of several hundred atmospheres may facilitate some of the chemical changes involved in the transformation of water and carbonic acid into the organic compounds met with in animals and plants of low organization found at great depths in the ocean, and thus to a certain extent compensate for diminished light. I, however, most willingly admit that very much remains to be learnt before we can say to what extent the principles I have described are applicable; and yet, at the same time, cannot but think that henceforth they must be taken into account in many departments of chemical and physical geology, and will readily explain a number of facts which otherwise would be very obscure.

May 7, 1863.

Major-General SABINE, President, in the Chair.

In accordance with the Statutes, the names of the Candidates recommended for election into the Society were read from the Chair, as follows:—

Edward William Cooke, Esq., A.R.A.
William Crookes, Esq.
James Fergusson, Esq.
Frederick Field, Esq.
Rev. Robert Harley.
John Russell Hind, Esq.
Charles Watkins Merrifield, Esq.
Professor Daniel Oliver.
Frederick William Pavy, M.D.
William Pengelly, Esq.
Henry Enfield Roscoe, B.A.
Rev. George Salmon, D.D.
Samuel James Augustus Salter, M.B.
Rev. Arthur Penrhyn Stanley, D.D.
Colonel Frederick M. Eardley Wilmot, R.A.

The following communications were read:—

I. "On the Physiological Properties of Nitrobenzole and Aniline." By Henry Letheby, M.B., F.L.S., &c., Professor of Chemistry, and late Professor of Toxicology in the Medical College of the London Hospital. Communicated by Dr. Sharpey, Sec. R.S. Received April 23, 1863.

It is on record that Thrasyas, the father of Botany, was so skilled in the preparation of drugs, that he knew how to compound a poison

which would remain for days in the living body without manifesting its action, and would at last kill by a lingering illness. Theophrastus speaks of this poison, and says its force could be so modified as to occasion death in two, three, or six months, or even at the end of a year or two years. The writings of Plutarch, Tacitus, Quintilian, and Livy are full of instances of what seem to be this kind of slow and occult poisoning. In fact, until recently there has been a common belief among the unlearned that a skilful poisoner could so apportion the dose and combinations of certain subtle agents that he could destroy the life of his victim with certainty, and at the same time measure his allotted moments with the nicest precision, and defy the utmost skill of the physician and the chemist. Even so late as the 16th century this belief was shared by the learned of the medical profession; for we are told, in Sprat's 'History of the Royal Society,' that among other questions which were drawn up by the earlier Fellows to be submitted to the Chinese and Indians was, "Whether the Indians can so prepare that stupefying herb, *Datura*, that they make it lie several days, months, years, according as they will have it, in a man's body without doing him any hurt, and at the end kill him without missing half an hour's time?"

Modern toxicologists have long since discarded these notions, and have set them down to the vague fears and exaggerated fancies of the ancients, rather than to the sober contemplation of facts. But the account which I am about to give of the physiological properties of nitrobenzole will show that there is one substance, at least, which realizes to a great extent the extraordinary opinions of the ancients. This compound may be given today, and yet, if the dose be not too large, it shall not manifest its action until tomorrow, or the day after, and shall then destroy life by a lingering illness, which shall not only defy the skill of the physician, but shall also baffle the researches of the medical jurist. These facts are so remarkable, that they would be hardly credited if they were not susceptible of the proof of demonstration. They are likewise the more interesting and important from the circumstance that nitrobenzole is now a common article of commerce, and is accessible to everyone.

In every manufactory where nitrobenzole and aniline are prepared on a large scale, the peculiar narcotic effects of these poisons are often observed. The vapours escaping into the atmosphere are breathed

by the workmen, and cause distressing headache and a heavy, sleepy sensation. For the most part these effects are not serious, but are quickly relieved by fresh air and a mild stimulant, as a glass of brandy and water. Now and then, however, the workmen, from carelessness in their habits, expose themselves to the action of comparatively large quantities of these poisons, and then the effects are most dangerous. Two fatal cases of poisoning by nitrobenzole have been referred to me by the coroner for investigation during the last two years, and in both instances they were the results of careless manipulation. In one case a man, forty-three years of age, spilt a quantity of the liquid over the front of his clothes, and he went about for several hours in an atmosphere saturated with the poison. In the other a boy, aged seventeen years, received a little of the liquid into his mouth while sucking at a siphon. The effects were nearly the same in both cases, notwithstanding that in one the poison was inhaled, and in the other it was swallowed. For some time there was no feeling of discomfort beyond that of drowsiness; gradually, however, the face became flushed, the expression stupid, and the gait unsteady—the sufferers had the appearance of persons who had been drinking. Little by little this stupor increased, until it passed into profound coma, and in this condition they died. The progress of each case was much the same as that of slow intoxication, excepting that the mind was perfectly clear until the coming on of the fatal coma. This was sudden, like a fit of apoplexy; and from that moment there was no return of consciousness or of bodily power—the sufferer lay as if in a deep sleep, and died without a struggle. The duration of each case was nearly the same; about four hours elapsed from the time of taking or inhaling the poison to the setting in of the coma, and the coma lasted for about five hours.

