

On the physiological and medicinal properties of bromine and its compounds : also on the analogies between the physiological and medicinal properties of these bodies, and those of chlorine and iodine, with their correspondent compounds : being the Harveian Prize Essay for 1842 / by R. M. Glover.

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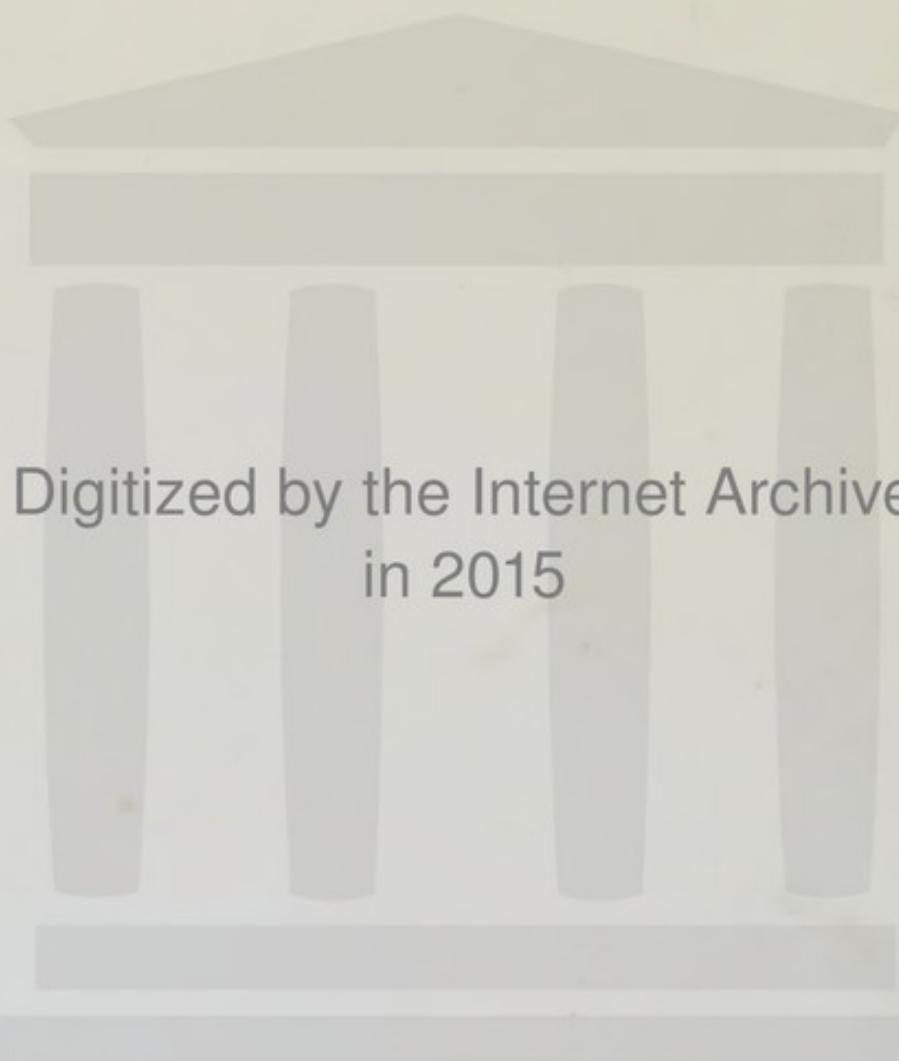
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ON
THE PHYSIOLOGICAL AND MEDICINAL
PROPERTIES
OF
BROMINE AND ITS COMPOUNDS;
ALSO ON THE
ANALOGIES BETWEEN THE PHYSIOLOGICAL AND
MEDICINAL PROPERTIES OF THESE BODIES, AND
THOSE OF CHLORINE AND IODINE, WITH THEIR
CORRESPONDENT COMPOUNDS;

BEING THE HARVEIAN PRIZE ESSAY FOR 1842.

By R. M. GLOVER, M. D., EDIN.
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(*From the Edinburgh Med. and Surg. Journal, No. 152.*)

BROMINE and some of its compounds are known to possess great energy of action on the animal system. The element and many of its compounds are interesting from the chemical analogies which they offer with well-known medicinal agents. Exact and beautiful chemical relations subsist between chlorine, bromine, and iodine, and between their compounds. Hence, a more complete investigation than has yet been recorded of the physiological and medicinal properties of bromine, and of the mode in which they are affected by combination of the element with other bodies, must appear likely, besides the more particular results, to contribute to the solution of a problem of the highest interest, viz. the extent to which the chemical analogies of bodies are accompanied by analogy of action on the living system.

Generalizations of the kind alluded to are valuable as guides in therapeutics on account of the great difficulty which exists in ascertaining the effects of remedies. Having before us as data, the possession of certain physiological and medicinal properties by chlorine and iodine, and their respective compounds, and the existence of bromine and its compounds in a definite chemical position between the two other classes of bodies, we then find for the group which more immediately concerns us a physiological place corresponding analogically to that which is held by it chemically, and we make use of the physiological relations which we have discovered as guides in the therapeutic part of our inquiry. If we do not thus dispense with the necessity of trying the medicinal properties of some of the bodies, we at least gain points of elevation whence to view the medical facts that may occur; or obtain useful guides and illuminating beacons amidst the obscure and contradictory evidence so often furnished from the treatment of disease.

The idea of a relation between the chemical and physiological properties of bodies, similar to that which exists between the external forms of many plants and the action of the same plants on the animal economy, has been more than once expressed. Mr Blake, in his laborious and ingenious researches into the action of inorganic bodies introduced into the circulation, endeavours to connect the physiological properties of the bodies with their chemical relations viewed through the medium of the doctrine of isomorphism. In the present crude state of this doctrine, it appears to me more satisfactory to take into account the broad chemical analogies of bodies than their relations solely as to crystalline form. If some isomorphous bodies are similar in physiological action, there are others between which it would appear difficult to trace any great resemblance; for example, the compounds of arsenic and phosphorus.* Mr Blake's statement, that the properties of a base are but little modified by combination with the strongest acids, if true, appears somewhat in contradiction with the prominence which he attaches to isomorphism as a guide to the physiological action of substances, for isomorphism is frequently to be traced as much produced by the acid as by the base. *Non omnia possumus omnes*; and it seems to me that the valuable re-

* I have experimented on rabbits with arsenic and phosphoric acids, and the alkaline arseniates and phosphates. Four grains of arsenic acid dissolved in two measured drachms of water and introduced into the stomach of a stout rabbit, killed the animal in four hours, with symptoms of strong irritant, and corrosive action and also of affection of the nervous system. Fifty grains of glacial phosphoric acid in the same quantity of water similarly administered to a rabbit supposed equivalent to the other, produced no effect. Great difference also appears to exist between the action of the alkaline arseniates and phosphates, so given to rabbits, the former being more irritant and acting more powerfully on the nervous system. These are, however, I conceive, exceptional cases: but such exceptions are probably very numerous.

searches of Mr Blake fall short of what this great question requires, since their author confines the chemical part of the question on the one hand, and that which relates to physiology on the other. He takes into account almost exclusively the effects of substances introduced directly into the circulation ; and many salts which are very different in general physiological properties, thus introduced, appear to produce very similar effects. Thus he has been led to connect potassa and its salts physiologically with ammonia and its compounds, rather than with the series of soda salts, which last named group he places beside the salts of silver, following in this respect the isomorphous relations as guides. Now, in general chemical properties, potassa, and soda, with their respective salts, are more allied than are the compounds of sodium and silver, and I venture to assert, that this also holds good physiologically. In this inquiry I am most fortunately situated, for, not only are there beautiful chemical analogies to be traced throughout the group of halogenous elements and their compounds, but in general the chloride, bromide, and iodide of a base are isomorphous.

Although desirous to avoid all chemical details, which are foreign to the subject, I proceed to indicate some of the leading chemical and physical analogies of this interesting group, for they have a distinct bearing on the inquiry.

In the first place, we are struck by the remarkable analogies of physical character in the elementary bodies, which may in general be traced in a modified form throughout the long series of compounds. Thus, at ordinary temperatures, chlorine is a light-green coloured gas ; bromine a liquid of a splendid red colour ; iodine a solid with an intense shade of violet. And the volatility of their respective compounds in general follows in each case the rule of the element. Hydrochloric acid is the most volatile of the three hydracids, and hydriodic acid the most fixed. The chloride of potassium is volatile at a brown red heat, while the iodide requires a much more elevated temperament.* Chloride of cyanogen is gaseous at ordinary temperatures when the bromide and iodide of the same substance are solid. The chlorides and bromides of olefiant gas and formyl are liquid, but the corresponding iodides are solid. The compounds of bromine are frequently of a deeper hue than those of chlorine, but the compounds of iodine are generally of the deepest shade of all. Nay, the respective specific heats of these bodies preserve a relation. It will be observed, in the tables given in the recent researches of M. Regnault on the specific heats of compound bodies, that the specific heats of bromides are less than those of chlorides, and greater than

* Berzelius, *Traité de Chimie*, T. iii. p. 374.

those of iodides of the same bases.* The three elements all undergo modifications of form by slight changes of temperature and pressure. Chlorine becomes a liquid under the comparatively slight pressure of four atmospheres. Bromine, which freezes at 10° , boils at $116^{\circ} 5'$, and iodine is melted and volatilized by a slight elevation of temperature.

Even the chemical equivalents of the elements exhibit the same traceable connection; the equivalent of bromine being nearer that of chlorine than it is to the equivalent of iodine. And passing from chlorine to bromine and iodine, we find their affinity for electro-positive bodies represented by hydrogen to decrease, while the affinity for electro-negative bodies represented by oxygen increases, which may be illustrated under the following heads:

1. Bromine does not, like chlorine, combine directly with hydrogen under the influence of solar light, although a small quantity of a mixture of bromine and hydrogen may be made to unite on introducing a red hot wire. It is still more difficult to combine iodine directly with hydrogen.†

2. Nitric acid decomposes all the three hydracids, but the hydrobromic and hydriodic acids are decomposed likewise by sulphuric acid.

3. Chlorine and bromine act more powerfully on organic matters than iodine, which pre-eminence they appear to owe to their greater affinity for hydrogen; they rapidly act upon alcohol, giving rise to the production of chloral and bromal, while iodine may be kept long in this fluid, before much effect ensue.

4. Iodine being more electro-positive than the other two elements, does not in every case dispossess oxygen from an electro-positive metal, which may be the reason why, in some cases, it forms iodides of oxides, where they create bleaching compounds.‡

5. Chloride of iodine and chloride of bromine are decomposed by alkaline solutions, with formation respectively of a hydrochlorate and iodate, and hydrochlorate and bromate, but the bromide of iodine is so decomposed with the result of a hydrobromate and iodate being obtained. Under the same head may be placed the difficulty of concentrating chloric and bromic acids on account of their tendency to decomposition, while iodine holds its oxygen more tenaciously.

* Ann. de Chimie, T. i. série iii.

† Balard, Ann. de Chimie, T. xxxii.

‡ I have observed a fact with regard to the action of bromine on one metallic oxide, which I have not seen noted. When solution of bromine in water is added to solution of nitrate of oxide of silver, a precipitate is formed, and the solution acquires the smell characteristic of the bleaching compounds of chlorine. On filtering the solution, it yields a further precipitate after filtration, and bleaches strongly and continues to furnish more precipitate for several days. The nature of the action is doubtless similar to that of chlorine on solution of nitrate of silver, or on red oxide of mercury. A hypobromous acid or a bromous acid must be formed.

6. Chlorine decomposes the bromides and bromine the iodides of electro-positive metals; but when we get to the electro-negative metals, there are indications of a tendency to inversion of these affinities. Thus iodine, heated along with calomel in water, gives rise to the formation of red iodide of mercury and corrosive sublimate; and hydrobromic and hydriodic acids decompose the terchloride of gold.

Among other remarkable relations between the halogenous elements may be mentioned their association together in the sea and its productions. I may here state incidentally, that I have found another instance of the coexistence of these bodies in a salt spring, that of Birtley, in the county of Durham, where bromine and iodine exist in very appreciable quantity.

On the whole, we may conclude from the chemical facts which I have thus connected, that bromine is more allied in chemical properties to chlorine than to iodine.

The subjects of this paper may be conveniently arranged as follow:—1st, Of the Physiological Properties of Bromine and its Compounds—the Hydrobromic Acid, Bromides of Potassium, Sodium, Magnesium, Barium, Zinc, Iron, Mercury, Cyanogen, and Olefiant Gas, with Bromoform, and of the analogies which they offer with Chlorine and Iodine, and their correspondent compounds, some of which we shall have to examine where they appear to need investigation; 2d, Of the Medicinal part of the Inquiry; 3d, General Conclusions.

PART. I.—PHYSIOLOGICAL PROPERTIES OF BROMINE AND ITS COMPOUNDS.

All substances which can exert a chemical action on component parts of the tissues of organized beings, and therefore, when applied to them, cause a physical lesion, must be irritant, or capable of giving rise to a series of phenomena which appear in such cases to be partly of a reactive character. The first question that we have to ask, therefore, regards the power of bromine to act chemically on the tissues. The exact nature of this action is yet obscure. Beyond the mere fact of the coagulation of albumen by bromine, but little information on this subject is to be found in works.* Indeed, great doubt may be entertained with regard to the nature of the action of all corrosive substances on the animal tissues. Thus, while Mulder describes a series of regular atomic compounds formed by the action of acids on albumen, such as the sulpho-proteic acid, $\text{Pr} + \text{SO}_5$, Dr Samuel Brown maintains that the action of acids on albumen is altogether catalytic.† If we look

* See Ann. de Chimie, T. xxxii. Raspail, Systeme de Chimie Organique, p. 201. Berzelius, Traité de Chimie, T. viii. p. 63.

† E. in. Academic Annual for 1840.

to the analogy of chlorine, we have the chloro-proteic acid of Mulder. In the few facts that I have to relate on this head, there is yet something which bears on the inquiry.

According to Balard, "bromine readily attacks organic matters, such as wood, linen, and especially the skin, which it colours strongly yellow; the tint which it communicates is less intense than that given by iodine, and disappears like it at the end of some time, but if the contact has been of some duration, only with the remains of the epidermis."* "In these circumstances," says Berzelius, "water is decomposed, the oxygen is carried to the organic substance, and the hydrogen forms hydrobromic acid with the bromine." It is not easy to see how, on the coagulation of albumen by bromine, a bromo-proteic acid could be thus the sole resulting compound.

