Almost all the zoologists and botanists will, however, return in September, with a ship hired for the purpose, and the remaining party will try to go further northward, west, or eastward, from the north-west part of Spitzbergen, where the expedition can obtain a sufficient depôt of English coal. We will also try to employ the brown coal of King's Bay; but I fear this supply is not to be relied upon.

XIII. "An attempt to apply Chemical Principles in explanation of the Action of Poisons." By W. H. Broadbent, M.D. Communicated by Dr. F. Sibson, F.R.S. Received June 18, 1868.

(Abstract.)

The starting-point in the inquiry has been the two following postulates :—

1. That there must be some relation between the substance administered and the animal organism, on which the effects depend.

2. That, so far as the substance is concerned, the basis of the relation can only be its chemical properties, using the term in its widest sense.

From these postulates follow certain corollaries :—

1. That the physiological and therapeutic action of the same substance must be similar in kind.

2. That the action of food, remedies, and poisons must be capable of explanation on the same principles.

3. That substances chemically allied should have similar physiological and therapeutic actions, or any diversity found to exist should be capable of explanation on chemical grounds.

The second of these deductions is taken as a guide in the present inquiry. Something is known as to the uses of the various classes of foods in the economy, and of the mode in which they subserve these uses; this knowledge may be applied in the endeavour to ascertain the mode of action of poisons.

The operations taking place in the animal organism may be divided into two great classes :—(α) for maintenance of structure, (β) for evolution of force. While mutually interdependent, they are distinct, and in character essentially antagonistic, structural and chemical elaboration on the one hand, oxidation or disintegration on the other.

The two great classes of food, organic and mineral, are in close relation with these. The organic foods build up the tissues, but ultimately undergo oxidation and yield force. The inorganic foods take a subordinate part in the composition of the textures; they do not yield force by oxidation, but they influence the nutritive processes. So also the organic remedies and poisons affect the evolution of force, mineral substances the organic processes.

(The action of mineral matters has been noticed elsewhere.)

The force evolved in the animal organism takes the form of heat, motion, and nervous action; but there are very important points of difference between heat on the one hand and nervo-muscular action on the other, both as to the part they take in the vital processes, and in the conditions of their evolution.

It is through their action on the nervous system that the powerful organic poisons destroy life; and in order to understand this action, it is necessary to consider closely the evolution of nerve-force, and to endeavour to realize the chemical conditions implied.

In the first place, the source of nerve-force is oxidation, and the seat of the oxidation is the nervous structures. This is generally admitted, and seems to be conclusively established by an analysis of the phenomena observed in experiments with a prepared frog's leg.

This admitted, it is to be noted—

1. That nerve-action is intermittent and of varying intensity, and that in addition to the presence of the oxygen brought to the nerve-structures by the blood, an impulse from without, or from some other part of the nervous system, is necessary to determine the evolution of the force.

2. Again, there is a storing up of potential energy in the nervous structures; witness the necessity for sleep, &c.

3. A due supply of oxygen is required. The phenomena of asphyxia show that the demand is most urgent in the hemispherical ganglia.

These facts indicate that the constituent of the nervous structures by oxidation of which the force is yielded, possesses what I have ventured to call chemical tension, a property which does not belong to non-nitrogenized matter, or to all nitrogenized matter. It will be further explained later; for the present, it is sufficient to refer to nitroglycerine as an extreme example.

The protagon of Liebreich, and the neurine recently identified by Wurtz, with hydrate of trimethyl-oxethyl-ammonium, have this characteristic in a certain degree.

Turning now to the poisons which kill by their powerful action on the nervous system. They all contain nitrogen, and all possess chemical tension; and these seem to be the only points common to the entire group.

Nitrogen cannot be the poisonous element; it has no great chemical energy, and it is present in large proportion in substances which are inert. It is nevertheless the pivot on which the deadly influence turns. Its affinity for H, O, and especially for C, is only feeble. When, therefore, in a molecule containing C, H, and N, or C, H, N and O, the elements are not so arranged that the mutual affinities of C, H, and O cooperate to maintain the integrity of the molecule; there may be a more or less powerful tendency on the part of C, H, and O to rearrange themselves without regard to the N, or to combine with O or H_2O if presented. This is what is meant by the term chemical tension. In the example given, nitroglycerine $\{C_3H_5(NO_2)_3O_3\}$, the dislocation is of O from N in favour of C and

H. Equally striking examples of dislocation of N from C or H cannot be given, and it is not easy in all cases to point out the source of the tension. A very important method in which the balance of affinities is deranged and the condition of tension brought about, is by departure from a stable type, as, for instance, in the nitrite bases, which are residues derived from ammonium-salts by dehydration. To this class belong morphia, strychnia, brucia, and most poisonous alkaloids. Additional interest is given to these compounds by the fact that Dr. Crum Brown and Dr. Fraser have shown that, by introduction into the molecule of methyl-iodide, carrying back the constitution a step in the direction of the ammonium type, the poisonous effects are greatly diminished, and entirely altered in character.