After death there were no appearances of convulsion, but rather of narcotism and apoplexy. The face was flushed; the lips were livid; the superficial vessels of the body, especially about the throat and arms, were gorged with blood; the dependent parts were turgid; the blood was everywhere black and fluid; the lungs were somewhat congested; the cavities of the heart were full; the liver was of a purple colour, and the gall-bladder distended with bile; the brain and its membranes were turgid, and in the case of the man there was much bloody serosity in the ventricles. Analysis discovered the

existence of nitrobenzole in the brain and stomach, and also of aniline.

These effects were so remarkable, that I determined to examine them still further by experiments on domestic animals. Dogs and cats were submitted to the action of from thirty to sixty drops of nitrobenzole which had been well washed with dilute sulphuric acid and water to free it from every trace of aniline. The poison was generally administered by pouring it into the mouths of the animals, but sometimes it was given by means of an œsophagus-tube. When the nitrobenzole had come into contact with the mouth, it always caused discomfort, as if from unpleasant taste, and there was profuse salivation. Its local action on the stomach, however, was never very great, for there was rarely any vomiting until the setting in of nervou symptoms, and this seemed to be due to sympathy rather than to any local irritation of the stomach. Two classes of effects were clearly observed: there was either the rapid coma which characterized the operation of the poison on the human subject, or there was a slow setting in of paralysis and coma, after a long period of inaction.

When the effects were speedily fatal, the animal was soon seized with giddiness and an inability to walk. The weakness of the limbs first appeared in the hind extremities, and was manifested by a difficulty in standing; but very soon it extended to the fore legs, and then to the head and neck. There was complete loss of voluntary power. The animal lay upon its side, with its head drawn a little back, and with its limbs in constant motion, as if in the act of walking or running. The muscles of the back were occasionally fixed in spasm, and every now and then the animal would have a sort of epileptic fit. It would look distressed, would howl as if in pain, and would struggle violently. After this it would seem exhausted, and would lie powerless. The pupils were widely dilated, the action of the heart was tumultuous and irregular, and the breathing was somewhat difficult. For some time, however, the animal retained its consciousness, for it would look up, and wag its tail when spoken to; but suddenly, and often at the close of a fit, it would become comatose—the eye would remain open, but the conjunctiva would be insensible to touch, and the movements of the limbs would nearly cease; the breathing would be slow and somewhat stertorous, and the animal would appear as if

it were in a deep sleep. This condition would last until it died—the time of death varying from twenty-five minutes to twelve hours after the administration of the poison.

When the action of the poison was slower, there was often no visible effect for hours or days. At first there was always a little discomfort from the taste of the poison, but this soon subsided, and then for a day or more the animal appeared to be in perfect health. It would go about as usual, would be quite lively in its movements, would eat its food heartily, and in fact would seem to be in no way affected by the poison. Suddenly, however, it would look distressed, it would have an attack of vomiting, and it would tumble over in an epileptic fit. When this had subsided, it was generally found that the animal was weak, or even quite paralysed in its hind extremities; and after two or three of such attacks, the loss of voluntary power would extend to the fore limbs. The animal would lie upon its side perfectly helpless; and then the progress of the case was much the same as that already described, except that it was considerably slower. Consciousness, for example, would be retained for days after the animal was paralysed, and, although it was quite unable to stand, it would take food and drink when they were put into its mouth. The condition in which it lay was most distressing: the look was anxious and full of fear; the limbs were in constant motion; and every now and then there would be a violent struggle, as if the animal was in a fit, or was making fruitless efforts to rise. This would last for days, and then there would be either a gradual restoration of voluntary power with complete recovery, or death from exhaustion. The time that elapsed from the administration of the poison to the coming on of the first symptoms, namely the epileptic fit, varied from nineteen hours to seventy-two—in most cases it was about two days; and the time of death was from four to nine days.

The *post-mortem* appearances were nearly the same in all cases, whether the death was quick or slow. The vessels of the brain and its membranes were extremely turgid; the cavities of the heart were full of blood; the lungs were but slightly congested; the liver was of a deep purple tint, and the gall-bladder distended with bile; the stomach was natural, without sign of local irritation; and the blood all over the body was black and uncoagulated. Whenever the progress of the case had been quick, and death had taken place within twenty-four

hours, the odour of the nitrobenzole was clearly perceptible in the stomach, the brain, and the lungs; and there was always unmistakeable evidence of the existence of aniline in the organs of the body. In the slower cases the odour of the poison had often entirely disappeared; but generally there were distinct traces of aniline in the brain and urine, and sometimes in the stomach and liver; occasionally, however, no poison was found.