When white of egg is coagulated by bromine, either pure or in solution in water, the colour of the element is lost. The coagulum is soluble in solution of caustic potash with or without the aid of heat. From this solution we can readily obtain evidence of the presence of bromine. If without dissolving the coagulum, we wash it on a filter with distilled water, the liquid that passes assumes a faint blue tinge, and is a solution of a small quantity of albumen in dilute hydrobromic acid. The coagulum cannot, however, be thus absolutely deprived of its bromine. Conceiving the existence of a chloro-proteic acid to be altogether hypothetical, since Liebig, Dumas, and Mulder, all vary in formularizing protein, and no chlorous acid of the composition Cl O_5 has been proved to exist in combination with any other base, I prefer explaining the changes described, by supposing that compounds of albumen, with bromine and hydrobromic acids, exist in the clot, the albumen serving as a feeble base; but when we wash the clot, these acids decompose each other, and a weak solution of albumen in hydrobromic acid passes the filter. Or this action might be regarded as a case of double catalysis, the bromine being enabled to decompose water by the presence of albumen, and the albumen coagulated by the presence of the bromine.

It may be questioned whether the action of metallic salts on albumen be not closely allied to that of acids. M. Lassaigne has controverted the notion of Orfila, and others, that metallic salts are necessarily decomposed when they act on albumen.† If we cannot wash the chloride of mercury from albumen, which it has coagulated, by water, we can remove it unchanged by means of ether.

A small quantity of bromine will not coagulate more than a certain amount of white of egg, nor will the latter substance change

* Bromine let fall on the arm speedily raises a blister, and if allowed to remain will soon effect greater mischief.

† Ann. de Chimie, T. lxxiii. Same author in Journ. de Chim. Medicale, Mars 1840.

the colour of an indefinite quantity of the former. The medium degree of saturation appears to be attained when 96.25 of solid ingredients in white of egg are added to 23.31 of bromine.

The action of hydrobromic acid on albumen presents a most beautiful analogy with that of hydrochloric acid. When white of egg is put into concentrated hydrobromic acid, it is at first coagulated, but by repeated agitation in excess of the acid it is dissolved, and with more facility by the aid of heat. The result is the formation of a deep-coloured solution, not of a deep indigo blue tint, as in the case of hydrochloric acid, but of a brownish purple hue.

There is great difficulty in bringing about a similar effect by pure bromine and white of egg. On heating and agitating large quantities of bromine in succession with white of egg and a little water, I obtained a strongly acid greenish coloured solution with a deeper coloured coagulum at the bottom.

When bromine in water is placed in contact with fibrin, the latter substance is converted into a bluish gelatinous looking body. The same circumstances are observed of fibrin in this state as of albumen coagulated by bromine.

A solution of colouring matter of the blood is coagulated by bromine, the hue of the mixture becomes olive green, and ultimately gray if excess of the element be employed. And it may not be without interest to observe that, on washing the coagulum, the iron of the blood is removed, and yet, when the washings cease to give evidence of containing iron, a large excess of bromine having been employed, the precipitate left on the filter, on being boiled with solution of caustic potass or soda, will give a colour nearly resembling that of the blood. This fact may be adduced in connection with the argument of M. Scherer, who has sought to prove that the colour of the blood is not entirely dependent on its iron.

Bromine exerts an action on the fatty principles of the tissues, and appears to be transformed into hydrobromic acid at their expense. The compounds formed are probably analogous to those so formed by chlorine.

Desire of brevity induces me to omit the detailed history of previous investigations into the physiological properties of bromine and its compounds; the results of these investigations are to be found in many elementary works. Sufficient evidence has been adduced by former investigators to show that the primary action of bromine introduced into the stomach, or into the circulation, bears considerable resemblance to that of chlorine or iodine, in so far as either of these bodies can be similarly administered.

The following facts, ascertained by former investigations, may, however, be stated with advantage. M. Balard, the discoverer of bromine, observed that a drop of it placed on the beak of a

small bird soon produced death. Barthez found ten or twelve grains of bromine dissolved in a sufficient quantity of water to occasion death when injected into the jugular of a dog. A single fit of tetanus only preceded death. Sometimes in such an experiment death did not take place, but there were restlessness, dilated pupil, frequency of the pulse, and sneezing. Blood-letting after the commencement of the symptoms favoured recovery in such cases. The following sentences from Devergie give a summary of what had been observed of the effects of bromine introduced into the stomach of animals. "Introduced into the stomach (of the dog) in a dose varying from thirty to forty drops, according to the state of the organ in regard to fulness, it causes death, and gives rise to the following symptoms:—nausea, attempts to vomit, vomiting, acceleration of the respiration and circulation, prostration going on augmenting till death, which takes place at the third or fourth day. *Pathological alterations*; more or less marked injection of the villous coat of the intestinal canal, corrugation of this membrane in the stomach; now and then grayish superficial ulcers; in some cases sufficiently evident softening." Butske found that a dog died in a few days after taking only "five grains dissolved in a few ounces of water, and the symptoms were laborious breathing, loud cries, and convulsions. In the dead body he found the stomach internally chequered with bloody mucus, the duodenal mucous membrane universally injected, but the rest of the intestinal canal in a healthy state."* I may observe that there must be some mistake in this statement,—five grains of bromine dissolved in a few ounces of water being quite incapable of killing a dog when introduced into the stomach.

These effects have much resemblance to such as have been observed to arise from the similar administration of chlorine and iodine. Iodine when introduced into the stomach of the dog produces the same prostration; the same kind of death without any phenomenon of general excitement. "After death we find numerous blackish ulcerations of the villous coat, sometimes surrounded with a yellowish areola along with general injection of the mucous membrane of the intestinal tube."† In animals killed by the injection of chlorine water into the stomach, the villous coat is also found blackened and ulcerated.‡ The introduction of tincture of iodine into the veins scarcely furnishes a fair comparison with the effects of pure bromine or those of the same substance dissolved in water. But effects are thus produced bearing some resemblance to those following the administration of bromine.§ Devergie, nevertheless, is not warranted in stating broadly

* Christison.

† Devergie.

‡ Dictionnaire de Matière, Médicale, Art. Chlore.

§ It is odd, that while Dr Cogswell found two drachms of tincture of iodine injected into the veins of a dog almost immediately fatal, Magendie gave a drachm without

that bromine has the same physiological action as iodine, at least from the facts before him. Where are the proofs that bromine can exert so powerful an action on the secretory and excretory organs as iodine is known to possess? This is part of the question for investigation.

Bromine is better fitted for physiological experiments than chlorine or iodine, since we can administer it pure or dissolved in water. The exact solubility of bromine in water is nowhere stated. According to my experiments, at the temperature of 60° , one part of bromine is soluble in 41.23 of water, so that a fluid-ounce of a solution of this strength, being what I understand by a saturated solution, would contain about 10.36 Troy grains of bromine.

No experiments have been made on the action of bromine on vegetables. In a large dose it must be destructive to plants on account of its chemical effects on their tissues. In a very minute dose it may prove stimulant to vegetation, as has been asserted, and denied of chlorine and iodine.

Expt. 1st. A gold fish, placed in a mixture of one part of saturated solution of bromine and two parts of water, had its whole surface immediately corroded, and life appeared to be extinct in less than a minute. Another fish placed in water tinged faintly yellow by bromine had the respiration quickened and apparently rendered more laborious. This animal showed no other signs of excitement and died in an hour; its surface was corroded; the gills of both were congested.

Expt. 2d. Four drops of bromine* were placed on the bill of a pigeon; the effects were corrosion of the bill where the bromine was placed; violent excitement of the bird followed by an apathetic state; death in two days, owing to corrosion and irritation of the air passages produced by inhalation of the fumes of the bromine.

Expt. 3d. By a suitable contrivance four drops of bromine were introduced into the external jugular of a strong male rabbit. He immediately shrieked; the respiration became laborious; the pupils were dilated; the heart's action quick and violent, but ceased after a few irregular beats; there were two or three convulsive struggles, and the animal was dead in seventy seconds from the performance of the operation. On opening the chest immediately, the irritability of the heart was found to be destroyed. The substance of this organ was corroded near the apex; and there were several marks of corrosion in the lung. The blood in the right ventricle and pulmonary artery was coagulated and corroded. Contractility of the voluntary muscles remained.

any effect, and says, he found no other effect from solid iodine introduced into the stomach of dogs than vomiting.

* Bromine is about three times as heavy as water.

Expt. 4th. A middle-sized bull and terrier bitch, strong and active, had an ounce of solution of bromine containing two and a half minims of the element injected into her jugular by a glass syringe; the symptoms were panting and tumultuous action of the heart, a spasm of opisthotonos followed by a terrific yell and escape of the urine and fæces. After the spasm had subsided, having lasted about a minute, the animal gave several heavy inspirations, and the heart's action was felt very feeble and irregular; the pupil was observed greatly dilated. General tremors of the muscles occurred before death, which was preceded by a deep inspiration, and took place within a second or two of three minutes from the period at which the solution was injected.

On inspection, the voluntary muscles contracted strongly when cut. The heart was gorged with black coagulated blood in its right cavity and with red fluid blood in its left, and was irritable five minutes after death. The lungs collapsed on opening the chest and appeared healthy.

Expt. 5th. A strong fox-hound, a year old, lamed, had half an ounce (by measure) of saturated solution of bromine injected into his jugular. After the operation he was seized with a fit of panting, which lasted nearly two minutes. After this both respiration and circulation were observed to be quickened. In seventeen minutes after the operation, he became affected with coryza and sneezing. Then rigors came on. During the first hour he passed fæces repeatedly. For some hours he continued feeble, and as if suffering from a pulmonary affection, but eventually to all appearance he recovered, and in three days after was again experimented on.

He had thirty drops of bromine introduced into the jugular of the side not operated on before; and as the fluid did not descend but coagulated the blood in the vein and destroyed the surrounding parts, an ounce of the saturated solution of bromine was thrown in afterwards. As soon as the solution entered, the animal gave a loud yell; the heart's action became violent and irregular, and the respiration of the same panting character that had been before remarked. Then followed violent movements succeeded by prostration and manifestations of suffering. Seventeen minutes after the operation he made efforts to vomit, and began to void blood from the mouth. The pupil was now greatly dilated. The animal appeared to possess perfect consciousness. He died in an hour and a quarter from the performance of the operation, having repeatedly voided blood from the mouth, and passed urine and fæces; death was preceded by great feebleness of the heart's action and muscular debility.

The most remarkable appearances after death were found in the lungs and stomach. The lungs presented a splendid appearance

of congestion, and several apoplectic-like spots ; slight pressure caused blood to flow from almost every part of the pulmonary tissue. The bronchi contained frothy blood, and in several places were occupied by strings of coagulated blood. On cutting near the border of the right lung, there appeared a vessel filled with yellowed and corroded blood, and around the pulmonary tissue contained much blood. The stomach contained about half-a-pint of grumous blood ; the mucous coat was much injected, and presented several large ecchymoses ; one of which near the cardia appeared to have been the chief source of the blood. The rectum exhibited marks of vascularity.

Remarks.—Bromine introduced directly into the circulation appears to exert a corrosive and irritant action on any organ to which it may be directed. In the fourth experiment we see it producing death by coagulating the blood, and so obstructing the circulation. The sudden stoppage to the circulation through the ~~left~~ side of the heart, and consequent compression of the nervous centres, may account, as shown by Mr Blake, for the nervous symptoms which occur in such cases.* The state of the stomach after death, in the experiment just related, may, perhaps, be accounted for by supposing that this organ affected since the first operation, was unable to withstand the sudden congestion it would undergo from obstruction to the circulation through the right side of the heart in the second operation. It is easy to see how blood-letting may remove some of the symptoms occasioned by the injection of bromine into the veins.

Expt. 6. Sixty minims of bromine were poured down a flexible tube into the stomach of a strong female cat. For two minutes no effect was perceptible. Then the respiration and circulation became greatly quickened ; inspiration being somewhat prolonged, but expiration made with rapidity, and accompanied by a wheeze. Saliva began to drop from the mouth, the eyes to water, and in the course of four or five minutes, clear fluid was running in a constant stream from the mouth and nose. About the fifth minute, the animal began to struggle violently, and made repeated efforts to vomit, but did not succeed in vomiting. The heart's action became very irregular, and after terrible convulsions, death took place in seventeen minutes from the time at which the poison was administered.

The appearances were all those of the most violent corrosion and irritation. The mucous membrane of the stomach would be separated in rose-coloured flakes. The lining membrane of the gullet was as if filled with a minute red injection. The appearances of corrosion were not confined to the digestive organs, but extended to the air passages and lungs. The peristaltic action of

* Ed. Med. and Surg. Journal, No. cxlviii. p. 121.

the intestines was stopped, and the small intestines had completely lost their tonicity. A more detailed account of the appearances is unnecessary, because the relation of the next experiment will show better the peculiarities of the corrosive action of bromine, and we may infer, of the halogenous elements generally in a high dose. In the present case, no proof was obtained of the absorption of the poison.

Expt. 7th. Two measured drachms of pure bromine were given to a strong and active terrier-dog in the mode related in the last experiment. For seven or eight minutes after the operation, he manifested no emotion. He then began to draw his belly along the ground, and then vomited matter which evolved fumes of bromine, and seemed to excite a disagreeable sensation in the mouth. For about an hour, the symptoms were of this character; occasionally fæces were passed, and there were frequent tremors, cries, and other expressions of pain. These symptoms gradually subsided, and he remained in a state of stupor, occasionally moaning; the respirations heavy and heart's action feeble. His death took place about five hours and a half after the operation. The inspection was not made until some hours had elapsed.

The lungs were found with several large spots towards their roots, and infiltrated with frothy serum. The blood was dark-coloured and coagulated on both sides of the heart. The peritoneum contained a dark-coloured semifluid matter, feebly acid, and exhibited many marks of inflammation. The greater part of the stomach had been dissolved, leaving only some blackened shreds attached to the duodenum, and another portion at the cardia, which might amount to a third of the organ. This part was marked with long black striæ, and presented a space near the entrance of the œsophagus where the mucous membrane was deeply injected. The mucous membrane of this remaining part was gelatinized, the remaining peritoneal coat was tinged blue, somewhat more of it was left than of the other coats. Great part of the lining membrane of the gullet was reddened and thickened. The duodenum and small intestines presented appearances altogether different from those offered by the stomach. The duodenum was yellowed internally by the poison, and retained a strong odour of bromine, which was not the case with the stomach. The mucous membrane of the duodenum, although thickened, felt harder than natural, and rather brittle, but was covered with a large quantity of matter, which appeared to be the secretion of the bowel acted on by the poison.* On cutting the jejunum or ileum across the walls of the tube did not collapse. The mucous membrane of these intestines was much thickened, and in the superior portion had a white and granulated aspect. At the inferior part of the small intestine, the mucous

* See Plate I. for a representation of these states of the stomach and duodenum.

membrane was thickened and softened, and began to exhibit traces of vascularity, which were very distinct in the sigmoid flexure and rectum, where there was little or no corrosion. The colon was empty. The lower part of the liver was corroded and of a bluish colour. The membranes of the brain were vascular.

A careful analysis of the heart and its contents showed that bromine had been absorbed into the blood.

