POSTOPERATIVE SALT INTOLERANCE*

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THE EXPERIENCE OF YEARS regarding the toxicity of isotonic sodium chloride solution has been forgotten. Trout and Evans urged caution in the use of isotonic saline solution over thirty years ago. The clinical experiments that Trout reported, although few in number, enabled him to draw conclusions that hold the essence of the whole problem. It seems appropriate then that Trout should be quoted: (1) "Even we surgeons know of the wonderful improvement in some patients with nephritis when placed on a salt-free diet, and all of us realize there is a transient renal irritation or possibly a nephritis following the majority of anesthetics and infections. In seven cases in our series the following coincidence has been observed; a transient albuminuria remained in every specimen for two days after an anesthetic when using salt solution per rectum. Water was then substituted, and at the end of 24 hours the albumin had disappeared. At this time a return was made to salt solution, with the appearance of albumin and a few hyalin casts in from six to 24 hours. Patients were then placed on a limited salt diet, and the urine in every case promptly returned to normal and remained so until discharged from the hospital. In none of these cases was there any edema. (2) In this entire series, in both the salt and water cases, there have only been 121 who complained of being thirsty, and of this number 112 of them were salt cases. There were 27, or over one-fourth of these cases, who complained of tasting salt when they had absolutely no way of knowing that they were being given saline by rectum, and the solution being prepared so as to be 0.6 to 0.9 per cent sodium chloride. Furthermore, the water cases have taken one-third more fluid by rectum than the salt cases, and the latter have required nearly twice as much water by mouth to relieve thirst. (3) It is true sodium chloride is the least toxic of the group of similar metal chlorides, but even at that it is a poison to all people when given in large doses, and occasionally very toxic in small doses to a certain class of cases; and we believe this peculiarity is apt to be present in patients whose resisting powers are lowered by operations and infections."

The purpose of this discussion is to retract the so-called clinical rule that was proposed in 1938, and to bring to your attention Trout's and Evans' conclusions. It is generally true that the body of a normal person is capable

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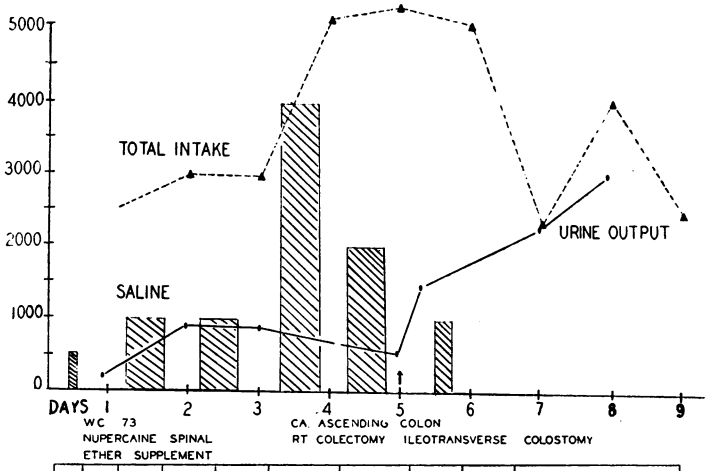
of handling relatively large amounts of isotonic saline solutions without showing signs that would indicate that a significant derangement in the regulation of body functions had occurred. However, there are many individuals who are incapable of tolerating relatively small excesses of salt solution, *during the immediate postoperative period.* The type of illness that may follow the administration of saline or Ringer's solution varies. There are three predominant and fairly distinctive symptom and sign complexes. The cases that are presented illustrate these arbitrary complexes.

CHART I



PO DAY	NPN	CO2 VOL.%	PLASMA CL' AS NACL	SALINE	TOTAL INPUT	URINE OUTPUT	EMESIS	WANG.	REMARKS
1				500	2500	200			
2				1000	3000	875	50	350	SUCTION STARTED
3				1000	3000	850		1600	DEEP RESPIRATIONS
4	101.6	46	438	4000	5900	625	200	1350	DROWSY, CONFUSED
5	113.7	59	445	2000	6000	350/1350		1150	MERCUPURIN-ADRENALIN
6	104.5	70	467	900	4900	3900		880	STILL IRRATIONAL
7	67.3		508		2300	2300	100		SL. IMPROVED
8					4080	2800	850		IMPROVED
9	49.1	62			2500	1975	200		IMPROVED
10	50.8			1000	3000	1950			IMPROVED
11					3555	3200	420		IMPROVED
12	37.5				2700	2350	500		EATING, DRINKING