It has appeared to me that the facts which are here elucidated are very remarkable; for they not only indicate a rare circumstance in toxicology, namely, that a poison may be retained in the system for many days without showing its effects, but also that the poison may be changed into an entirely different substance. The importance of these facts cannot be overrated; they are alike interesting to the chemist, the physiologist, and the medical jurist; for, without dwelling on a very possible occurrence—namely, the criminal administration of this poison, with the knowledge that the effects would be delayed, that the symptoms would correspond to those of natural disease, that the progress of the case would be lingering, and that there would be either no discovery of poison in the body, or the discovery of a thing different from that administered—it will be manifest that the study of these facts by the medical jurist is of public importance. To the physiologist they are also interesting, insomuch as they indicate a reducing power in the animal body by the conversion of nitrobenzole into aniline. I have endeavoured to ascertain whether this is due to a living or a dead process. In the first place, I find that dead and decomposing organic matter will effect the change alluded to; for when nitrobenzole is placed in the dead stomach, or is kept in contact with putrid flesh for several hours, there is a partial reduction of it into aniline. This may be the source of the poison found in the dead body; but, on the other hand, there is a great similarity in the physiological effects of nitrobenzole and those of aniline.

When aniline is given to dogs and cats in doses of from twenty to sixty drops, it causes rapid loss of voluntary power. The animal staggers in its gait, looks perplexed, and falls upon its side powerless. Its head is drawn back, the pupils are widely dilated, there are slight twitchings or pasms of the muscles, the breathing is difficult, the action of the heart is tumultuous, and the animal quickly passes into a state of coma. From this it never recovers, but remains upon

its side as if in a deep sleep, and so dies in from half an hour to thirty-two hours.

The *post-mortem* appearances are much the same as the last: the brain and its membranes are turgid, the cavities of the heart are nearly full of blood, the lungs are but slightly congested, and the blood all over the body is black and uncoagulated. In every case the poison was easily discovered in the brain, the stomach, and the liver.

While, however, there seems to be a probable conversion of nitrobenzole into aniline in the living animal body by a process of reduction, there is also undoubtedly a change of an opposite character going on upon the surface of the body, whereby the salts of aniline are oxidized and converted into *mauve* or *magenta* purple. Some remarkable facts illustrative of this have been brought under my own notice, and have been the subject of clinical observation.

In the month of June 1861, a boy aged 16 was brought into the London Hospital in a semi-comatose condition. He had been scrubbing out the inside of an aniline vat, and while so doing he breathed an atmosphere charged with the vapour of the alkali, and became insensible. He did not suffer pain or discomfort, but was suddenly seized with giddiness and insensibility. When he was brought to the hospital he looked like a person in the last stage of intoxication: the face and surface of the body were cold, the pulse was slow and almost imperceptible, the action of the heart was feeble, and the breathing was heavy and laborious. After rallying a little, he complained of pain in his head and giddiness. It was then noticed that the face had a purple hue, and that the lips and lining membrane of the mouth and the nails had the same purple tint. The next day, although the narcotic effects of the poison had passed away, he was still remarkably blue, like a patient in the last stage of cholera.

In the early part of last year, sulphate of aniline was given in rather large doses to patients in the London Hospital affected with chorea. The doses ranged from a quarter of a grain to seven grains. They were frequently administered, so that large quantities of the salt were taken in a very short time. In one case as much as 406 grains were given in the course of a few days. No very remarkable effects followed beyond this—that after a few doses had been taken, and the system had become, as it were, saturated with the salt, the

face became of a leaden blue colour, the lips and gums looked as if the patients had been eating black currants, and the nails also acquired a purple hue. The colour faded a little before the time came for the administration of another dose, but soon after taking it it appeared again; and this was the subject of constant observation. Dr. Fraser and Dr. Davies have recorded the results of their experience in five cases *, from which it would seem that, although the free alkali is a powerful poison, the sulphate of it has but little action upon the animal body.

The general conclusions which appear to me to be warranted by these investigations are:—

1st. That nitrobenzole and aniline in its free state are powerful narcotic poisons.

2nd. That they exert but little action, as local irritants, on the stomach and bowels.

3rd. That although the effects may be quick, and the fatal termination of them rapid, yet nitrobenzole may remain in the system for a long time without manifesting its action.

4th. That the salts of aniline are not nearly so poisonous as the free alkali.