Remarks.—Two series of effects are produced by the introduction of bromine in large doses into the stomach. We have the action due to volatilized bromine getting into the fauces and air-passages, and so into the lungs, and the corrosive and irritant action on the stomach and intestines. Another series of effects might be due to the entrance of bromine into the circulation. To the first series must be referred the coryza, sneezing, salivation, and affection of the respiration. The solution of a great part of the stomach in the seventh experiment, may be accounted for by supposing that, after a time, the stomach became unable to transmit its contents into the duodenum, when the bromine remaining in the organ becoming converted into hydrobromic acid dissolved the coats. The intestines being not so well adapted for the lodgement of the poison, the appearances they presented differed from that of the stomach, being the effect of the element, and not of the hydracid. An experiment will be afterwards detailed, in which it will be found that hydriodic acid dissolves a portion of the stomach. The peculiar blue colour appears characteristic of the action of the hydracids on this organ, and resembles the appearance of the stomach, showing the action of the gastric juice after death, as given in Carswell's plates. I could not, as has been related, exactly imitate the process which I suppose to have taken place in this experiment, by acting on white of egg by bromine.

The absorption of hydrobromic acid is corroborated by numerous analogical facts. Chlorine and sulphuretted hydrogen pass into the urine, * also arsenious acid; and I shall afterwards bring forward evidence of the absorption of the acid bichloride of mercury. The hydracids of chlorine, bromine, and iodine are peculiarly likely to be absorbed, since the two former form soluble compounds with albumen, and we may assume as much of the other.†

* Becquerel, *Séméiotique des Urines*, pp. 128–180.

† In my essay, given in for competition on the 1st of January, I stated this absorption of hydrobromic acid, the argument above given in favour of the absorption of other acids, and the evidence of the absorption of corrosive sublimate. Orfila announces in a letter of very recent date (See *Echo du Monde Savant*, 28 Avril 1842) that he has now established the absorption of muriatic, nitric, sulphuric, and oxalic acids. As yet he has given no details. He has also detected mercury in the urine. The absorption of the oxacids may be accounted for from their compounds with albumen being soluble in a large quantity, the absorption of corrosive sublimate is explained by its compound with albumen being soluble in solution of the electro-positive chlorides. (May 12th.)

Expt. 8th. A strong male rabbit had ten minimis of pure bromine introduced by a flexible tube into his stomach. No particular effects followed the operation. Three days after this, he was poisoned by prussic acid, when the mucous membrane of the cardiac portion of the stomach was found reddened, somewhat thickened and softened, and dotted with numerous minute white spots of corrosion.

Expt. 9th. Another rabbit like the former had the same dose administered in the same manner. Three hours after the operation, the respiration was wheezing, and saliva flowed from the mouth. He got well, and was killed a week after by prussic acid. An ulcer of the size of a shilling, of a triangular shape, was found near the cardia.

Expt. 10th. Two ounces by measure of a saturated solution of bromine were injected into the stomach of a stout male rabbit. Death took place in five minutes and a few recent symptoms, tetanic convulsions, a peculiar rapid movement of the fore-legs; after this pulse slow and feeble, respiration slow and forcible, pupils at first contracted, afterwards dilated, salivation just before death.

Chief appearances after death; bloody froth in the mouth and air passages; several apoplectic spots towards the roots of the lungs; heart not irritable three minutes after death; blood dark and fluid in both cavities. The mucous membrane of the stomach was of a white and corroded aspect over the greater part of the organ, deeply injected at the depending part. The same appearances extended to the duodenum. The epithelium of the stomach came off in washing the organ.

Expt. 11th. Half the quantity of the solution of bromine given in the former experiment was administered to a strong male rabbit. Death took place in a quarter of an hour. Symptoms; loss of power over the voluntary muscles; breathing became embarrassed and made with great muscular effort; frothing at the mouth, and violent convulsions like those described in the preceding case.

The appearances were in general similar to those observed in the former experiment. The left side of the heart contained dark clotted blood. In both these cases the voluntary muscles contracted, and the peristaltic action continued. No evidence of the absorption of bromine was obtained from the analysis of the organs.

Expt. 12th. In this case the introduction of two measured ounces of the saturated solution of bromine into the stomach of a rabbit gave rise to a different train of symptoms. The solution was introduced in two portions, the second dose being given five minutes after the first. An hour after the operation, he was affected by coryza and salivation. This was at 6 P. M. Next morn-

ng at nine he was found lying on his side, the eyelids closed, respiration slow and forcible, accompanied with a slight wheeze; pulse scarcely perceptible; the fore legs were regularly moved towards the head, and these brought back; some flow of saliva; the animal heat low; death took place about five o'clock.

In this case no corrosion was found in the stomach, but very curious marks of irritation. The stomach, which was contracted, on a little semidigested food, showed its cardiac portion of a deep purple hue separated by a distinct line of separation from the pyloric portion, which was pale and œdematous. The epithelium was removed, and the mucous membrane over the cardiac was occupied in several places by irregular patches of ulceration. The same disorganization was exhibited in the upper part of the small intestines. The blood was coagulated in the abdominal veins and ascending cava; the heart pale and empty.

The blood collected from the veins gave evidence of the presence of the poison.

Expt. 13th. Two strong male rabbits had each two ounces by measure of the saturated solution of chlorine in water introduced into the stomach in the usual way. Forty hours after this the animals were poisoned by prussic acid. The stomach of one was found with its villous coat inflamed, and softened over the cardiac portion; that of the other, in addition to this general appearance, had three somewhat oval green-coloured ulcers with the mucous membrane around them deeply injected. One of these near the pylorus was about half the size of a sixpence; another of about twice this size next the œsophageal opening; and the largest, about as big as a shilling, was opposite this, at the lowest part of the cardiac sac.

Expt. 14th.—Forty grains of finely levigated iodine were suspended in an ounce (by measure) of water, and injected into the stomach of a stout male rabbit. Then an ounce of water was thrown down the tube, with the view of washing all the iodine into the stomach. Death took place in half-an-hour.

Symptoms.—Loss of power over the voluntary muscles; dilated pupil; slowness and feebleness of the heart's action; slow and forcible respiration; salivation. Shortly before death the animal ran suddenly into a corner, where it was found extended on its side. The respirations were now ten in the minute; and each was attended with a convulsive shudder.

Inspection.—The voluntary muscles contracted on being cut; the auricles of the heart moved five minutes after death; the lungs were congested, and contained much frothy serum; both sides of the heart contained dark fluid blood; the stomach, on an external view, showed its vessels much congested; the mucous membrane was much corrugated; and over the cardiac portion

presented an appearance like cork corroded by iodine, with deep-red coloration in the centre of the depending part; the bladder was full of urine, which contained no iodine.

Remarks.—Bromine is more irritant when diluted than when pure. It is an irritant independent of its corrosive action; the effects of chlorine and iodine introduced into the stomach of rabbits closely resemble those produced by bromine considering certain modifying circumstances. The experiment last related is, I believe, the only one on record where an animal is killed speedily by the corrosive and irritant action of pure iodine. Supposing the chemical affinities of the halogenous elements for albumen to be the same, which I have already shown is not in all probability the case, an equal quantity of chlorine should be more powerfully corrosive than bromine, and the latter body than iodine, because of the difference in their chemical equivalents.

Expt. 15th. A lively terrier dog, about five months old, had three ounces by measure of the saturated solution of bromine introduced into his stomach by a flexible tube, the penis being secured by a ligature. Three minutes after the operation he vomited much frothy mucus and a little semidigested food; the vomited matters exhaled vapours of bromine. Repeated vomiting of bloody mucus and purging succeeded. This state continued an hour, the animal manifesting great uneasiness. After this he lay in a state of great feebleness, but did not appear to suffer from pain. Half-an hour after the operation, the ligature was removed from the penis. He forthwith passed urine which, on analysis, was found to contain bromine. Urine passed four hours after the operation gave no proof of containing the poison. Next day he seemed recovered, and the same dose was again administered; effects similar; less vomiting. The day after this second dose he had another; after this he could not retain his food. Two days after this third dose he was found completely prostrated; the respirations abdominal; heart's action slow and feeble; pupils dilated; salivation; body cold; death was preceded by stupor and frothing at the mouth.

On inspection the stomach exhibited several mottled erythematous like patches. There was a distinct line of separation between the cardiac and pyloric portions; the former presented an appearance of softening, and had assumed a yellowish hue except in the site of the patches described. It had also lost its epithelium in several parts. The pyloric portion was red, contracted, and rugose; the lungs, which were slightly affected with tubercle, were infiltrated with bloody serum, and partly with a purulent secretion. Black coagulated blood was found in both sides of the heart; no bromine could be detected on analysis of the blood and organs.

Expt. 16th. A middle sized mongrel dog had two ounces, by measure, of the saturated solution of bromine introduced into the stomach. He passed fæces almost immediately. In the course of an hour the respiration became affected; salivation, coryza, and retching ensued. About the third hour the symptoms had subsided. This dog had the above-mentioned dose given every second or third day for a month, *i. e.* time was allowed for the irritation of one dose to subside before another was given. During this time he got very thin, was much purged, and acquired a great appetite.

Expt. 17th. Eight drops of bromine were placed on the tongue of a small mongrel dog; he made efforts to reject the poison, the fumes of which were disengaged from the mouth. In the course of a few minutes the respiration became doubled in rapidity, inspiration being accompanied with a mucous rattle and expiration, attended with wheezing and hiccup. The respirations gradually became slower, and the heart's action irregular. He passed fæces repeatedly, and retched violently; the mouth and eyes watered; the pupils became dilated; the animal, after these symptoms had subsided (after having lasted about an hour) became greatly depressed.

Remarks.—The last series of experiments were intended to exhibit the effects of the inhalation of bromine vapour, and those which are manifested on the *primæ viæ*, independent of the corrosive action, and further, to test the rapidity of the absorption of the poison, and possibly to throw some light on the question of its cumulative action, which we cannot but ask in regard to a substance so nearly related to iodine. The purgative action of bromine is sufficiently evident on dogs, but something similar is produced by almost all irritant and corrosive poisons. We might fancifully ascribe the vomiting and purging which take place in such cases to efforts of the *vis medicatrix naturæ*. It is shown that bromine passes speedily into the urine, and we may also infer from experiment 15th, that it is thus removed from the system. Every thing that has yet been observed with regard to bromine seems to show that, besides its primary action and the effects of the irritation thus induced, which may be repeated so as to accumulate the deleterious influence on an animal, there can be no proper cumulative action. Compare experiment 16th with experiments on the cumulative action of iodine.* The dose of bromine administered was as great as could be given without inducing excessive irritation, which would defeat the end in view.

There is similarity between the effects observed to proceed from the inhalation of chlorine, and those which are detailed in the last experiment as occasioned by bromine.

This appears to be the proper place to relate the observations

* See Cogswell on Iodine, pp. 60–62.

of M. Fournet on the physiological effects of bromine, which were manifested on some patients affected by chronic arthritis, to whom bromine was administered by him, then an interne under Andral.* The remedy was given suspended in mucilage. The dose was at first two drops, but was raised by two drops daily, until it amounted to sixty drops in the twenty-four hours, which should be sufficient, in a treatment of three months, to afford a good example of the action of the substance. The quantity of mucilage employed to suspend the substance was always four ounces. Two drops thus taken occasioned only a hot sensation in the back of the palate. "In a little stronger dose, the patient experienced in a quarter of an hour, itchings in the hands and feet, and shocks in the feet and near the knees. A quarter of an hour after these first sensations he had borborygmus and colic. During the night the sensations in the hands and feet were now and then repeated. As the dose became stronger, there was a sensation of heat in the chest, accompanied with attempts to vomit, but without any vomiting. At first a peculiar sensation of weakness and fatigue in the chest accompanied these first efforts, but as the patient became habituated to the preceding phenomena, these symptoms disappeared. The patient who experienced these itchings in the fingers was always the most sensible to the effects of the bromine. A quarter of an hour after ten drops were taken, he complained of a sensation as of enormous weight on the stomach, with desire to vomit, colics, and gargouillements. An hour after, he had a feeling of tightening from the shoulders, to beneath the elbow, on each side, as if these parts had been compressed in a vice; these lancinating pains were felt in the fingers and circumference of the head; but these symptoms disappeared, and the patient enjoyed a remarkable degree of calm. Every day, at each administration of the remedy, the preceding symptoms were renewed. At length there was joined to them a feeling of shooting pain round the orbits. The shocks which the bromine determined on traversing the digestive tube became greater with each increase of dose. This shock was followed by a feeling of heat internally, which lasted for about ten minutes; and was greatest when the bromine was on the point of entering the stomach. When the dose became forty-five drops, the sensation of acidity and burning which followed the administration of the remedy was so violent, that the patient exhibited for some time a convulsive state of the face and members. Then he experienced an inclination to vomit but never vomited. In five minutes these symptoms disappeared, and his ordinary state returned. After this crisis he experienced no other disagreeable sensation. The appetite was good, the digestive functions unimpaired, his fatness and appetite increasing."

The writer of this paper took the watery solution of bromine

* Bulletin General de Therapeutique, Fevrier 1830.

for a month. The dose was at first forty drops of the saturated solution in half a tumbler of water with a little syrup, three times a-day. This was increased to half a wine glassful of the solution, which was as much as could be taken at a time. The taste in the palate after the taking of this dose was truly horrid. Slight pain in the stomach was sometimes felt. The appetite improved, and there was slight action on the skin and kidneys; but he experienced more notable effects; "a drop and a-half of bromine in half an ounce of water gave him heat in the mouth, œsophagus, and stomach, followed by colicky pains. Two drops occasioned nausea, hiccup, and increased secretion of urine." Franz, by breathing the vapours, had "violent cough, and a feeling of suffocation, followed by headach." Of these effects, I have had abundant experience.

The tonic and diuretic effects of bromine were experienced by a syphilitic patient of mine, who took the solution. Mr R. Fentress, of this town, having given a glandered horse five ounces of the saturated solution of bromine twice daily, observed increase of the appetite of the animal. After death, we found the villous coat of the stomach and intestines in a healthy state.

An operation on the nervous system is manifested by bromine; dilated pupil and stupor occurred in several experiments. And in an experiment where I injected solution of bromine into the peritoneum of rabbits, the same symptoms were observed along with the peritoneal inflammation which killed the animals. Large doses of hydrochloric acid have occasioned somewhat similar cerebral affection in man.*

M. Fournet relates that frictions of bromine produced an erythematous eruption, preceded by a prickly sensation. Mr Wallace describes a similar effect as proceeding from the application of chlorine gas to the skin.†

On the whole, there can be little hesitation in placing bromine intermediate in physiological properties between chlorine and iodine, but more nearly related to the former than to the latter body.

TESTS AND ANTIDOTES FOR BROMINE.

This part of the inquiry has no other interest but what a rational spirit of scientific investigation can confer. The tests for bromine in general require the presence of the element to be manifested by the peculiar colour of the body. There is, however, an exception to this rule in a new test which was suggested to me by my friend, Dr George Wilson, viz. the chloride of gold; the solution of this salt giving a red tinge with hydrobromic acid or an electro-positive hydrobromate.

* Pereira, Mat. Med. Part. i. p. 153.

† Wallace on Chlorine, p. 99.

