the nuclear chromatin must reside the main heritable and character-determining material. The conclusion is inevitable that the essential biophoric molecules are conveyed in the nuclear chromatin. The cell wall, or membrane, the cytoplasm and the nuclear membrane, are all conservative agents, tending to preserve the biophores from sudden change from without, but while conservative, this system is exposed to constant change, particularly in the more active tissue cells. The system is not inert, but is constantly reacting with the external

medium in which the cell finds itself. The semi-permeable cell membrane, while preventing the entrance of some substances, freely permits the entrance of others, whether directly or after a preliminary dissociation into smaller molecules by the action of extracellular enzymes. Once foodstuffs are taken into the cytoplasm they are, if necessary, broken down into yet simpler molecules by intracellular enzyme action. Foodstuffs are not utilized by the cell as such, but only after dissociation and disintegration, and then either by oxidation to supply energy or, on the other hand, to be built up in growth.

This matter of growth is wholly neglected by the biologists. They speak of inorganic bodies (crystals) growing by agglutination, organic bodies by intussusception. "Intussusception," "imbibition," "intercalation," and "interpenetration" are all inane terms; they cannot possibly explain how two molecules of living matter appear where there was but one before, two grains of wheat where but one was put into the ground. Growth is one of the great underlying phenomena of living matter, and zoologists and botanists have in a simple Topsy-like manner been satisfied that the phenomenon occurs—and have left it at that. Increase in the amount of living matter means multiplication of the molecules of living matter, and this multiplication can only take place after the manner of the growth of a crystal, by ions arranging themselves into radicles, and radicles arranging themselves in a particular order, until in orderly sequence the necessary radicles become built up, identical in arrangement with the pre-existing molecule, in association with which the group has become developed. This conception is materially aided by the recognition that crystallization does not of necessity demand the production of rigid rectilinear figures. Lehmann in 1904 first called attention to the existence of "fluid crystals"; in 1906 Adami and Aschoff pointed out that these fluid crystals are frequent in the animal organism. As D'Arcy Thompson remarks, "The phenomenon of liquid crystallization does not destroy the distinction between crystalline and colloid forms, but gives added unity and continuity to the whole series of phenomena."

The lecturer then passed rapidly in review certain conclusions which develop out of this conception of living matter. Weismann's doctrine of the continuity of the germ plasm was shown to be erroneous; it is not the germ plasm which is eternal, merely there is a potential continuity of molecular arrangement and constitution. The functional and vegetative activities of the organism and the cell were passed in review, along with the essential nature of metabolism and enzyme action, all these in order to emphasize that these matters of adaptation and evolution have to be approached from the aspect of function and the dynamics of living matter, rather than from the point of view of cell statics. "Function precedes structure," and the study of cell function must afford the key.

As regards the acquirement of the new power of digesting and utilizing a foreign protein, it is seen from what has been said that these proteins are complexes of amino-acids, and the number of the individual amino-acids is limited. Proteolytic enzymes, already in existence, whether intracellular or extracellular, do not attack the foreign protein as a whole, but must be regarded as dissociating certain everyday amino-acids from the complex. But doing this, to take the simplest case, the relative number of molecules of the different amino-acids presented to the cell may come to differ from the normal; or, again, the simpler complexes due to the breaking down of the foreign proteins may not be identical in constitution with those which the cell and its biophores had been accustomed to utilize in growth. In either case the constitution of the biophores may become altered as they are built up. Where enzyme-like bodies such as the toxins and phytotoxins become introduced into the cytoplasm, their toxic function must be regarded as due to their power of dissociating the living molecules, by detaching certain radicles. If the toxin molecules be not present in too great a number, time is given for the living molecules to attract and build up again the lost radicles, and by the law of habit, if this process be constantly repeated, particular radicles are now built up in excess of the needs of the cell, and undergoing discharge become the antitoxin bodies of the blood and body fluids.

That this conception of the mechanism of immunity and

progressive adaptation is substantially correct was, he urged, strongly supported by the long-continued and admirable studies of Professor Victor C. Vaughan of the University of Michigan, and the later work of Abderhalden of Berlin and his pupils. These observations and their significance were discussed in some detail.

Colonel Adami next attacked the prevalent conception of the Mendelians that the parental unit-properties remain segregated in the germ cells. In the zygote, the fertilized germ cell, and in all the tissue cells derived therefrom, it is inconceivable that two orders of biophores or active living molecules can exist floating in a common nuclear sap, undergoing growth, building up side-chains and radicles, discharging certain of these or undergoing dissociation from time to time, without the two reacting upon each other and without a certain amount of interchange, without the one having a greater affinity for side-chains elaborated by the other, and building these into its system. There must be this interaction, and at a slower rate, due to their more latent state, this same interchange must take place in the germ cells. Along these lines it is still possible to interpret the facts of Mendelism, and indeed interpret not a few phenomena which by the hypothesis of determinants fail to obtain explanation.

Briefly, each species must be regarded as having for its essential living matter a distinct organic compound—a compound as distinct as any inorganic salt, but differing from that simpler salt in that whereas the central ring or chain is to be regarded as having a relatively fixed constitution, the radicles composing that ring or chain are to be regarded as capable of attracting and then reproducing a series of side-chains which may vary in constitution, so that within the species there may be various strains, just as we may speak of various strains of crystalline haemoglobin obtained from different samples of human blood.

