namely, it releases the mesenteric occlusion of the duodenum by removing the downward traction of the mesentery and the weight of the dilated stomach. We should expect that it would be more efficacious than the gastric lavage, since experimentally it was found that the factors which permit of the absorption of intestinal poisons, i. e., obstruction with distention, are far more important than the production of these poisons. This type of toxemia in dogs can be successfully controlled by the frequent administration of large amounts of Ringer's solution or salt solution intravenously or by hypodermoclysis. There is no reason why such treatment may not be tried in clinical cases.

ABSTRACT OF DISCUSSION

DR. JAMES J. MOORHEAD, Terre Haute, Ind.: Speaking of acute dilatation of the stomach from the clinical standpoint, I recently had this rather unusual experience: A patient was admitted to the hospital suffering from a gunshot wound of the lower abdomen received thirteen hours previously. An enormous distention of the stomach was relieved by the use of a tube, and the patient was prepared for laparotomy. During the intra-abdominal work—six perforations of the small intestine were closed—a recurrence of the gastric dilatation subsided following the treatment employed in the first instance. Dr. Dragstedt's paper emphasizes the value of animal experimentation in the solution of clinical problems.

DR. JOHN J. GILBRIDE, Philadelphia: I was interested to hear from the pathologist as to his views on the etiology of acute dilatation of the stomach. My acquaintance with the subject was made in 1901 when I came across a little booklet of lectures on "Tumors of the Stomach," by the late Sir William Osler, which he delivered at Johns Hopkins Hospital. There is shown a plate of a necropsy in which the abdomen is opened and in which an acutely dilated stomach practically fills the entire abdomen. Acute dilatation of the stomach occurs most frequently after operations on the upper abdomen. However, it may occur after operation on any part of the body. It has occurred after operation on the head, and it has also occurred after the application of a cast or other apparatus for a support in disease of the spine. Both the motor and secretory functions of the stomach are profoundly affected. The stomach becomes hugely and rapidly dilated. There appears to be a profuse secretion into the stomach. This comes mostly from the stomach, and it is probably augmented by secretions from the pancreas and the liver. It appears to me that obstruction as an etiologic factor does not explain the condition. Personally, I believe that the statements made about compression of the duodenum by the superior mesenteric vessels are more mythologic than real. Gastro-enterostomy does not accomplish anything in these cases. Paterson had acute dilatation of the stomach occurring in two cases in which he had performed gastro-enterostomy for ulcer.

DR. A. J. CARLSON, Chicago: This work seems to link several known facts, particularly in connection with intestinal obstruction and intestinal intoxication, so that the interpretation offered must be refuted by something more substantial than mere guess. The work suggests a more rational therapy of that condition than gastro-enterostomy, because gastro-enterostomy would not necessarily relieve an obstructed duodenum. Dr. McKenna suggested some years ago the production of a fistula in the duodenum for the relief of general peritonitis, on the theory that some of the symptoms of general peritonitis involve interference with the duodenal functioning (obstruction). Would it not be feasible to introduce a duodenal tube for drainage of the obstructed duodenum via the mouth? This should be superior to the duodenal fistula operation for an obstructed duodenum, as this operation at times induces a more severe obstruction than the one we attempt to relieve by it.

DR. LESTER R. DRAGSTEDT, Chicago: We have never produced acute dilatation of the stomach in an experimental animal. A toxemia of high intestinal origin will cause death with practically all of the symptoms of acute dilatation of the stomach. There is no experimental evidence that dilatation or distention of the stomach will reflexly produce the symptoms we see in this condition. The beneficial effects of the adoption of the prone position with elevation of the pelvis and the use of the stomach tube can really be explained on the basis of the pathogenesis of the disease presented. The dehydration must be regarded as a result of the profuse secretion into the upper intestine and stomach, brought about by the toxic secretagogues and cannot be considered a primary factor. It would be relieved by the intravenous or hypodermic administration of Ringer's solution, which in addition would dilute and promote the excretion of toxic materials in the blood.

CONTRIBUTIONS TO THE PHARMACOLOGY AND THERAPEUTICS OF IODIDS *

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I shall present here a summary of the results of certain studies of the pharmacology and therapeutics of iodids carried on in the Section on Dermatology and Syphilology of the Mayo Clinic during the last two years. Detailed accounts of methods and data covering each phase of the work will be published later.

Throughout these studies the method of Kendall¹ for the determination of iodine has been scrupulously followed. The advantages of this method are numerous, chief among which are its delicacy and accuracy with minute amounts of iodine, and, therefore, its adaptability to small amounts of blood and spinal fluid.