When bromine exists in an organic mixture, since it is sure to be in a state of combination, caustic potass should be added to the mass, which should then be reduced to an ash, exhausted by distilled water, and chlorine passed through the solution, or the chloride of gold added to it previously carefully neutralized by hydrochloric acid. When chlorine is used, starch may render the presence of the element more perceptible. I have tried experiments on the relative delicacy of tests, and prefer the chloride of gold. Nitrate of silver is a delicate test where the bromine is not mixed with chlorine; the bromide of silver is distinguished from the chloride, by heating with hydrochloric acid, and chlorite of lime, when ruddy fumes are evolved if bromine be present.

M. Barthez has proposed magnesia as an antidote for bromine. From experiments to be related, it will appear that the bromide of magnesium is by no means an active salt; neither is it inert. From experiments performed on rabbits, I conclude starch in solution and white of egg to be excellent antidotes to the poison.

PHYSIOLOGICAL PROPERTIES OF HYDROBROMIC ACID.

Expt. 18th. Five minims of bromine, partly dissolved, partly suspended in an ounce by measure of water, were converted into hydrobromic acid, by means of sulphuretted hydrogen, and being freed from sulphur, and excess of sulphuretted hydrogen were injected into the external jugular of a terrier dog selected to correspond with the subject of the fourth experiment. The symptoms which resulted were strong, quick, and irregular action of the heart, and a curious succession of fits of panting, occurring at intervals of three or four seconds, and lasting each time for ten or twelve seconds. This state endured for about twenty minutes, the animal remaining pretty quiet, but before the expiry of this time, the fits were not so frequent as at first. In two hours he was quite well.

Expt. 19th. 80 grains of the bromide of barium dissolved in water, were decomposed by dilute sulphuric acid in the way I have elsewhere recommended;* and thus a solution of hydrobromic acid in seven fluid drachms of water obtained, which, according to the tables of Berzelius, would give 95.958 grains of bromine in the form of the hydracid. This solution was then injected into the jugular of a cur bitch of middle size. The symptoms were an immediate spasm of opisthotonos with escape of urine and fæces, loud cries, and frothing at the mouth. The tetanic spasm lasted a minute and a-half. After it subsided, the respiration was slow and forcible; the heart's action slow and feeble; death took place in three minutes from the commencement of the operation. The heart was found gorged with dark clotted blood in both ca-

* Philosophical Magazine, No. 121, Third Series.

vities. The irritability of the organ remained after death. The blood in the heart did not redden litmus; the urine contained bromine.

Expt. 20th. Ninety minims of bromine in two ounces of water being converted into hydrobromic acid, half-an-ounce of the solution was introduced into the stomach of a stout male rabbit. Effects,—restlessness; quickened respiration and circulation; great uneasiness manifested; and now and then a sharp cry; loss of power over the voluntary muscles; discharge of urine; slight convulsions; death in ten minutes from the administration of the poison.

The most remarkable appearances were, congestion of the lungs, which were infiltrated with frothy serum, and with a few apoplectic spots in their tissue; the bladder was full of urine; the whole of the mucous membrane of the cardiac portion of the stomach exhibited a uniform gray erosion, was much softened, and had the epithelium removed.

Expt. 21st. Two fluid ounces of saturated solution of bromine were converted into hydrobromic acid solution and given to a rabbit, without any effect being produced.

Expt. 22d. Three drachms of iodine were suspended in two fluid ounces of water, and nearly all converted into hydriodic acid by sulphuretted hydrogen. An ounce of this solution was introduced into the stomach of a strong male rabbit. At first the motions of the animal were quickened, but in the course of seven or eight minutes they became feeble. The respirations at the end of this time were panting. At the tenth minute there was partial loss of power over the inferior extremities. At the fifteenth minute, he moved a little and passed urine. At the twentieth minute he lay on his belly; the hind legs outstretched; the heart's action very feeble. After this he was in a state of complete prostration, but apparently conscious; the animal heat declining rapidly. Death took place in an hour and forty minutes from the administration of the poison.

On inspection immediately, there was no contractility of the voluntary muscles; no movement of the heart (which was empty) on the application of stimulus; nor peristaltic action of the intestines. The stomach was largely perforated, or rather dissolved at the cardiac extremity and greater curvature, and that portion which remained was of a blue colour, and had several pieces of semicoagulated blood at its surface. The small intestines exhibited marks of corrosion and irritation; the colon was full of fæces; the bladder empty and contracted; the peritoneum contained a quantity of dark-coloured fluid blood.

Remarks.—These experiments show that hydrobromic acid is less powerfully corrosive and irritant than the element. The last experiment confirms the statement made some pages back with re-

gard to the capability of hydrobromic acid to dissolve the coat of the stomach. A comparison between experiments 4th, 18th, and 19th will show that hydrobromic introduced into the blood is less energetic than bromine. The effect of the hydrobromic acid in coagulating the blood in Expt. 19th corresponds with what is related of the effect of hydrochloric acid similarly administered.

Dr Buchanan maintains that all the beneficial effects due to the administration of iodine are owing to the conversion of the element into hydriodic acid, which passes into the system, and that the primary irritant action is due to the element alone.* In the rabbit poisoned by hydriodic acid, I found that the iodine was retained in the tissues by a base, since they could be charred, and the iodine detected in them without the necessity of having recourse to caustic potass. According to Rees, the iodine is sometimes converted into iodic acid in the system,† which is according to the view I have given of the action of bromine on albumen to which that of iodine corresponds, as I have ascertained, though this latter action is of a more feeble character. The suspected existence of iodate of potass in the urine, where the hydriodate has been taken internally, may receive some elucidation from facts which I shall afterwards bring forward tending to show that the activity of salts depends, in great part, on the facility with which they undergo decomposition in the system.

The hæmadynamometer, which has been so recommended in physiological experiments of the kind related, and so much used by Mr Blake, was not employed in the experiments on bromine and hydrobromic acid, because both these bodies must obstruct the circulation in the capillaries of a part to which they may be sent, on account of their chemical action on the blood and the walls of the vessels.

PHYSIOLOGICAL PROPERTIES OF THE BROMIDES OF POTASSIUM AND SODIUM.

It may be proper to remark, in the first place, that these salts have little action of a corrosive character. Solution of albumen is faintly troubled by the bromide of potassium in contact with it. The solutions of both salts added to the blood give a brighter colour to this fluid.

M. Barthez reports that the bromide of potassium resembles the iodide of the same base. He found it kill dogs when injected into the jugular, coagulating the blood, and causing convulsions. He introduced a drachm of the salt into the stomach of a dog without any ill effect, except vomiting. But two drachms, and even a drachm and a-half, killed dogs in three days when retained in the stomach by a ligature of the gullet, with marks of inflam-

* Med. Gazette, Vol. xiii. p. 515.

† Rees on the Analysis of the Blood and Urine, p. 88.

mation of the gastro-intestinal mucous membrane. Maillet gave two ounces to a dog without any ill effect; and he observes, according to the principle, that the dose of a saline substance for the horse should be eight times that for the dog, that a pound of the bromide of potassium would have no ill effect on a horse.* Devergie was accustomed to state in his lectures, that an idiosyncrasy on the part of dogs affected the action of this substance on their stomachs. But this notion apparently arose from an expectation of finding more active properties in the bromide than in the iodide of potassium.

The bromide of potassium is often impure; I have found it adulterated with one-third its weight of the chloride. There are three methods by which this adulteration may be detected. One is given by Pereira, quoted from Rose (*Ann. de Pharmacie*, t. 23.) "If pure bromide of potassium mixed with excess of bichromate of potass be distilled with concentrated sulphuric acid in a tubulated retort, to which is adapted a receiver, containing excess of solution of caustic ammonia, pure bromine distils over, and the ammoniacal liquid remains perfectly colourless. But if the bromide contained a chloride, both bromine and the chloride of chromium distil over, and the ammoniacal liquid becomes yellow. Chromic acid may be detected in the solution by the usual tests." Another method of detecting a mixture of a chloride with a bromide is that of M. Caillot,† and consists in mixing the salt with equal parts of persulphate of mercury, and peroxide of manganese, and heating until decomposition; then on adding a few drops of a solution of chromate of potass, if the chloride of mercury be present, red spots will appear, due solely to the decomposition of the chromate by the chloride. On this head, the following is extracted from the third part of Professor Kane's new work;—"The commercial article is frequently adulterated with chloride of potassium, the presence of which may be detected as follows: Dissolve 100 grains of the salt in four ounces of water, and decompose it by an excess of nitrate of silver, collect the precipitate, wash it carefully, and dry it in a capsule till it ceases to lose weight, then weigh it. If it were perfectly pure, the bromide of silver should weigh 158.8 grains; but the presence of chloride of potassium would have the effect, from the smaller equivalent of chlorine, of increasing the weight; therefore, if the precipitate, when quite dry, weighs more than 158.8 grains, the sample is impure, and the quantity of chloride present may be calculated from the overplus weight, for 100 grains of the chloride of potassium should give 192.6 grains of precipitate. Thus, if there were 10 per cent. of impurity, the precipitate should weigh 162 grains, if 20 per cent., it should weigh 165.4. Thus the precipitate increases in weight about 3.3 for each 10 per cent. of chloride present."

* Pereira, *Mat. Med.*, 1st ed., part i. p. 287.

† *Ann. de Chim.*, t. 45.

Expt. 23d. Forty grains of the bromide of potassium dissolved in half-an-ounce (by measure) of water, were injected into the jugular of a large and strong old greyhound dog. A tetanic spasm was produced, with tumultuous and irregular action of the heart and discharge of urine and fæces. Twenty minutes after the operation, he appeared quite recovered. Eighty grains dissolved in the same quantity of water were then injected. There was sudden cessation of the motion of the heart, and of the respiration, along with a tetanic spasm (opisthotonos,) which lasted about a minute and a-half, and was attended with disengagement of urine. After this had subsided, he drew two deep inspirations; a universal trembling of the muscles took place, and lasted for three minutes and some seconds,* when every other sign of life had disappeared.

The chest was immediately opened; the voluntary muscles contracted on being cut; the lungs collapsed on opening the chest; the heart was without motion; and had lost its irritability in less than two minutes after death. This organ was gorged with clotted blood, red in the left ventricle, and dark-coloured in the right. The lungs appeared quite healthy, the tips of the rugæ of the stomach were somewhat redder than natural.

Expt. 24th. A middle-sized French poodle-dog had sixty grains of the bromide of potassium dissolved in half a fluid ounce of water injected into the jugular. The symptoms were stertorous breathing, escape of urine and fæces, tumultuous and irregular action of the heart, which suddenly ceased, frothing at the mouth, cries, dilated pupil, and death before the animal could be untied, or in about two minutes from the injection of the salt.

On inspection, the voluntary muscles contracted strongly on being cut; five minutes after death, the heart had lost its irritability, and was gorged with fluid blood, red in the left ventricle. The lungs were quite healthy.

Expt. 25th. A middle-sized messet bitch had twenty grains of the salt dissolved in a fluid drachm and a-half of water injected into her jugular. Death took place in forty or fifty seconds. The symptoms were sudden cessation of the heart's action, preceded by a few stertorous respirations, escape of urine and fæces, and dilated pupil. The heart was found to have lost its irritability, and to be gorged with blood, which was fluid in the right ventricle, red and coagulated in the left.

Expt. 26th. A hæmadynamometer was connected with the femoral artery of a middle-sized, strong, and lively terrier dog; and sixty grains of the salt dissolved in half an ounce of water (by measure) were injected into the carotid in the direction of the

* This appears to be a similar phenomenon to that described by Mr Blake as produced by salts of oxide of lead, strontia, and baryta. I have observed it most remarkable in rabbits poisoned by cyanide of ammonium.

heart. Previously to this, the mercury was raised two inches and eight lines. As the solution was introduced, the pressure in the instrument was augmented, and when the whole of the salt had entered, the mercury had risen to five inches. This elevation was only for a minute, during which period the oscillations were also greater, owing perhaps to the struggles and hard breathing of the animal. After a minute the mercury suddenly fell below the former level, and continued to fall until, in about two minutes and twenty seconds, all pressure in the arterial system seemed removed: death then took place in about two minutes and a-half from the period at which the salt began to be injected. The animal voided urine and fæces during the experiment, and seemed spasmodically agitated. On inspecting the chest, much the same appearances were observed as in those experiments where the salt was injected into the jugular. The brain was healthy.

Expt. 27th. Forty grains of the salt dissolved in three fluid drachms of water were injected into the femoral artery of a lively terrier-bitch in the direction of the circulation. Spasmodic extension of the limb was followed by spasmodic action of the muscles of the chest, and by extension of the other limbs, with excited action of the heart and dilated pupil. This state lasted for about five minutes, and then subsided.

Expt. 28th. One hundred grains of the bromide of potassium dissolved in three drachms of water were introduced through a flexible tube into the stomach of a strong male rabbit. Five minutes after the operation he fell flat on his belly; loss of power over the hind legs became apparent, and he made ineffectual efforts to crawl. The breathing became quicker than natural, embarrassed and abdominal; the action of the heart irregular and feeble. This state continued for half an hour, during which time fæces twice escaped, and the iris seemed paralysed. His eyelids winked; a stroke appeared to excite convulsive strikings out of the limbs. Towards the close of the half hour he seemed greatly agitated, and recovered for a short time the use of his limbs. After this his head was moved forwards and backwards with great velocity, and the body bent in a crouching form while he stood on his legs. He was then agitated with convulsions, (both *emprosthotonos* and *opisthotonos*.) At length he fell on his side. In this position similar rapid movements of the fore legs were observed to those which occurred in rabbits poisoned by bromine. These movements lasted for a minute, when he lay apparently insensible, and died after a few deep inspirations.

Inspection.—The muscles contracted feebly on being cut. The auricles contracted feebly; ventricles did not move nor respond to the stimulus of the knife two minutes after death. The peristaltic action continued. Lungs greatly congested toward the dependent part, and contained much frothy serum. Pericardium

contained serum ; blood dark-coloured and fluid in both cavities of the heart. The stomach was contracted towards the pylorus, loose at the cardiac extremity. On washing this organ the epithelium came off. The mucous membrane over the cardiac portion was softened, gray, but dotted with numerous purple ecchymoses. Beneath, the muscular tunic was greatly congested. There were two large bloody patches—one where the œsophagus enters the stomach—the other at the lower portion of the cardiac sac. The upper part of the small intestines exhibited appearances approaching those of the stomach. The lower part of the liver was darker coloured than natural. The membranes of the spinal chord showed marks of congestion, and there was some effusion of serum into the ventricles of the brain. The bladder was full. Bromine existed in the blood, liver, and urine.