5th. That in rapid cases of fatal poisoning, both the poisons are readily discovered in the dead body.

6th. That in slow cases the poisons may be entirely changed or eliminated, and therefore not recognizable.

7th. That both of the poisons appear to be changed in the body by processes of oxidation and reduction, nitrobenzole being changed into aniline, and aniline and its salts into mauve or magenta.

In an appendix † are given notes of the two cases of fatal poisoning by nitrobenzole referred to in the paper, and a detailed account of twelve experiments on animals with nitrobenzole, and three with aniline; also the process employed for the recognition of aniline and nitrobenzole in the dead body, as follows:—

1st. The matters to be analysed were bruised in a mortar with a little water, and very slightly acidulated with dilute sulphuric acid.

* Medical Times and Gazette, March 8th, 1862, p. 239.

† Preserved in the Archives.

2nd. They were then submitted to distillation in a glass retort—the distilled products being saved in three or four separate portions by changing the receiver at different stages of the process. In this way the presence of nitrobenzole was discovered.

3rd. The residue in the retort, when reduced to a pulpy mass by the distillation, was treated with strong spirit of wine and filtered.

4th. The filtered alcoholic solution which contained the aniline was treated with a slight excess of subacetate of lead, and again filtered. In this way gum, dextrine, &c. were removed.

5th. The filtered solution was treated with a slight excess of a saturated solution of sulphate of soda in water. In this manner the excess of lead was precipitated as a sulphate.

6th. The clear solution was then made very alkaline with caustic potash, and distilled to dryness from an oil-bath. The aniline, together with ammonia from the animal matters, was found in the clear, colourless, distilled spirit.

7th. This was neutralized, or rather made acid, with a slight excess of dilute sulphuric acid, and evaporated nearly to dryness in a white porcelain dish. If necessary, the spirit was saved by distillation.

8th. The residue was of a pinkish colour if aniline was present, and occasionally there were little streaks of blue around the edges of the white porcelain dish. If the quantity of the saline residue was not more than a grain or so, it was at once tested by dissolving it in a few drops, or even in a single drop, of dilute sulphuric acid (1 to 1). A small portion of it was then placed upon a strip of bright platinum; and the platinum having been connected with the positive pole of a single cell of a Grove's battery, the liquid was touched with the negative pole: in a few seconds, if aniline was present, the liquid would acquire a bronze, a blue, or a pink colour; the kind of colour being dependent on the amount of aniline present—bronze being the result of much aniline, and pink of a very little. In this way at least the $\frac{1}{2000}$th part of a grain of aniline was easily recognized.

To another portion of the acid liquid placed upon a white porcelain plate, a little peroxide of lead or red prussiate of potash was added, and a blue or purple reaction followed. This test is not so delicate as the last, for it fails when the amount of aniline is less than the $\frac{1}{1000}$th of a grain.

Other tests may be resorted to if necessary, as when the quantity

of aniline is large. Thus peroxide of manganese or bichromate of potash may be used in the same way as the red prussiate of potash in the last experiment; but these tests will not answer with less than the $\frac{1}{500}$th of a grain of aniline. Lastly, a drop of a solution of chloride of lime may be added to the acid liquid, and if the quantity of aniline exceeds the $\frac{1}{100}$th part of a grain it will cause a purple reaction.

9th. If the quantity of saline residue from the last operation is large, and there is reason to believe that much ammonia is present, this alkali must be got rid of, for it greatly interferes with the success of the colour-experiments. The residue, therefore, is made moist with water, and rubbed down with about twice its bulk of neutral carbonate of soda. It is then exposed to the air for a short time until the odour of ammonia has passed away. It is then treated with strong alcohol, filtered, acidulated with dilute sulphuric acid, and again evaporated. The aniline is now fit for the colour-experiments.

There are no fallacies to these experiments; for although, as I have elsewhere shown, strychnia will give nearly the same colour-reactions, yet in the first place this alkali is not volatile like aniline, and will not therefore distil over as the latter does; and in the next place, while the best effects, in respect of colour, are developed with dilute acid and aniline, strychnia requires the concentrated acid. These differences are sufficient to prevent any embarrassment as regards the two alkaloids.

II. "On the Immunity enjoyed by the Stomach from being digested by its own Secretion during Life." By Frederick W. Pavy, M.D. Communicated by Dr. Sharpey, Sec. R.S. Received April 29, 1863.

(Abstract.)

The author stated that the opposition which his view on the above subject received the evening of its announcement, in his former communication read January 8, 1863, had induced him to perform a series of additional experiments. As from these experiments some important confirmatory evidence was supplied, he deemed it desirable to present a further communication to the Society on the subject.

He had again denuded the stomach of a patch of mucous mem-