ADMINISTRATION BY MOUTH

It is well known that small doses of iodids by mouth are rapidly absorbed and eliminated. The recent use of massive doses of iodids has raised the question of whether large doses are absorbed proportionately and, if they are absorbed, whether the iodine is excreted more rapidly or less rapidly than with small doses. The significant facts obtained from a study of the results after doses of 1, 5 and 20 gm. of sodium and potassium iodide by mouth are as follows:

1. Sodium iodide is excreted faster during the first hour than potassium iodide. The percentages for the one-hour interval following the administration of 1 gm. of sodium iodide and 1 gm. of potassium iodide, respectively, are 5.3 and 2.2; 7.3 and 7.2 for 5 gm., and 10.9 and 2.0 for 20 gm. This fact is of importance when the mechanism of absorption is considered.

2. No appreciable difference could be noted in the amounts of iodine eliminated after sodium and potassium iodide had been taken by mouth; the percentages were on the average a trifle higher with the sodium

* From the Section on Dermatology and Syphilology, Mayo Clinic.

* Read before the Section on Pharmacology and Therapeutics at the Seventy-Third Annual Session of the American Medical Association, St. Louis, May, 1922.

1. Kendall, E. C.: The Determination of Iodine in the Presence of Other Halogens and Organic Matter, *J. Am. Chem. Soc.* **34**: 894-909, 1912; The Determination of Iodine in Connection with Studies in Thyroid Activity, *J. Biol. Chem.* **19**: 251-256, 1914; The Determination of Iodine in Connection with Studies in Thyroid Activity, *ibid.* **43**: 149-159 (Aug.) 1920. Kendall, E. C., and Richardson, F. S.: Determination of Iodine in Blood and in Animal Tissue, *J. Biol. Chem.* **43**: 161-170, 1920.

iodid. My observations tend to show that the individual varies under different conditions.

3. The highest point of concentration of iodine in the urine is reached between the second and fourth hours after administration. The curve of urinary concentration of iodine does not always parallel the curve of iodine excreted because of the varying amounts of urine passed for each unit of time. There is no evidence that the amount of urine influences the amount of iodine excreted. Water intake effects are under investigation.

4. There is no difference in the length of time sodium and potassium iodide are retained in the body. They are practically entirely eliminated by the end of ninety-six hours, regardless of the size of the dose.

5. During the second twenty-four hour period after administration, approximately the same percentage of total iodine is eliminated, regardless of drug or dose.

No appreciable amount of iodine appears in the stools. Following the dose of 5 gm. of sodium iodide, 200 mg. of iodine was found in the feces, and after the 20 gm. of potassium iodide, 250 mg. of iodine appeared in the feces. Thus, 96 per cent. was absorbed from the gastro-intestinal tract, and this in spite of the fact that 20 gm. doses were followed by a mild watery diarrhea.

From experiments performed on two patients, it was found that no appreciable differences could be noted in the rates of elimination when the drug was given before or after meals. As in the case of the single dose, from four to five days was required for the entire elimination of the drug. During this series of experiments, blood was drawn at exactly two and three hour intervals after the second, or noon, administration. The blood concentration of the iodine was essentially the same in every instance. Many pharmacologists recommend the coincident administration of fats in the form of milk and cream on the theory that the lipid substances hasten absorption of the iodine. My observations indicate no difference in the rate of absorption due to fats in ordinary meals, as compared with the empty stomach. Patients note less gastric irritation if the drug is taken on an empty stomach one-half hour before meals. I am unable to state at present whether or not the administration of iodides before meals lessens the liability to iodism.

Sodium iodide is usually better tolerated than potassium iodide. Two patients were observed recently who tolerated sodium iodide by mouth and intravenously, but who reacted markedly to potassium iodide by mouth.

COMPARATIVE RATES OF ELIMINATION FOLLOWING ADMINISTRATION BY MOUTH AND INTRAVENOUSLY

The intravenous administration of sodium iodide is being commercialized as a method superior to the oral administration, because of the supposed intensive effect and the slower excretion. The important facts to be noted from a study of results obtained following doses of 5, 10 and 20 gm. of sodium iodide are:

1. There is no striking difference in the rate of elimination of sodium iodide given intravenously, as compared with that given by mouth. Mendel has contended that sodium iodide administered intravenously is retained in the body for a longer period. My observations indicate that there is practically no difference between the two methods in the rate of elimination, and large doses are eliminated as rapidly as small ones.