Remarks.—These experiments appear sufficient to enable us to compare the operation of the bromide with that of the iodide of potassium, as shown by analogous experiments. According to Mr Blake, the salts of potass, when injected into the veins, destroy the irritability of the heart, and when introduced into the arteries obstruct the circulation through the systemic capillaries.* The experiments just related prove both these properties to be possessed by the bromide of potassium. In one of the cases where the salt was thrown into the jugular, the blood was fluid in both cavities. Death then was owing to destruction of the heart's irritability. In experiment 26th we see the salt first obstruct the systemic capillaries, and then, when it reaches the heart, we have destruction of the heart's irritability as in those cases where the poison was introduced at once into the organ. The convulsions which occurred when the salt was introduced into the circulation might be owing to the sudden arrestment of the circulation, or to a specific action of the salt on the nervous system.

Expt. 27th shows the effect of the salt in causing muscular contractions.

All these effects are very similar to the properties eliminated in similar experiments from hydriodate of potass ; although no experiment exactly similar to my 26th and 27th experiments is on record as performed with this latter salt.

Devergie observed oscillations of the fibres of the tongue after death, in a dog killed by injection of the iodide of potassium into the jugular. These oscillations might correspond to the muscular contractions related in experiment 23d.

The experiment on the rabbit shows a very similar action on the stomach of this animal to that described by Dr Cogswell, as possessed by the iodide, "Several small coagula of blood were scattered over the inner surface, and the lining membrane itself

* Edin. Med. and Surg. Journal, July 1, 1841, p. 123.

was penetrated with crowds of small bloody extravasations bordered by brownish red areolæ.”*

I had made some experiments with an impure bromide before my attention was drawn to its adulteration.

A mongrel dog had a drachm and a-half of the impure salt introduced into his stomach. This was at mid-day. During the ensuing night he was much purged. The same dose was given every day for a week; he became thinner and lost power over his limbs to some extent, but retained his appetite. A drachm of the salt introduced into the cellular tissue on the back of a rabbit produced much local irritation. Three drachms of it killed a rabbit in less than an hour and a-half, with symptoms which, so far as were observed, resembled those related in experiment 28th, and, with very similar morbid appearances, similar purple patches of ecchymosis being found in the stomach.

The physiological effects produced by the salt in small doses, on man for example, are exceedingly obscure. It acts as a diuretic; in some cases it occasions diarrhœa, and possesses somewhat of that action on the secretions and excretions which renders the corresponding iodide so powerful as a deobstruent. Here I may refer to the second part of this paper, in which the medicinal properties of the bodies are to be related.

The bromide of potassium is evidently less powerful than the iodide of the same base; the chloride is by no means devoid of the properties which its analogous bodies possess. I found fifty grains of the chloride dissolved in half an ounce of water capable of killing a dog when injected into the jugular, with symptoms closely resembling those produced by the allied bodies, the heart's irritability being destroyed.

Expt. 29th. The hæmadynamometer was connected with the femoral artery of a lively cocker-dog; and fifty grains of the bromide of sodium, dissolved in two drachms of water, were injected into the jugular. The mercury, whose highest mark was two and three-quarter inches, fell immediately to the level, and remained there for from fifty to sixty seconds, no oscillations being distinguishable. In a minute after the operation, the column began to rise, and soon regained its former level, the oscillations less frequent, but stronger than before the operation. Four minutes after the operation, the heart's action seemed quite restored, and he was set loose. He had completely lost the power of moving his limbs, but evidently retained consciousness. The pupil was dilated. The heart's action became synchronous with the respiration; being 54 in the minute. An hour after the operation he remained much in the same state, but gradually recovered.

Expt. 30th. One hundred grains of the same salt, dissolved in three fluid drachms of water, were injected into the jugular of a

* Cogswell on Iodine.

lively terrier bitch rather larger than the subject of the preceding experiment. The only symptom produced appeared to be excessively quickened and excited action of the heart. The animal on being set loose appeared lively and excited.

Remarks.—The bromide of sodium appears to bear a close resemblance to common salt in physiological properties. Its taste is exactly like that of common salt, nor does it appear to be much more energetic. The iodide of sodium seems, however, to be not destitute of activity.*

PHYSIOLOGICAL PROPERTIES OF THE BROMIDE AND IODIDE OF BARIUM.

These salts are included under the same head, because I am not aware of any experiments on either of them having been published. They both crystallize in needles. According to Berzelius, the crystals of the bromide have no resemblance to those of the chloride, which I presume means that they never affect the tabular form.

Expt. 31st. A scruple of the bromide of barium, dissolved in a small quantity of water, was injected into the stomach of a stout male rabbit. At the end of the first minute after the operation, the heart's action was feeble and irregular, and respiration hurried. In two minutes, loss of power over the voluntary muscles was perceptible; and ineffectual efforts to crawl were made. Towards the third minute, the animal kept moving its head from side to side. Between the fourth and fifth minute, a violent convulsion occurred, which flung the animal from a table on which it was placed. After this there were few signs of life, and these were altogether absent towards the seventh minute.

Inspection immediately.—Legs outstretched; neck rigid. There was but slight contractility of the voluntary muscles, and that of the heart was extinct. The peristaltic movement of the intestines was also absent. The blood in the great veins was of a treackly consistence; the jugular was full of blood. The blood was dark and partly coagulated in both sides of the heart. Lungs somewhat congested; as were the membranes of the brain. The stomach was vascular externally; the mucous membrane was red and softened at the cardiac extremity.

Expt. 32d. Six grains of the iodide of barium, dissolved in two fluid drachms of water, were injected into the stomach of a stout male rabbit at seven o'clock in the evening. For two hours and a half no effect except disinclination to move was manifest. Next morning at nine o'clock he was found lying on his belly making ineffectual efforts to crawl; fæces had been passed during the night. The heart's action was very feeble; respiration natural; pupils dilated, and the iris not affected by light. The eyelids closed when touched,

* Christison on Poisons, p. 605.

and the animal appeared to possess consciousness. The most remarkable phenomena were, convulsive strikings out of the limbs, tremors of the neck and shoulders, with occasional grinding of the teeth, and violent shaking of the head from side to side. On pricking the anus reflex phenomena were excited. At seven P. M., this state still continued, but the pupil was contracted. The temperature of the animal was now very low. He died at half-past eight.

On inspection, the state of the muscular system was the same as in the subject of the preceding experiment, but the irritability of the heart was not altogether absent. The left ventricle was empty. Peristaltic motion of the intestines continued. The mucous membrane of the stomach was rose-red at the cardia, and softened; its epithelium was removed, and some small dark patches of extravasation appeared at the surface. The small intestines appeared healthy; the colon contained fæces, and the bladder was full. The membranes of the brain and cord were congested, and there was considerable softening of the substance of the cerebellum and spinal chord.

Remark.—These experiments show that the bromide and iodide of barium possess the physiological properties of the class of salts to which they belong, and in particular, closely resemble the chloride of the same base.

PHYSIOLOGICAL PROPERTIES OF THE BROMIDE OF MAGNESIUM.

Expt. 33d. Three drachms of this salt, dissolved in a fluid ounce of water, were given to a stout rabbit.

Symptoms. Violent and irregular muscular contractions, chiefly affecting the muscles of the neck; feebleness; slowness of the respiration, with slow and weak action of the heart; death took place in eight minutes. The chief appearances on inspection were slight corrosion and reddening of the gastric mucous membrane.

Expt. 34th. Another rabbit had a drachm and a-half of the same salt dissolved in three fluid drachms of water injected into the stomach: No immediate effect was perceived. But although he took his food, debility gradually came on, and he was found dead on the third day after the operation. The epithelium of the stomach was removed, and the mucous membrane softened. Near the pylorus was a small oval slough with a raised border, and here there was a reddish coloration through to the peritoneal coat of the viscus. The small intestines exhibited several patches of inflammation; and the kidneys, liver, and membranes of the brain were congested.

Remarks.—There seems every reason for concluding that this compound of magnesium participates in the general physiological

action of the magnesian salts. Although this body is much less active than the bromide of zinc, yet the effect on the stomach, as displayed in the experiment just related, and also the general depression produced, resemble exceedingly the action of this more powerful salt when similarly administered. Mr Blake shows that the magnesian salts when introduced into the blood give rise to phenomena very similar to those brought about by the salts of zinc applied in that way.

PHYSIOLOGICAL PROPERTIES OF THE BROMIDE OF ZINC.

This salt is deliquescent as well as the chloride, to which, as to the iodide, it bears a close chemical resemblance. It is capable of coagulating albumen and solution of the colouring matter of the blood, to which it gives the brick-red tint produced by other salts of the same base. It is a compound of some interest in a physiological point of view.

Expt. 35th. Half a drachm of the salt, dissolved in two measured drachms of water, was injected into the jugular of a middle-sized, lively, and strong mongrel dog. The entrance of the fluid was followed by spasmodic dilatation of the chest, sudden cessation of the heart's action, and convulsive tremors of the limbs, with discharge of urine and fæces. On unbinding the animal, it was found dead in about two minutes from the time at which the operation was performed. The chest was immediately opened. The heart was found without motion, and gorged with blood, but, on irritating the organ with the point of a scalpel, feeble contractions were excited. The blood was perfectly fluid in both ventricles, florid in the left. The lungs were congested, and contained much froth. The voluntary muscles contracted on being cut.

Expt. 36th. Half a drachm of the salt, dissolved in three fluid drachms of water, was injected into the carotid artery of a strong mongrel bitch, in the direction of the heart, a haemadynamometer being connected with the femoral artery. As the injection was slowly made, the mercury, which oscillated at from three and a half to four inches above the level, gradually rose to six and a quarter inches. It continued at this height for a minute and a half, the oscillations being greater. It then fell to two inches, but speedily rose, and oscillated slowly for five minutes at nearly the elevation it had attained before the salt was injected. It then fell, and remained without movement. An universal spasm with escape of urine preceded death.

Three and a half minutes after death the heart was without motion, but contracted on being irritated. It was gorged with fluid blood, which was red in the left cavity, and of a lighter colour than usual in the right side. The lungs were affected with vesicular emphysema, and did not appear much congested. The voluntary muscles contracted on being cut.

Expt. 37th. A mongrel dog had fifty grains of the bromide dissolved in three measured drachms of water injected into his stomach by a flexible tube.

Symptoms.—Excessive vomiting and purging, with great prostration of strength. Recovery nine hours after the operation.

Expt. 38th. Sixty grains of the salt dissolved in half a fluid ounce of water were injected into the stomach of a stout rabbit. This was at six P. M. The respiration continued more frequent during the remainder of the evening. At six A. M. next day the animal was found dead; the legs outstretched; teeth closely set, and body very rigid.

The lungs were found dotted with congested spots, and much frothy serum exuded on cutting their tissue. About half an ounce of serum by measure was effused into the chest. The right side of the heart contained dark fluid blood; the left side was empty. The peritoneum contained a little serum; the bladder was full. The greater part of the stomach was in a state of decomposition. There was difficulty in washing it without removing the villous coat, which over the cardiac portion was completely softened and blackened, as in a state of gangrene. The epithelium was removed from the pyloric portion, which, as well as the small intestines, had little suffered. The surface of the liver touching the stomach was corroded.

Bromine was detected in the blood and heart, and in the corroded liver.

Remarks.—It thus appears that the bromide of zinc, when thrown into the venous system, puts a stop to the motions of the heart without, however, totally destroying the irritability of the organ; and that, when this salt is introduced so as to pass through the systemic capillaries before reaching the heart, it obstructs them temporarily, but exerts its deleterious influence on the central organ of the circulation when it arrives there in quantity.

Mr Blake states that he found sulphate of zinc without the property of obstructing the arterial systemic circulation. But the bromide appears to be a more active corrosive than the sulphate. I take this opportunity of saying a word with regard to the influences on the pulmonic and systemic capillaries, and on the heart's irritability, ascribed to many salts by this writer, and employed by him as differential tests or criteria. Those salts which obstruct the circulation through the systemic capillaries are, I think, capable of producing the same effect on the pulmonic vessels, unless they have also the power of arresting the heart's action. Should they produce this effect on the heart, the velocity of the flow of blood towards the lung is soon diminished, and the circulation arrested before congestion of the lungs can occur. Thus, when we introduce substances capable of so affecting the heart into the jugular,

we find no congestion of the lung produced, but sudden cessation of the heart's action. And we may suppose a dose of the salt large enough to congest the pulmonic capillaries, to be capable of putting a stop to the motions of the heart, *i. e.* where such a power is possessed. Moreover, I think that all irritants, and especially corrosive substances of the saline class, have more or less the power of obstructing the capillaries, when introduced so as to circulate directly to them.

Dr Cogswell found the heart of a dog, into whose jugular he had injected the iodide of zinc, in a state similar to that described in experiment 35th. The organ was gorged with blood, fluid in both ventricles, and red in the left; it was without motion when the chest was opened, but contracted on being irritated.* Experiment 38th bears a great resemblance to an experiment related by the same author, on the effects of the iodide introduced in the same dose as I employed of the bromide, also into the stomach of a rabbit.†

From the effects observed in experiment 37th, where the salt was introduced into the stomach of a dog, there can be but little doubt of the participation of this salt in the general action exerted by the salts of its class on the stomach and intestines when not in excessive or poisonous dose. In short, sufficient has been brought forward to enable the body to be brought under the general head of zincoid compounds as regards physiological properties.

PHYSIOLOGICAL PROPERTIES OF THE BROMIDE OF IRON.

This substance resembles the preceding salt in its action on albumen.

Expt. 39th. Forty grains of the bromide of iron dissolved in three fluid drachms of water, were injected into the jugular of a cur bitch, of middle size and strength. The operation was followed by cries, convulsive struggles, voiding of the urine and fæces, irregularity of the heart's action, and laborious respiration. On being set loose she lay quiet for a few minutes, and then tried to pass fæces. A quarter of an hour after the operation the respirations were 72, panting, and the heart's action feeble. After this, tremors frequently occurred; fluid stools were passed; and saliva flowed. The respirations became less frequent, the heart's action feeble, and the general appearance of the animal denoted great weakness. An hour after the operation she vomited. After this, moaning and tenesmus; great efforts of the muscles of respiration; fæces and urine often discharged. The urine contained both bromine and iron. Death took place at the expiration of three hours and a-quarter, being preceded by great prostration of strength and slow and difficult respiration.

* Cogswell on Iodine, p. 153.

† *Op. cit.* pp. 149-50.

On inspection there were strong contractions of the muscles; five minutes after death the heart's motion had ceased, and the organ could not be irritated; the peristaltic motion of the intestines continued. The blood in both sides of the heart was dark and fluid. There was some effusion of serum into the pericardium and pleuræ. The lungs showed marks of congestion; the intestinal veins, and those of the liver and spleen were engorged; the whole mucous membrane of the intestinal tube, from the stomach to the rectum, was affected; the villous coat of the stomach presented a violet tinge, gradually deepening towards the pylorus, and along the duodenum; the affection became greater in descending to the lower part of the canal; the jejunum and ilium had their villous coat of a deep purple hue, contained a large quantity of grumous blood, showed the Peyerian patches remarkably distinct and swollen, and several deep-coloured ecchymoses. The rectum was vascular, corrugated, and mottled with dark patches.