It is possible to replace an impossible hypothesis based upon supposititious, independent, and transposable determinants by one based upon our present knowledge of the composition and properties of the main and outstanding constituent of living matter—the proteins. To one who regards life, not from the morphological point of view, in terms of form, but from the physiological, in terms of function, who regards life as a moving equilibrium, who regards it as in essence “a state of persistent and incomplete recurrent satisfaction and dissatisfaction of certain proteinogenous molecules” and metabolism as the primary and basal characteristic of living matter—for such a one Professor Bateson’s stumbling-block does not exist.

The Batesonian hypothesis of a backward evolution by the progressive removal of inhibitory factors, like the baseless fabric of a vision, fades into nothingness once it is confronted by the proof that direct positive acquisitions can be brought about experimentally. It enters into the limbo of the past as an example of the Spencerian tragedy—that of a deduction destroyed by a fact.

Memoranda:

MEDICAL, SURGICAL, OBSTETRICAL.

X-RAY TREATMENT IN LICHEN PLANUS.

In the following case the immediate relief and rapid disappearance of intense itching, the prompt subsidence of the eruption, and the restoration of healthy circulation in the hands under x-ray treatment, as evidenced by the freedom from cold hands, swollen fingers, chilblains, and frost bites during the past exceptionally severe winter, are worthy of notice.

The patient was a girl aged 12 years, of delicate constitution, subject to cold hands and swollen fingers even in the summer, and to very severe chilblains and frostbites in mild winter even. She was given galvanic and faradic Schnee baths on September 19th, 23rd, 27th, and 30th, October 7th and 20th last, with the view of improving the feeble circulation in the hands. On October 7th the patient complained of slight pain and smarting at the séance. On October 20th the pain and smarting were worse, and on careful examination a few scattered papules were noticed on the hands and more on the forearms. The swollen condition of the fingers and the cold feeling in the hands improved under galvanic and faradic treatment. By October 28th the eruption had extended to all the fingers of both the hands and more up the forearms, becoming confluent in most places. It was very itchy, and consisted of slightly elevated

violaceous papules of the size of pinheads, with flattened glistening top, slight central depression, and dry rough surface. There was a return of the swelling of the fingers. No more Schnee baths were given.

In spite of ointments and internal medicine there was a rapid extension of the eruption, and a decided aggravation of the itching and other symptoms. The itching was so troublesome as to interfere with proper sleep.

A mild stimulating dose of x rays was given on November 15th. This was followed by marked relief of the itching, which disappeared altogether in about a week. There was no further extension of the eruption, which looked darker and flatter. A second dose was given on November 22nd. The patient was now quite free from the troublesome itching, and there was a retrogression of the eruption. By December 4th, when a third treatment was given, the eruption had almost disappeared from the right hand and forearm, and only a little was left on the other side. The swelling of the fingers had also subsided. The last x-ray treatment was given on December 18th. Desquamation commenced soon after and continued till about December 31st. The remnants of the eruption and every trace of the complaint had altogether disappeared by that time.

Note.—The patient, it appears, had some spots on the forearms for a couple of months before the Schnee baths were given. Apparently the baths, instead of acting beneficially, aggravated the complaint.

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PREVENTION OF CEREBRO-SPINAL FEVER.

COLONEL PARKES’S communication¹ with reference to this subject is most interesting and instructive, especially to any one connected with soldiers. Last winter somewhat the same procedure was carried out by me in the battalion of which I am medical officer. I used three ounces of formalin to the gallon of water in a “Killgerm” sprayer. I had no opportunity to have the sick with infective throats examined bacteriologically, but all sick with any “catarrhs” were sent each morning to a large room in a billet, and whilst this was being sprayed the men were kept in it for twenty minutes. We had not the success of the New Zealanders in eradicating the disease. Out of a battalion whose strength at that time averaged 2,500 men, three cases of cerebro-spinal fever developed in the season.

The same treatment has been used again this season. The sprayer is set going in a large room each morning, and all “catarrhal sick” are put there for twenty minutes. I have varied the solution, sometimes using formalin and at others “pacolol,” which is really Pearson’s lysol. The latter is less irritating, and much preferred by the men. We have had so far one case of cerebro-spinal fever whose history is somewhat instructive. In the case of this patient there was no question of overcrowding. His room was on the sea front, containing 1,680 cubic feet, and there were four men in it.

Pte. N., after eleven weeks’ service, was passed fit for draft leave, January 31st to February 5th, 1917. On February 8th he reported sick, with eighteen of the same company, with sore throats and the usual catarrhal symptoms. He had no fever. Was ordered “medicine and no duty” on this and the following day; and “medicine and light duty” on February 10th. From the 10th to the 15th he went on duty and was apparently perfectly well.

On February 15th, at sick parade (7 a.m.), he reported ill, with diarrhoea and sickness. He was ordered “medicine and no duty.” At 2 p.m. he again reported, as directed; his temperature was then 103°, and he was dazed and almost collapsed. He was sent to hospital, and next day cerebro-spinal fever was diagnosed.

As a means of attacking the nasopharynx the steam sprayer is very well worth trial. I intend to use the 1 per cent. sulphate of zinc solution to see if there is any virtue in this drug.

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¹ BRITISH MEDICAL JOURNAL, February 24th, 1917, p. 262.

ACCORDING to the *Med. Klin.*, medical practitioners in Vienna are experiencing increasing difficulties in getting to and from their patients, owing to the shortage of vehicles and motor power. There are only a few motor cars and cabs available, and their proprietors refuse all but short journeys. For several months the electric trams have enabled practitioners to carry on, but, owing to the shortage of coal, this service has had to be greatly restricted. It is therefore proposed that doctors with patients in distant parts of the town should communicate over the telephone with colleagues living in these parts and get them to attend to the distant patient.