2. There is a rapid adjustment of the body fluids to the hypertonic sodium iodide solution (10 per cent.). After 5 gm. of sodium iodide intra-

venously, the concentration of iodine in the urine rises immediately; while, after the 10 gm. dose, it is a trifle slower. With the relatively large dose of 20 gm., the urinary concentration remains comparatively low until the end of the first hour, after which it rapidly rises to a maximum during the fourth hour. Clinical experience coincides with these findings. Practically every adult patient tolerates 10 gm. of sodium iodide intravenously (100 c.c. of 10 per cent. solution) very well because the body is able to adjust itself to that amount. Above 10 gm., symptoms may develop from the effect of the hypertonic solution. No accumulation of the drug in the body after the large daily doses intravenously occurs. On 30 to 45 gm. daily, the same percentages were obtained as with small doses, and the drug did not remain in the body any longer.

RECTAL ADMINISTRATION OF IODIDES

Two patients were given ascending doses of potassium iodide three times a day by drop proctoclysis, with practically identical results. The maximal efficiency, with regard to the percentage of iodine excreted in the urine as compared with the amount administered by rectum, was reached with the smaller doses of approximately 3 to 10 gm. of potassium iodide a day. The iodine excreted varied from 16.9 to 43.3 per cent. of the amount administered. Increasing the dose above 10 gm. daily did not produce a corresponding increase in absorption. In both cases, severe rectal irritation developed when the dose reached 30 gm. of potassium iodide daily. Accordingly, it appears that approximately 20 to 25 per cent. of iodide given by rectum is absorbed with doses up to 10 gm. daily. Since 96+ per cent. is absorbed after administration by mouth, a daily dose of from 2 to 3 gm. by mouth is equivalent to the maximal dose by rectum; thus it would seem that rectal administration of iodides offers no significant advantage.

STUDY OF THE BLOOD CHEMISTRY OF IODIDES

In my first few series of experiments, blood serum was obtained after clotting had taken place. Since then I have found that oxalated blood serum is somewhat more convenient. Only the most minute traces of iodine were found in the packed cells, indicating that practically all, if not all, of the iodine is in the serum fraction of the blood.

SODIUM, POTASSIUM AND IODINE CONCENTRATION OF BLOOD SERUM AFTER IODIDES BY MOUTH

Doses of 1, 5, and 20 gm. of sodium and potassium iodide by mouth were used in this series of experiments. The potassium and sodium determinations were made after the methods of Kramer and Tisdall² under the direction of Dr. Rowntree. The most important facts noted were:

1. Following the administration of sodium iodide by mouth there was a definite marked rise in the sodium content of the blood serum proportional to the size of the dose, with no change in the potassium content.

2. In contrast to this finding, administration of potassium iodide by mouth did not produce a corresponding rise in the potassium content of the blood serum; but,

2. Kramer, B.: Direct Quantitative Determination of Potassium and Sodium in Small Quantities of Blood, *J. Biol. Chem.* 41: 263-274, 1920. Kramer, B., and Tisdall, F. F.: A Simple Method for the Direct Quantitative Determination of Sodium in Small Amounts of Serum, *J. Biol. Chem.* 46: 467-473 (May) 1921; A Clinical Method for the Quantitative Determination of Potassium in Small Amounts of Serum, *ibid.* 46: 339-349 (April) 1921.

on the contrary, a definite rise in the sodium content almost equal to that following the sodium iodid. Following the 20 gm. dose, only a slight rise in the potassium content was noted.

3. The iodine content of the blood serum is, in general, proportional to the dose administered. With doses of 1 and 5 gm., the highest concentration is reached about one hour after administration; while, with the 20 gm. dose, the peak is reached at the two-hour period.