Expt. 40th. Forty grains dissolved in half-an ounce by measure of water were injected into the stomach of a stout rabbit. This was at six P. M. Next day, at eleven A. M., there was feebleness of the heart's action, and panting respiration; animal able to move. At three P. M. he was found lying on his side; heart's action scarcely perceptible; respiration slow; pupil greatly dilated. Death took place at four P. M.

Inspection.—The muscles contracted; not so the heart three minutes after death; peristaltic motion went on. Blood accumulated in the right side of heart; lungs slightly congested; stomach contained some food, and was greatly distended with flatus; the mucous membrane at the pylorus was pretty healthy; that of the cardiac portion showed the epithelium removed, and was softened in several places, especially around a number of irregular patches of a brownish hue, which had a gritty feel; the small intestines were healthy; the sigmoid flexure and colon empty; bladder full of dark-coloured urine.

On analyzing the stomach, its coats were found to afford evidence of containing iron, but not bromine; both the elements were found in the urine.

Remarks.—These experiments establish the analogy of the bromide of iron with other salts of the same base, and more particularly with the iodide, as its effects are shown in Dr Cogswell's thirteenth and fifteenth experiments. When injected into the veins it appears, as far as can be made out without the aid of the hæmadynamometer, to obstruct the pulmonary circulation, and weaken the action of the heart; when these effects are in some degree subsided, a powerful secondary action on the intestinal canal becomes apparent.

When I come to speak of the medicinal properties of this salt,

I shall have to relate some of its less striking physiological properties.

In experiment 40th, the salt appears to have undergone decomposition in the stomach, the oxide of iron being retained there.

PHYSIOLOGICAL PROPERTIES OF THE BROMIDE AND SUB-BROMIDE OF MERCURY.

These salts bear the most remarkable resemblance in chemical properties to the chloride and subchloride, to which also their physiological affinity is strict.

Expt. 41st. A scruple of the bromide, wrapped in blotting-paper, was pushed by a bougie into the stomach of a stout male rabbit, a little water being thrown into the stomach afterwards. In two minutes the respirations became fifteen in the minute. Inspiration was apparently made with great difficulty. The heart's action was quickened, being at the rate of 200 beats per minute, and enfeebled. The animal remained in this state till the end of the sixth minute, all the time on his legs, but apparently in a state of stupefaction. At this period he made an attempt to run, but was seized with convulsions, and fell on his side. Several convulsive movements of the whole body followed, and he died in about seven minutes from the operation.

The most remarkable circumstance on inspection was the solidification of the blood in the right side of the heart and veins, along with effusion of the fluid parts into the cavities of the pleuræ and ventricles of the brain. The muscular contractility remained, as did the peristaltic action after death, though the heart's irritability was gone.

Expt. 42d. Two and a-half grains of the bromide dissolved in two measured drachms of water were injected into the jugular of a lively and strong terrier bitch.

Effects.—Feebleness and irregularity of the heart's action; tetanic spasm lasting about a minute; slow and spasmodic respiration; attempts to vomit; tremors of the limbs; dilated pupil. Death took place in three minutes from the time the salt entered.

On inspection, the voluntary muscles contracted when cut; the heart's action had ceased, but the organ contracted when irritated, three and a-half minutes after death. The peristaltic action continued; lungs congested; bronchi filled with frothy serum. Right side of the heart gorged with blood, showing here and there brick-red spots; left side moderately distended with blood somewhat darker than natural.

Remarks.—The solidification of the blood in experiment 41st could not be a chemical phenomenon; because such is not the character of the chemical action of the bromide of mercury on blood. I performed several repetitions of this experiment—some before Dr Lonsdale and Mr Skae; but although I have seen a treackly appearance of the blood produced, I never again saw this

curious phenomenon. I do not allude to the solidification alone, but to the connection of this with effusion of the serum. As these experiments may be supposed to show the analogy of the bromide with the chloride, the following experiments were made with the chloride, in order to elucidate some points of doubt with regard to both salts.

Expt. 43d. Half an ounce of corrosive sublimate was introduced into the stomach of a strong terrier, and the gullet tied. The animal died in an hour. The mucous membrane of the stomach was found of a nearly uniform colour—of a blue slate tint, with scarcely a trace of vital action; but in the duodenum, and still more in the small intestines, where the quantity of the poison was diminished, there were abundant marks of vital action, *i. e.* irritation. The heart and about eight ounces of blood carefully collected from the great veins were digested for two days in nitric acid, successive portions of the acid being added. The mass was then set aside for a week, and a fresh digestion made. Then the acid liquid filtered through asbestos was heated to expel acid, water being repeatedly added. The solution was then carefully neutralized by pure caustic potass. When the point of neutralization had been nearly attained, each addition of caustic potass caused a faint lemon-coloured precipitate, which was speedily redissolved. On adding the carbonate instead of the alkali, a distinct red tint was assumed, which disappeared when the effervescence had ceased. I divided the liquid into three portions: one portion was evaporated to dryness, and strongly heated in a tube of Bohemian glass; protochloride of tin was added to another portion; a third portion was exposed to the action of tin-foil, which became dull.

Results. The first process gave very faint evidence of the presence of mercury; the protochloride gave a faint gray precipitate; the tin-foil on being heated did not give any perceptible mercurial vapour. As the reagents were pure, notwithstanding the imperfect evidence of the reduction test, there could be no doubt that the blood acted on by the nitric acid contained mercury, probably in the state of pernitate and corrosive sublimate.*

Since I gave in my essay containing this fact, for competition for the Harveian prize, M. Orfila has established the absorption of corrosive sublimate in the most satisfactory manner. His memoir is published in the *Journal de Chimie Medicale* for July; I performed the experiment just related in October 1840, assisted by my friend, Dr Embleton.

Expt. 44th. Ten grains of corrosive sublimate dissolved in half a fluid ounce of water, being thrown into the jugular of a dog, produced almost instant death, the heart's irritability being destroyed.

* The sub-bromide, like the subchloride, is converted by digestion in nitric acid into the bromide and nitrate, or per-bromide and per-nitrate, according to the nomenclature preferred.

Expt. 45th. Five grains of the same substance, dissolved in the same quantity of water, were injected into the carotid of a stout terrier bitch in the direction of the heart, the hæmadynamometer being connected with the femoral artery. The effect of the salt in obstructing the circulation through the capillaries was manifest; this obstruction was overcome in between two or three minutes; and the pressure in the instrument was diminished. On setting the animal loose, she lay on her side; the respiration of a spasmodic character, but the heart beating regularly; the eyelids closed, and no manifestation of consciousness; the limbs rigid, and tail bent backwards. She continued in this state for half an hour, when death took place, with no other previous symptom than relaxation of the sphincters.

On examination, the heart had no irritability five minutes after death; the blood was fluid and dark in both ventricles; the lungs appeared healthy. The membranes of the brain, especially at the base, were very vascular; the cortical substance of the brain was of a livid colour for about two and a-half lines from its margin, round the whole circumference of the organ, on section of which numerous dark spots were observable. The surface of the spinal cord throughout its extent showed the same lividity; the membranes were also vascular, and bloody serum was effused into the theca. The peristaltic action continued; there was some vascularity of the rugæ of the stomach.

A French writer has insisted much on the greater mildness of the physiological action of the bromide in comparison with that of the chloride.* I am willing to believe that its effects are not quite so great as those of the formidable and well known salt, not so much from actual observation, which will scarcely bear out so nice a distinction, as from more general considerations. To come to the point at once, I am induced to frame a law to the effect, that, among chlorides, bromides, and iodides of electro-positive metals, the iodide is the most active physiologically, then the bromide, and lastly the chloride; but this law is inverted when we get to the electro-negative metals, and their haloid salts. There the chloride is the most active, then the bromide, and lastly the iodide; thus in all cases the activity will be as the solubility of the salt, and as its facility of decomposition, according to what has been said of the affinities of chlorine, bromine, and iodine for electro-positive and electro-negative substances in the introductory part of this paper.

By way of example, the chlorides, bromides, and iodides of potassium and sodium may be cited in support of one part of the pro-

* M. A. Bonnet (*Bulletin General de Therapeutique*, Juillet 1837) maintains that the bromide is less apt than the chloride, during a long administration, to occasion pains of the head, chest, and abdomen.

position, the chloride, and red iodide of mercury, in support of the other. But, as a still more marked example in support of the latter part of the proposition, take the chloride and iodide of platinum. I found the former of these salts introduced in solution in a dose of ten grains into the stomach of a rabbit, to give rise to prostration of strength, slimy stools, abdominal respiration, finally death in six hours, preceded by great feebleness of the heart's action. After death the stomach exhibited a uniform brownish-gray corrosion over the cardiac portion. But the iodide in a dose of fifteen grains, similarly administered to another rabbit,* produced no effect.

The sub-bromide is strictly analogous to calomel in physiological properties.

Before concluding these observations on the action of the saline compounds of bromine, I may remark that we are yet completely in the dark whether any substances can obstruct the capillary circulation, but such as are capable of exerting a chemical action on the vessels or their contents.

PHYSIOLOGICAL PROPERTIES OF THE BROMIDE OF CYANOGEN.

Expt. 46th. Five grains of this compound, prepared according to the process given by Berzelius,† were dissolved in half an ounce by measure of distilled water, and injected into the jugular of a strong terrier bitch; she shrieked and struggled; a spasm of opisthotonos occurred, which lasted about a minute, during which the urine was discharged. The heart beat two or three times; and on complete relaxation from the spasm, the animal was dead.

The voluntary muscles contracted on being cut, the heart was without motion five minutes after death, but contracted on being irritated; the peristaltic action continued. The lungs displayed marks of congestion. The blood was found of its usual colour in both cavities, and partially coagulated.

Expt. 47th. Two grains of the same body dissolved in the same quantity of water as above were similarly administered to another dog. A tetanic spasm followed, attended with discharge of urine and fæces, and cessation of the heart's action and respiration for about a minute. The animal recovered, apparently without having sustained any permanent injury.

Expt. 48th. Ten grains of the substance were dissolved in two fluid drachms of water, and poured down the throat of a remarkably strong terrier dog. He immediately broke loose from those who were holding him, and rushed violently about, uttering frightful cries. This lasted about a minute, when he fell suddenly on

† *I. e.* suspended in water.

† After Serullas; see *Traité de Chimie*, t. i. p. 345.

his side, and lay apparently without consciousness ; no respiration audible, although the heart beat slowly and feebly. This state lasted for two minutes and some seconds. He then began to respire, at first slowly, and with much muscular effort. For half an hour he lay stretched out in a spasmodic state ; the legs stiff, and tail extended. The respirations gradually became quicker and more forcible. Towards the close of the period mentioned, they were 120 in the minute, and made with a loud rattle chiefly attending inspiration. The heart during the same time beat slowly and forcibly at about half the frequency of the respirations. The eyes were dull ; the pupils dilated ; the eyelids winked occasionally. During the time that he was in this state, he twice voided urine, and seemed insensible to several mechanical stimuli applied. The symptoms became gradually milder, but during the next forty minutes were still of a similar character. At the end of this time he got on his legs, having previously manifested symptoms of returning sensibility. He then vomited a quantity of slimy matter. He staggered and reeled in attempting to stand. The symptoms of affection of the nervous system subsided, but in their place signs of the most extensive and excessive irritation came on. The respiration continued husky and laborious ; the animal was debilitated to the last degree. Bloody foam issued from the mouth, to which there was constantly a large portion adherent. Large quantities of blood were vomited along with the shreds of mucous membrane. Bloody stools were passed. The great original strength of the animal enabled it to live for several hours in this dreadful state, when at last it was spined.

On inspection, the appearances of irritation were most extensive. The lungs were congested in several spots, and the bronchi filled with a mixture of bloody mucus and frothy serum. The mucous membrane of the trachea and part of the bronchi was removed. The lining membrane of the gullet was softened and dotted with ecchymoses. The outer surface of the stomach was intensely vascular ; and its villous coat appeared as if soaked in blood ; black tarry blood occupied the spaces between the rugae, which were very prominent. This state continued more or less intense throughout the entire length of the intestines. The membranes of the brain and spinal cord were vascular, and several bloody spots were visible on section of the former organ.

Expt. 49th. Five grains of the bromide dissolved in the same quantity of water as above were introduced into the stomach of another terrier, in order that the effects of antidotes might be tried. When the spasm appeared commencing he was treated with the cold affusion, and solution of ammonia applied to his nostrils. The effect of these remedies in recovering him was apparent. The dose of the bromide was repeated ; symptoms of irri-

tant poisoning came on, similar to those with which the subject of the preceding experiment was affected. The dog was hanged eight hours after the second operation. The bronchi and trachea did not show those excessive marks of irritation visible in the former case, but the digestive tube was in a similar state. Several singularly well-defined abrasions of the mucous membrane were visible in the stomach.*

Expts. 50th and 51st. In these experiments the bromide was injected into the peritoneum and stomach of rabbits, with the effect of producing death, attended by all the symptoms of speedy poisoning by prussic acid. In one case the irritability of the heart was extinguished, and the contractility of the voluntary muscles rendered very slight. The substance, judging from the diffusion of its odour, appeared to penetrate the tissues rapidly.

Expt. 52d. Thirty minims of the liquid ammonia of the P. L. strength mixed with seven fluid drachms of water being introduced into the stomach of each of two rabbits; one of the animals had five grains of the bromide dissolved in a fluid drachm of water injected into its stomach immediately after. Instead of being killed in less than a minute, as would certainly have been the case, but for the ammonia, it lived five minutes, without any symptom, and then was seized with the characteristic convulsions. But after all motion of the heart and lungs had ceased, a curious set of muscular tremors or vibrations commenced, affecting especially the muscles of the chest, and continued for not less than from ten to twelve minutes. This effect I ascribe to the action of the cyanide of ammonium formed by the resolution of the bromide of cyanogen into that salt and the bromide of ammonium. The other rabbit lived about twenty-four hours.

Remarks.—The bromide of cyanogen appears to possess two kinds of action; one on the spinal cord—perhaps primarily on the sympathetic system, closely resembling the primary effect of prussic acid. But the secondary or irritant action far exceeds in intensity that of prussic acid, and probably that of any known irritant. This body has little corrosive power, it coagulates white of egg but slowly, and is as nearly as possible a pure irritant in its secondary action. In the 48th experiment, the great irritation exercised on the respiratory passages was probably owing to some of the poison having entered them. Ammonia cannot be useful as a chemical antidote either to this body or to prussic acid; neither can chlorine be otherwise beneficial than as a stimulus, for, according to Serullas, the chlorocyanic acid is no whit inferior in activity to the compound whose effects we have just seen. The iodide of cyanogen appears to be nearly as powerful as either of the other bodies.†

* This is the stomach represented in Plate IV.

† Magendie has admitted this body into his formulary.

PHYSIOLOGICAL PROPERTIES OF THE BROMIDE AND CHLORIDE OF OLEFIANT-GAS, OF BROMOFORM, CHLOROFORM, AND IODOFORM.