Let the deduction as to the evolution of nerve-force be accepted, and we have in the introduction into the blood of substances having varying degrees and directions of tension an intelligible method of influencing its manifestations.

Looking now upon nerve-action as a result of oxidation, in the various methods by which this oxidation may be influenced, analogies may be traced with conditions which affect ordinary combustion. These conditions are—

1. The supply of oxygen.

2. The character of the combustible.

3. The presence of products of combustion, or of bodies having a similar influence.

It is of course necessary to bear in mind the peculiarities of the oxidation yielding nerve-force, the differences between combustion and oxidation in the moist state, and the special modifying conditions of the animal organism. For example, while in asphyxia the deprivation of oxygen arrests all nervous action, the respiration of undiluted oxygen does not intensify it, either because the blood will only take up a certain proportion of oxygen, or more probably because the effects of the O are expended in altering the blood, which is thus oxidized instead of being oxygenated.

The analogies to the above conditions found in the action of substances on the nervous system are—

1. The liberation in the nascent state in the nervous structures of C and H, which appropriate the O brought by the blood, and so produce a result equivalent to the exclusion of O. The C and H are set free by the dislocating influence of N, and the example of this mode of action is furnished by prussic acid.

The converse of this, the liberation of O by a similar process, is not likely to occur, as O is never present in an organic body in excess of the proportion which would fully oxidize the other elementary constituents.

2. The analogy to the influence on the energy of combustion by the

character of the combustible, is found in the introduction into the blood of substances having chemical tension, holding different relations to the tension of the nervous matter.

3. The action of anæsthetics on the nervous system furnishes a strict parallel to the influence of CO_2 on combustion.

The rationale here given as to the action of anæsthetics is, for the purposes of the present paper, taken as established by the late Dr. Snow. Objections which have been made to it are capable of removal by experiments and considerations which need not here be adduced.

Considerable importance is attached to the establishment of the explanation here given of the action of prussic acid. Stated more explicitly, this explanation is, that the prussic acid is carried by the blood to the nerve-centres; that under the influence of the affinities thus brought to bear upon it (affinities which normally determine the oxidation by which nerve-force is evolved), its elements are dislocated from each other, and the C and H liberated in the latent condition appropriate the O destined for the evolution of nerve-force which is thus arrested.

This explanation is suggested by the composition of hydrocyanic acid, H Cy. Cyanide of potassium KCy, again, is used as a powerful reducing agent in chemical processes. Its liability to the change which will permit its elements to exercise their individual affinity for O, is indicated by its spontaneous decomposition in water, by its position as a nitrile (formio-nitrile). Corroborative evidence that it is by means of such a change that it acts, is furnished when the elements are held together by some supporting affinity, as in ferro-cyanogen. But the best example is in sulphocyanogen and hydrosulphocyanic acid, which of themselves are poisonous (*i. e.* cannot resist the dislocating influences), but, reinforced by a base, are innocent. [A parallel to this is seen in aniline, which is poisonous, and in sulphate of aniline, which is not. See Lond. Hosp. Reports, Dr. Letheby.]

The phenomena by poisoning by prussic acid are perfectly consistent with this view. All observers have noted their similarity to those of asphyxia.

Still more striking is the fact that artificial respiration, and especially with oxygen, is the great means of neutralizing the effects of this poison.

Probably this chain of facts would be considered conclusive, were it not that the hypothesis as to the mode of death by H Cy is paralysis of the respiratory movements. This hypothesis, however, still leaves unexplained the cause of the paralysis itself, and therefore the real mode of action of the poison. It is, moreover, inconsistent with certain of the phenomena; the respiratory nerve-centres are actually the last to be paralyzed, except those concerned in the action of the heart.