SODIUM, POTASSIUM AND IODINE CONCENTRATION OF BLOOD SERUM AFTER SODIUM IODID INTRAVENOUSLY

Sodium, potassium, and iodine determinations were made on blood serum at varying intervals after intravenous injection of 10 gm. of a 10 per cent. solution of sodium iodid. As would be expected, no change occurs in the potassium concentration. The sodium content remained high for twelve hours, and returned almost to normal at the end of forty-eight hours. The iodine content, which was 43 mg. for each 100 c.c. of blood serum at the one-hour interval, dropped rapidly during the first four hours to 24.7 mg. for each 100 c.c., and then gradually to 7.1 at the end of twenty-four hours. By the end of the fourth day, a trace was found in the blood serum. In comparing these results with the iodine concentration of the blood serum after iodids by mouth, it is apparent that a dose of 5 gm. of sodium or potassium iodid three times a day by mouth will maintain blood serum concentration of 20 to 40 mg. of iodine for each 100 c.c. of blood serum for at least ten to twelve hours. Three grams of sodium or potassium iodid will give a blood serum concentration of from 13 to 30 mg. for each 100 c.c. for at least three hours after a single dose. It is apparent that a dose of from 9 to 15 gm. a day in three doses of from 3 to 5 gm. each by mouth is comparable to 10 gm. in a single dose intravenously, and has the added advantage of producing a uniformly sustained concentration of iodine during the day. It seems, from these data, that unless the intravenous method is used as an adjunct to the mouth administration, there is no special advantage in giving small doses intravenously. The giving of large doses by vein produces a very much higher concentration for a much shorter period. Mouth administration creates a moderate sustained concentration; intravenous administration of large doses creates peaks of very high concentration followed by rapid declines. The therapeutic significance of these contrasting procedures remains to be determined.

IODINE CONTENT OF BLOOD SERUM PROTEINS AFTER SODIUM, AND POTASSIUM IODID

I have employed two methods for the precipitation of the serum proteins, the tungstic acid method of Folin and Wu,³ and the alcoholic precipitation. My results thus far are as follows:

1. Only traces of iodine were found in the serum proteins after the administration of sodium iodid by mouth.

2. In direct contrast to this finding, from 7 to 26 per cent. of the iodine following the administration of potassium iodid by mouth is found in the serum proteins. The average is 16.8 per cent.

3. Following sodium iodid intravenously, from 6 to 9.9 per cent. of the iodine is found in the serum proteins.

IODINE CONTENT OF BLOOD SERUM LIPOIDS

In a series of ten determinations, only traces of iodine were found in the alcohol, ether, and chloroform soluble fractions of blood serum following potassium and sodium iodid by mouth and sodium iodid intravenously.

COMMENT

These studies indicate that an exchange of ions occurs in the process of absorption of potassium iodid. Evidently the potassium is replaced by sodium to a large extent. Whether, in this exchange of ions, the iodine from potassium iodid is absorbed in the same form as after sodium iodid is open to question. Since the potassium is evidently absorbed to a very slight degree, the question naturally arises of whether the iodine after potassium iodid unites with the protein, the fat, or the inorganic constituents of the blood. My investigations suggest that the iodine given in the form of potassium iodid by mouth forms a sodium protein combination, while in the case of sodium iodid by mouth only traces of iodine enter into combination with the proteins. In a study not yet completed of two patients exhibiting symptoms of iodism following the administration of sodium iodid by mouth, the iodine united with the protein fraction to a greater extent than in normal persons. The foregoing observations have a direct bearing on the relative effectiveness of potassium and sodium iodid by mouth and the latter intravenously. If iodine, when administered in the form of potassium iodid, unites with the serum proteins to a greater extent than when administered as sodium iodid, the question at once arises as to whether it is this sodium-protein-iodine combination that is responsible for the action of iodids. What rôle, moreover, does this sodium-protein-iodine combination play in the production of iodism? These points must be made the subject of further study.

ABSTRACT OF DISCUSSION

DR. G. P. GRABFIELD, Boston: By the administration of small doses of iodids we were able to double and treble and in one case quadruple the nonprotein nitrogen of the blood. Dr. Osborne has used larger doses; and the question is whether our findings may be related to the protein combination that he suggests. After such doses of iodid, increase of the blood nitrogen begins about the second or third day, and continues for four or five days and gradually comes back to the previous level. Apparently, this is associated with an adjustment of the body fluids to the iodid in the blood. We have used both potassium and sodium iodid and have found the same result in the two cases. In two experiments so far done this is apparently also associated with some renal retention. If, however, the iodid is given in a single dose, this change in blood nitrogen does not occur. The chlorids remain unchanged. We are planning further work on this relation between iodid administration and the nitrogenous constituents of the blood. This will probably prove to be related to Dr. Osborne's work, and the two may prove to be mutually explanatory.

DR. E. D. OSBORNE, Rochester, Minn.: The question of iodism and anaphylaxis, so-called, as applied to cutaneous medicine has been opened up for study. The preparation of the iodine-protein combination is now being carried out. We expect in the near future to report a study on cutaneous diseases, employing this combination. Of course the relationship of the iodids to the bromids and to other such drugs in the production of skin diseases is of great importance, and this subject is just now receiving attention.

3. Wu, H.: Separate Analyses of the Corpuscles and the Plasma, *J. Biol. Chem.* 51: 21-31, 1922. Folin, O., and Wu, H.: A System of Blood Analysis, *J. Biol. Chem.* 38: 81-110 (May) 1919.