The only experiment on an animal with any of this class of bodies is one related by Dr Cogswell with iodoform, which he terms sesquiodide of carbon, but which we now know to be a compound of three atoms of iodine with one of formyl. The curious results of this experiment led me to investigate this class of bodies which, from the results of my experiments, appear to form a new class of poisons, and to be possessed of properties not unlikely to be beneficial in the treatment of disease.

The composition of these bodies, taking the compounds of chlorine as examples, is $C_4 H_5 Chl.$ + $H Chl.$ for the chloride of olefiant gas; and $C_2 H Chl_5$ for chloroform.

In the investigation of the properties of these bodies, I shall first show the striking resemblance in leading characters among the members of the group, and then take chloroform as an example of some of their more minute properties.

Expt. 53d. Thirty minims of the chloride of olefiant gas were introduced into the jugular of a small but lively mongrel dog eight months old. Immediately the animal commenced a series of short barking yells, each of which was synchronous with expiration. Before the operation the respirations were 48; after it they became 68 in the minute; expiration made with great effort of the abdominal muscles. The heart's action was quickened and irregular, but masked by the state of the respiration. From the first he lost all power of locomotion, but retained consciousness. In twenty minutes, his chest being pressed with a view to auscultation, he redoubled the barking yells. He was now placed near the fire, where he remained lying on his side; the eyelids at first half-closed. Large bubbles could be heard in the chest, and there was a clacking noise in the mouth proceeding from movements of the soft palate. In an hour and a-quarter from the operation, he made an effort to get on his legs, and succeeded, but speedily fell again on his side, and lay in this position. At this time the respirations were 82, and distinct crepitations could be heard. The bubbles continued of the same extensive character. A singular phenomenon appeared about the second hour. This was a suspension of the respiration during a period of fifteen seconds, the length of which never varied, but which occurred at irregular intervals, on the average, at every half-minute. This suspension might be a protracted expiration. The respirations gradually became slower, the heart's action imperceptible; the animal heat declined rapidly; towards the third hour, a little before death, the temperature was 63° in the axilla, 72° in the groin, and 82° in the rectum; the temperature of the room being 62° .

Inspection.—The mouth was open and tongue pendent; the smell of the chloride, which had been felt in the breath almost as soon as the substance was introduced into the jugular, still remained at the mouth. The voluntary muscles contracted when cut; five minutes after death the heart had no irritability. Peristaltic movement of the intestines continued. Nearly an ounce by measure of bloody serum was found in each pleura. The right side of the heart contained a little fluid blood; left side nearly empty. The left lung was so black and engorged as to surpass any pathological state previously witnessed by Dr R. Elliot or myself. The organ was only crepitant in one or two spots near the entrance of the bronchi. The texture was easily broken down, and the whole might be described as one vast apoplectic spot. The right lung presented a very similar state. On cutting into the pulmonary tissue much blood and bloody froth issued; the latter filled the bronchi. The membranes of the brain and spinal cord were vascular; section of the brain showed several bloody spots.

Expt. 54th. This experiment, with the bromide of olefiant gas, was the first that I tried with this class of bodies, and I employed an unnecessarily large dose of the substance. Three measured drachms of the substance were injected into the jugular of a healthy female ass of eleven months old. On the entrance of the fluid the respirations were quickened, and the animal was seized with a short dry cough. The heart's action became quick, at first irregular, then very feeble. A few convulsive movements of the limbs took place, the cough was exchanged for a kind of husky expiration, and death took place within three minutes from the operation. In about thirty seconds after the substance entered, its smell was perceptible in the expired air.

The inspection was immediately made. The voluntary muscles contracted strongly; the heart was without motion, and did not contract when irritated. The blood in both the cavities was somewhat frothy and mixed with large masses of coagula. In the left ventricle was found a mass of clear coagulated lymph. The lungs were in many parts of a light purple colour, but their lower border almost black. Everywhere they were scattered with congested spots. Towards the lower part the tissue was broken down in many parts, and saturated with blood. The bronchi contained a large quantity of frothy serum, and their lining membrane was deeply injected. The organs of the nervous system showed no morbid appearances. The smell of the compound was perceptible directly the chest was opened.

Expt. 55th. Forty minims of the chloride were introduced into the stomach of a stout male rabbit. Immediately after the operation symptoms similar to those observed in experiment 53d came on. For the first forty minutes the respiration might be

styled asthmatic, inspiration being quick and expiration protracted, and made with a wheezing noise. During this time the heart's action was quick, feeble, and irregular; the pupil dilated, and iris little contractile; the eyes suffused with watery fluid. There was great loss of power over the voluntary muscles. He partly recovered from this state, but was found dead ten and a-half hours after the operation.

Inspection.—Body very rigid; jaws firmly closed; nose and mouth bloody. The principal internal appearances were congestion of the lungs, dark fluid blood in both sides of the heart, and pink-coloured froth in the bronchi, with slight congestion of the brain, and softening of the gastric mucous membrane, which was dotted here and there with dark spots.

Expt. 56th. Fifty minims of the bromide were introduced into the stomach of a suitable rabbit. The effects closely resembled those described in the former experiment. Although the power of locomotion was gone consciousness remained. Death took place in two hours, being preceded by convulsive movements of the head and fore legs, and twitchings of the upper lip. In this case the body was opened immediately after death. The voluntary muscles contracted very feebly; the auricles were contracting, and contractions of the ventricles could be excited by stimulation. The peristaltic action went on. The odour of the poison was perceptible in the muscles, and in fact everywhere throughout the body. Similar appearances were found in the chest to those described in the preceding experiments. The membranes of the brain and spinal cord were healthy. The stomach had its mucous membrane blackened over the cardiac portion, especially towards the greater curvature; here and there were purple patches surrounded by flakes of mucus; there were also marks of congestion. The organ was quite flaccid. The upper part of the small intestines was affected as the stomach.

Expts. 57th and 58th. In the former of these experiments sixty minims of chloroform killed a poodle dog when injected into the jugular, in forty-five seconds, with symptoms similar to those occasioned in experiment 54th. In the 58th experiment, twice the quantity killed a large dog of Newfoundland and greyhound breed, with about the same degree of rapidity, and much the same symptoms. In both cases when the chest was opened, with the least possible delay, the heart was found gorged with clotted blood and its irritability destroyed. The muscles of voluntary motion contracted after death, and the peristaltic action went on. The lungs were congested to a surprising degree, and the bronchi filled with frothy serum.

Expts. 59th and 60th were performed on rabbits, into whose stomachs chloroform and bromoform were introduced, when effects

were produced similar to those resulting from the similar administration of the chloride and bromide of olefiant gas.

Expt 61st. A bitch full grown, between the beagle and pointer, was the subject of this experiment. Thirty minims of chloroform were injected into the jugular vein, a hæmadynamometer being connected with the femoral artery. In three or four seconds after the chloroform was introduced, the mercury fell from six inches above the level at which it had been oscillating, in a minute and a-half it had fallen to an inch, the heart's pulsations were manifested regularly during the descent, and were slower and more regular than before the operation. At the lower level, the oscillations became more considerable, sometimes carrying the mercury up to three inches, owing probably to struggles and expiratory efforts. In about two minutes the mercury began to rise, and attained the level of two inches. It continued to oscillate more regularly from this to a few lines higher, until ten minutes after the operation, when the animal was unbound; she was in a state of excessive prostration, but gradually recovered.

Expt. 62d. Sixty minims of chloroform were very slowly injected into the jugular of a large shepherd's dog.

Symptoms.—Irregular and hurried action of the heart; struggles; quick and forcible expiration, accompanied with a short bark; dilatation of the pupil; discharge of urine, and a temporary spasm, during which he was bent backwards. All this took place in two minutes. After this he lay still for three minutes; no respiration perceptible; the heart's action excessively feeble. He then began to breathe again, and gradually recovered, the recovery being attended for some time with great disorder of the respiration, loss of power over the voluntary muscles, and great prostration. Next day he was unwilling to move, and the respiration continued laborious. Four days after the operation he was poisoned by prussic acid, when the lungs were found to retain marks of the great congestion produced by this class of poisons.

Expt 63d. The same quantity of chloroform as in the preceding experiment was injected into the carotid of a lame pointer bitch, in the direction of the circulation. No struggle followed the injection of the fluid. A forcible inspiration, succeeded by a single expiration, ensued. The urine was voided. The heart continued to beat feebly, when every other sign of life was extinct. The animal was quite dead in a minute and a half.

The chest was immediately opened. The muscles contracted strongly on being cut. The heart, which was gorged on its right side, relieved itself of some of its contents on incision being made into it; the left side contained dark-coloured fluid blood. The lungs had collapsed on opening the chest, and seemed quite healthy. The membranes of the brain were much congested; there

was much serum in the ventricles ; and bloody serum at the base of the brain.

Expt. 64th. Sixty minims of chloroform were injected into the peritoneal cavity of a large male rabbit. Death ensued in seventeen minutes.

Symptoms.—Slight transitory excitement ; loss of power over the limbs ; profound coma ; excessively dilated pupil ; heart's action feeble ; great excitement of the respiration and dilatation of the chest ; a few slight movements of the limbs synchronous with the respiration. No motion could be excited by pricking or pinching the limbs ; nor did the eyelids move on approaching an object to the eye. He passed urine a few minutes before death.

Inspection.—Small intestines greatly congested externally, and their coats hardened where the chloroform had touched ; a large oval ecchymosis, which might equal the superficies of a half-crown, was visible between the muscular and peritoneal coats of the stomach. On cutting into the chest, the lungs collapsed, but contained much dark-coloured blood. The heart had dark blood in both its cavities, and retained its irritability. The peristaltic action was stopped ; and the voluntary muscles had little contractility. The brain was healthy ; the smell of chloroform was distinct in the chest and in the urine passed a few minutes before death.

Expt. 65th. Sixty minims of chloroform, in this experiment, killed a rabbit in half an hour when injected into the stomach. The symptoms were first those of action on the spinal cord, or primarily possibly on the sympathetic system ; the respiration became affected, and coma supervened.

After death the mucous membrane of the stomach was found white and corroded near the œsophagus ; over the rest of the cardiac portion dotted with purple patches of ecchymosis. The epithelium was removed from the pyloric portion and the mucous membrane reddened.

In other experiments with this substance on rabbits, the animals which recovered from the primary effects of its introduction into the stomach were sometimes found to die of the acute gastritis thus induced.

Remarks.—Great resemblance exists among the properties of this class of bodies which appear to form a new order of poisonous substances, uniting in themselves physiological properties which are not found united in any other known class of poisons. The distinguishing characteristics are first, the remarkable power they possess of obstructing the pulmonic circulation, whether they are injected into the veins or introduced into the stomach ; then the action on the spinal cord and afterwards on the brain ; and lastly, the corrosive and irritant action exercised on the stomach. In the case where chloroform was injected into the carotid, death appears to have been produced by the loss of nervous action conse-

quent on the direct action of the poison on the brain. This effect might be accounted for by the obstruction to the flow of blood through the capillaries of this organ thus induced. The mechanical properties of this class of bodies may peculiarly fit them for obstructing the circulation through the lungs. It was shown, for instance, that, when injected into the jugular, their smell is almost instantly perceptible in the expired air, so that the vapour getting into the air-cells may place the blood much in contact with the substance. The action on the spinal cord is very different from that of strychnia, to which my friend Dr Cogswell compared it in the case of iodoform. Strychnia destroys the influence of the will over the muscles, but appears to excite the spinal cord, which loses its sensibility under the action of this class of poisons. The blackening of the mucous membrane of the stomach which these substances produce is another curious property. This effect appears to be compounded of the corrosive and irritant action of the poison, its effects on the colouring matter of the blood, and that congestion of dark blood found in the stomach in certain cases of coma.

Where the poison was introduced directly into the circulation, we had the heart's action put a stop to, and its irritability destroyed, where the dose was large. In other cases a smaller dose caused obstruction to the flow of blood through the lungs, while the heart's action continued; and in one case this obstruction was shown by the haemadynamometer. In that case the pressure in the arterial system was diminished, but the heart's action continued.

The difference between the action of iodoform and that of the other members of the group, is, that this body produces the peculiar effects more slowly, owing, doubtless, to its solid form.*

The whole group have a surprising power of penetrating the tissues. Dr Cogswell found iodine where iodoform was given into the stomach, after death, in the blood, brain, and muscles; and I have observed the most distinct smell of the substances to a similar extent.

PART II.—MEDICINAL PROPERTIES OF BROMINE AND ITS COMPOUNDS.

Bromine was first used as a medicinal agent by M. Pourché, a townsman of Balard. Previous to this, a person named Desorgues, calling himself *simple magistrat*, had written to the Academy of Medicine, proposing the employment of bromide of mercury in the treatment of syphilis.

* I have used iodoform with great benefit externally in many obstinate skin affections, such as *lepra*, *psoriasis*, chronic eczema; and internally with benefit in a very old case of bronchocele, and in scrofulous enlargements of the glands. I gave it in doses of two grains thrice a-day in pill, with mucilage and bread crumb; externally, in the form of an ointment of half-a drachm to the ounce of simple cerate. I believe that this may prove one of the most valuable remedies that we have.

M. Bonnet, in a paper published in the *Bulletin Général de Therapeutique*, July 1837, gives a complete digest of what had been then observed in France with regard to the medicinal uses of bromine and its compounds. He refers to the researches of M. Pourché. In a case of scrofulous enlargement of the glands of the neck in a woman of 22 years of age, who had been affected for seven years, a cure was effected in three months by the external and internal use of bromine. At first six drops dissolved in three ounces of water were given in the day, in three doses. Next day, ten drops were given. In ten days, the dose was increased to fourteen drops daily, and at last to thirty drops in the same quantity of water. Cataplasms, moistened with solution of bromine, were applied to the swellings. The same physician had great success in the treatment of scrofula by the internal and external use of the hydrobromate of potass.

M. Bonnet attributes great advantages to the bromide and sub-bromide of mercury, as constitutional remedies in comparison with corrosive sublimate and calomel. He states, that the sub-bromide has less action than calomel on the salivary glands, and more effect on the urinary secretion; that the former substance is therefore preferable where the idiosyncrasy of the patients renders them liable to salivation. After stating that the bromide is less soluble in water than the chloride, he recommends a solution in ether for medicinal use, and gives the observations of an Austrian physician, which prove the antisiphilitic virtues of the remedy, and contends that it is not so liable as corrosive sublimate to affect the head, chest, and stomach during its medicinal use.

In the cases of M. Fournet, already referred to, the therapeutic action of the bromine is exceedingly obscure. Frictions of bromine to the swollen articulations appear to have been useful, but as their application was conjoined with alkaline baths, and, moreover, the bromine was mixed with alcohol, which would soon change it into bromal and hydrobromic ether, these cases prove very little.

Magendie employs bromine and its preparations in scrofula, amenorrhœa, and in hypertrophy of the ventricles. He expresses his conviction that future observation will establish the great therapeutic powers of bromine.