Experiments nevertheless have been made for the purpose of ascertaining whether the previous respiration of undiluted oxygen would retard, or in

any measure prevent the action of prussic acid. The results have been by no means uniform; but instances have occurred (rats being the animals used) in which, after the injection of an overwhelming dose, the fatal effect has been delayed quite beyond the operation of accidental causes; and again, in which a dose fatal to two rats, and barely survived, after a long train of symptoms, by one other, produced comparatively little effect on another after the respiration of oxygen.

It has been found also that a proportion of prussic acid diffused in equal volumes of air and of oxygen, has a decidedly less powerful action on the animal in the latter case.

With frogs the results were most contradictory and embarrassing, till it was discovered that prussic acid injected under the skin had scarcely any action on them. But if they were subsequently placed under a glass shade, or in some other confined atmosphere, into which the acid diffused, it would gradually affect them. It seems probable that the affinities in operation in the nervous structures of the frog are not sufficiently energetic to determine the decomposition of the H Cy, which will then act upon this animal as an anæsthetic.

Nitroglycerine was at first made the subject of experiment, under the idea that possibly oxygen might be evolved from the NO_2, which is substituted for three equivalents of H in the typical molecule. Subsequent reflection showed that this is not likely to occur; but the fact remains, that it is a substance liable to change, and very highly charged with oxygen, as compared with the ordinary constituents of the body.

It is a very powerful poison, having, however, entirely different effects on frogs and rats.

In frogs it very speedily induces powerful tetanic convulsions (a single drop of a solution of one pint of nitroglycerine in four parts of methyl in alcohol placed on the back of a frog is followed in five or eight minutes by stiffness of movement, and in thirteen to sixteen minutes by most violent spasms). In rats an hour or more elapses before any symptom is manifest, and then death is by a gradually increasing feebleness of movement, in two or three hours, without convulsion.

It is unquestionable that this difference in the effects has a relation with the oxygen contained in the nitroglycerine. The contrast with prussic acid in the action on warm and cold-blooded animals is suggested.

A very extended and comprehensive inquiry, both as to the conditions in the nervous system associated with convulsions, tetanus, delirium, &c., and into the relations and constitution of the poisons which give rise to these symptoms, is necessary before the second analogy can be followed out with any confidence. Experiments are being made with substances of known composition and constitution, with a view to elucidate this part of the question.

In conclusion, two points are considered which cannot be passed over in

any attempt to apply the principles of physical and chemical science to the case of poisons.

The first is as to the minuteness of the fatal dose. Any explanation, before it can be accepted, must show that the cause is adequate to produce the effect. This is a difficulty in the path of any rational explanation. It is attempted to meet it by showing, on the one hand, that the equivalency of nerve-force is extremely small, by reference to its analogy with electrical currents, and by other considerations, and that therefore the degree of chemical change involved in its evolution is also small; and, on the other hand, the maximum of force to be obtained from an organic body is through the exercise of the affinities of its individual elements.

The second point is as to the special action of certain poisons on particular nervous centres,—strychnia on the cord, morphia on the brain, &c., the substances being carried by the blood to all alike. It is as necessary to explain why no effect is produced on those centres, or tracts which do not suffer, as to explain the action on the one which does. The explanation is sought in the fact that the difference in the functional activity of the brain and cord, the need for sleep by the brain, not experienced, at any rate in the same degree, by the cord, point to a difference of tension, and therefore of relation with the substances which act as poisons. This consideration will apply where the differences of susceptibility and of tension are not so marked.

But this is only part of a still wider question—the different action of poisons on different classes of animals. The explanation is still the same. Difference in the functional energy or activity of corresponding nerve-centres implies difference of tension.

The following facts bear strikingly on this point:—

1. Anæsthetics affect all classes of animals alike, *i. e.* when the effect is a general arrest of oxidation.

2. Strychnia, which acts on the cord, affects all animals alike. The spinal system is the centre which is most similar in its endowments in all classes of vertebrates.

3. The poisons which have the most diverse action on different animals are such as in man act on the cerebral ganglia.

XIV. "On the Communication of Vibration from a Vibrating Body to a surrounding Gas." By G. G. Stokes, M.A., Sec. R.S., Fellow of Pembroke College, and Lucasian Professor of Mathematics in the University of Cambridge. Received June 18, 1868.

(Abstract.)

In the first volume of the Transactions of the Cambridge Philosophical Society will be found a paper by the late Professor John Leslie, describing