Dr Williams has used the bromide of potassium with success in cases of enlarged spleen. The first case which he gives is that of a boy, aged 14, admitted into St Thomas' Hospital on the 13th of September 1833. Both the liver and spleen were enormously enlarged. Their edge was hard, and substance unyielding. The abdomen contained much fluid; the countenance was sallow and emaciated; the legs dropsical; belly protuberant. The prognosis was most unfavourable. After unsuccessful trial of the super-

tartrate of potass and iodide of potassium, the iodide of mercury was used. This last remedy removed the dropsy, but the liver and spleen remained enlarged. On the 13th of May, the patient commenced with a grain thrice a day of the bromide of potassium, which dose was gradually increased to four grains. On the 10th of July he became slightly jaundiced. From apprehension that the bromide might have caused this, he had doses of the sulphate of magnesia instead until the jaundice had disappeared, when, on the 11th of August, the bromide was recommenced in four grain doses. On the 15th, the dose was increased to five grains thrice a day, and continued for fourteen months. Under this treatment, he gradually improved, and was dismissed with the liver and spleen only one-third of their former size.

In a second case of enlarged spleen with ascites, in a woman aged 30, the bromide could not be given in larger doses than four grains three times a day, on account of its tendency to disorder the bowels. After nine months treatment by the bromide, she was dismissed with the spleen still above the natural size. Dr Williams gives two more cases in which the results were of the same character.

I shall give a summary of my own results.

CASE I.—Eczema of the legs and arms in a married woman aged 40, of strumous habits, the mother of a large family. The disease, an inveterate form of eczema, had lasted a twelvemonth; for six months she had been under the care of Mr Brady of Gateshead, who had tried a variety of remedies without success. The eruption became moist every morning about three o'clock, and continued so for an hour, it then turned dry, and was accompanied by heat, redness, and itching. A saturated solution of bromine mixed with water until it ceased to give pain, and applied by means of lint and oil-skin, caused a decided improvement to take place. In two months the patient was cured.

CASE II.—Specific ulcers of the legs of long standing. This was a case treated in the Edinburgh Infirmary under the care of Dr Handyside. The man, aged 22, had been suffering for thirteen years from the effects of a kick of a horse, which had produced lacerated wounds on the anterior surface of the tibiæ at their middle third. According to his own account these never entirely healed. On admission, there were several small ill-conditioned sores over the seat of the former injury. From the 9th of May to the 20th of June, various metallic washes were applied to the ulcers without success. Then, the ulcers were treated with a strong ethereal solution of bromine, which acted as a caustic, and lint steeped in saturated solution of bromine placed over them, covered with oil-skin. Next day the same process was repeated. The application produced pain and intense redness, and after the

second time was not repeated. The ulcers healed rapidly afterwards, and cicatrization took place.

CASE III.—A case of carbuncle, under the care of Mr Bennett of Gateshead, which after resisting the hydriodate of potass used externally and internally, was cured by the external use of a solution of bromine—forty minims to the pint of water—in between six and seven weeks. Mr Bennett has used the lotion of bromine with success in many cases of skin affections, and in a case of purpura.

CASE IV.—Anomalous syphilitic tubercles of the legs. This was a strong man of 36 years of age, who had been affected with syphilitic and mercurial symptoms for eight years. For six years, he had a discoloration of the skin of the right fore-arm and left thigh, accompanied with pain of the bones at night. For several years, swellings have formed on these parts, which broke, leaving deep ill-conditioned ulcerations. The case was under the care of Mr Dawson of this town, who commenced the treatment on the 14th of May 1841. At first, the lotion of bromine—ten minims to the pint, was employed for a month, with the effect of cleaning the ulcers, and removing the discoloration, in a great degree; after this, he had an ointment composed of eight minims of bromine, and half a drachm of the bromide of potassium to an ounce of lard, which was ordered to be well rubbed on daily. Under this application, without internal treatment, the sores had healed, and the discoloration was removed by the 15th of December. Previous to the commencement of the treatment, the disease had a very formidable appearance.

CASE V.—Sarcomatous tumour of the knee, of about the size of an apple, spongy, not painful, in a woman aged 44; removed in a month by frictions of an ointment composed of thirty minims of bromine and a drachm of the bromide of potassium to an ounce of lard.

CASE VI.—Purulent ophthalmia in a child, where Mr Brown of Jarrow substituted a lotion of bromide of potassium, three grains to the ounce, with success, for the sulphate of zinc previously added.

CASE VII.—Scrofulous ulcer of the leg in a boy aged 12. Admitted into the Newcastle Infirmary under the care of Sir J. Fife, July 5th 1839. A large foul scrofulous ulcer occupied nearly the whole of the inner aspect of the left leg. There was a similar ulcer of the size of a half-crown on the back of the right wrist. There was great pain in the ulcer of the leg, the appetite was bad, and he slept little. The sore on the leg had lasted for three years. Tonics and hydriodate of potass internally were conjoined with the external use of creosote and ioduretted solution of hydriodate of potass. No benefit was produced. In the be-

ginning of December, the bones of the leg and carpus were obviously diseased, and symptoms of hectic appeared. The hydriodate of potass was again tried; no benefit was derived, and the lotion of bromine in the dose of forty minims to the pint of water was applied externally three times a-day by means of lint and oil skin, while the bromide of potassium was given internally.

Under this treatment the ulcers assumed a more healthy aspect, and gradually diminished in size while their foetor and pain were lessened. In six weeks the ulcer on the leg was nearly healed; that on the wrist continued open. He was then made an out-patient, and died in the course of the winter, I understand, of diabetes. The bromide of potassium was at first given in the dose of three grains thrice daily in pill. After three days this dose was increased to four grains, and so every three days until twenty-four grains were taken daily. Under this treatment the appetite improved, the night-sweats diminished, and the urine increased in quantity. Bromine was several times found in the urine during the treatment.

CASES VIII. IX. X. and XI.—These were cases of malignant ulcer of the face, and syphilitic ulcers, where the bromide of mercury was employed internally in the dose of the eighth of a grain thrice a-day, while the solution of bromine of the strength described in the preceding case was used externally. All the patients were men, and the cases were observed in the Newcastle Infirmary. The syphilitic ulcers rapidly healed, but during the internal treatment in three of the cases, symptoms of physiological action were observed exactly like those of corrosive sublimate. Very severe head, chest, and stomach affections were produced. The case of malignant ulcer was somewhat improved, and in this case, although the urine was increased in quantity during a treatment of a month, no head, chest, nor stomach affection was observed. There was slight salivation.

CASE XIII.—Mesenteric tumour in a weaver aged 22, Edinburgh Infirmary. Here the bromide of iron was used internally without success, so far as the swelling was concerned, but with improvement of the appetite. The dose was twelve grains in twenty pills, two morning and evening, from the 12th to the 21st of August 1840.

CASE XIV.—Here the bromide of potassium was employed internally in a case of scrofulous enlargement of the glands of the neck in a pitman aged 19, the same salt with bromine being used externally in the form of ointment. Five grains of the salt were given internally every three hours; and the ointment was composed of thirty minims of bromine, and a drachm of the salt to the ounce of lard, and rubbed on thrice a-day. In three weeks the glands were reduced to a third of their size, and some pain which

had been felt in the throat was no longer experienced ; then the glands began to suppurate ; the internal treatment produced no constitutional effect. I owe this case to Mr Brown of Jarrow.

CASE XV.—Scrofulous enlargement of the glands of the neck in a girl aged 16, treated by the bromide of iron internally, and ointment of bromine and hydrobromate of potass externally. The internal remedy was given in the dose of forty drops of a solution of one drachm in two fluid ounces of water twice a-day ; the external application was of the same strength as in the preceding case. The treatment was continued from the 22d of June 1841, to the 11th of August, when the general health was much improved, but little effect had been produced on the tumours.

CASE XVI.—Hypertrophy of the submaxillary gland in a youth aged 18. Treatment and result similar to that in the preceding case. The internal remedy caused some degree of diarrhoea.

CASE XVII.—Case of rupia treated by lotion of bromine externally, and the bromide of iron internally. The patient, aged 23, was treated in the Newcastle Infirmary by Dr Cargill. While the sores of one leg were treated by the lotion of bromine of the strength of forty minims to the pint, those of the other leg had nitrate of silver applied ; the superiority of the latter application was very evident. The bromine produced soreness, and a serous exudation from the ulcers ; the ointment of nitrate of silver, on the other hand, only caused temporary pain, and was soon the means of forming a dry scale. Two drachms of the bromide of iron were dissolved in two fluid ounces of water, and the patient had twenty drops three times a day. The treatment was commenced on the 22d day of February 1841. The external treatment by bromine was soon suspended. The dose of the internal remedy was gradually increased to 100 drops three times a day. This large dose on the 22d of March had produced no unpleasant symptom, but great improvement of the appetite and increase of strength appeared to have resulted from its use. The rupia got well under the application of nitrate of silver.

CASE XVIII.—Chronic rheumatism in a man aged 24. Here the internal use of the bromide of iron in the dose of six grains thrice a day gave rise to severe pain of the head and chest. (Newcastle Infirmary.)

Remarks.—The cases whose prominent features I have thus endeavoured to describe can be only supposed to give the slightest possible foundation on which to frame inductions with regard to the real therapeutic power of bromine and its compounds. I should be induced to recommend the external use of bromine in scaly darts affections of a peculiarly inveterate character, in specific and malignant ulcers where there is defective action, and in the form of lotion the element furnishes an elegant and cleanly

application. The solution is slowly changed by the action of light; the hydrobromic acid being formed. Oil skin should be employed to cover the lint in which the bromine is dipped, in order to prevent the evaporation.

Internally the use of bromine must necessarily be very limited. The sensation which attends the swallowing of it is, I repeat, truly horrid. The bromide of potassium is less powerful than the iodide, and might perhaps be used with advantage where the latter is apt to disagree with the stomach. The bromide of iron is perhaps the most agreeable of the strong preparations of iron. I have prescribed it frequently as a general tonic, and in hysteria and leucorrhœa. I conceive it to be less liable to decomposition than the iodide. A most exaggerated notion has been entertained of its power. The bromide and sub-bromide of mercury appear to have the good and bad properties of corrosive sublimate and calomel.

PART III.—GENERAL CONCLUSIONS.

1. Bromine appears to resemble chlorine much more than iodine in its physiological properties.

2. All the bromides seem to bear a closer relation to the chlorides physiologically than to the iodides.

3. The chemical and physiological relations of the group of halogenous elements and their compounds are in strict accordance.

4. Although in general the compounds of chlorine, bromine, and iodine with metals appear to resemble other salts of the same bases, in their action on the animal economy, yet we may perceive that the haloid salts are for the most part marked by peculiar resemblances.

5. As far as we can observe, the class of medicinal agents which bromine and its compounds furnish, is intermediate in medicinal action between the two allied groups, but nearer that of chlorine than that of iodine.

CORRIGENDA.

Page 11, 5th line from the bottom, *for would read "could."*

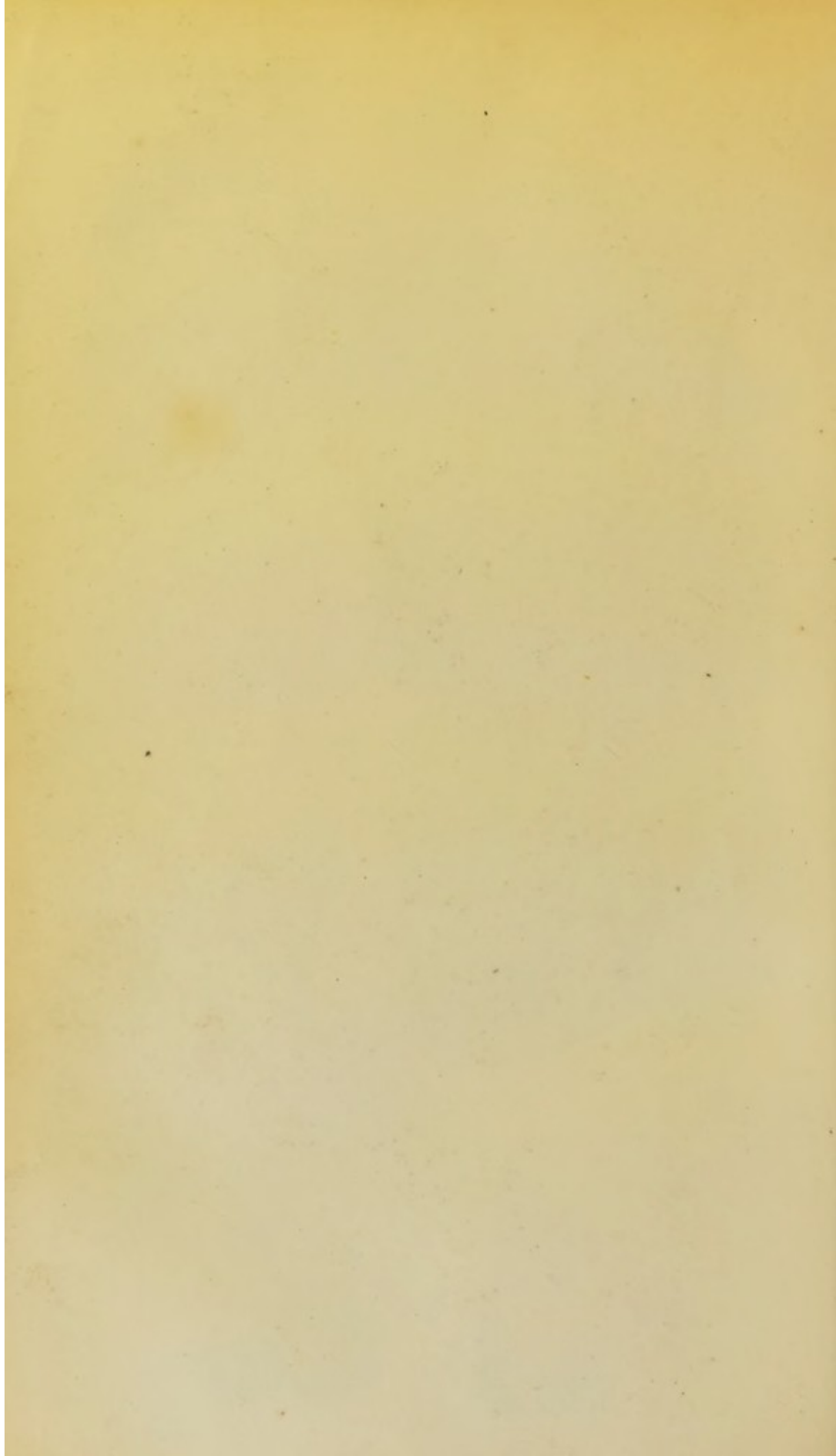
In note, p. 13, *for soluble in a large quantity read "soluble in a large quantity of water."*

P. 14, 16th line from top, *for recent symptoms read "seconds : symptoms."*

15, 4th ——— *for these read "there."*

D^R GLOVER'S PAPER.





*Stomach of dog destroyed by Bromide of Cyanogen
with abrasions of mucous membrane.*

D^r GLOVER'S PAPER



Geo. Akeman sc.