Case 1 represents the most insidious and, in our experience, the most common form of "salt intolerance." The symptoms and signs are primarily referable to the central nervous and digestive systems. They are weakness, disorientation, anorexia, nausea, vomiting, distention and an increasing depth of respiration. The rate of urine excretion decreases slowly, the N. P. N. of the blood increases, the carbon dioxide combining power falls, and the plasma chloride level tends to remain constant although a large amount of salt may be administered in an attempt to raise it should it be below normal. Recovery is slow. Paradoxically, as the person improves the plasma chloride level, if it is low, rises without the administration of the chloride ion.

Case 1.—W. C., male, age 73, was operated upon under a spinal anesthetic that

CHART II

M.L. ♀ 61 yr. Adenocarcinoma rectum. Comb. Abd.-perineal resect. Spinal anesth.

	Pre-Op.	Oper.	1	2	3	4	5	6	7	8
Oral	0	0	0	0	0	200	0	0	200	0
Saline		3000	3000					700	300	300
Glucose				3000	2000	2000	3000	2000	2000	2000
Lactate					250	250			500	
Blood		500								
Urine O-P		990	1380	1750	1125	1700	1750	1850	1150	1150
Emesis			150			750	700	100		
Wangensteen					1050		800	50		
NPN mg/100	25	22		19		31				
CO_2 vol %	59	56		55		77	77			68
Chloride mg%	634	634		622		535				568
Progress	Consid. a good risk	Duration 2½ hours No shock		Nausea, emesis Drowsy. Abd. Dist. Colos. not funct.		Emesis. Abd. Dist.		General Improvement obvious. Alert. Abdomen soft.		

had to be supplemented with ether. A resection of a neoplasm of the ascending colon and an ileotransverse colostomy were performed. On the first postoperative day, oliguria was present. During the first five postoperative days a positive fluid balance of five liters was amassed. With it the clinical signs of acidosis developed and a chemical analysis of blood on the fourth postoperative day substantiated the clinical opinion. The plasma chloride level was found to be low; the apparent deficiency of chloride was thought to be due to an excessive loss through gastric drainage and transudation into the small gut. As a consequence, upon the basis of the "clinical rule,"* 4000 cc. of saline were given intravenously in addition to 1900 cc. of 5 per cent glucose. His condition deteriorated rapidly, the distention increased in spite of massive gastric drainage, edema appeared, he became completely disoriented, and his urinary excretion decreased. However, the plasma chloride level remained stationary instead of rising to about 560 mg. per cent as had been anticipated. The next morning 2000 cc. of saline and 1000 cc. of glucose solutions were given and by evening he had excreted only 225 cc. of urine (12-hour period). His condition was precarious; respiration was noisy and difficult, the edema had increased, and cyanosis had appeared. It was realized then that the initial low chloride content of his plasma represented an attempt to compensate for an acidosis which likely had both an inorganic (urinary suppression) and a respiratory component (distention and emphysema).

Three liters of 10 per cent glucose, mercupurin, and epinephrin in oil were given to him. In the next 12 hours 1350 cc. of urine were excreted. The CO_2 combining power rose, the N. P. N. began to fall, and respirations became dry and easier. On the sixth postoperative day the intern, from habit, ordered saline, and 900 cc. had

CHART III

O.P. ♂ 78 yr. Adenocarcinoma rectum. Colostomy. Spinal Anesthesia.

	Pre-Op.	Oper.	1	2	3	4	5
Oral	0	0	0	0	0	1730	1910
Saline		2000	3000				
Glucose				3000	2000		
Lactate				250			
Urine O-P		1550	850	1505	2550	2000	1125
NPN mg%	43	41		41			
CO_2 vol%	33	35		42			
Chloride mg%	534	648		607			
Progress		Disoriented.		Drowsy. Abd. dist. Edema eyes, ankles.	Improved mentally Dist. less. Edema less	Clinically improved. Cheerful, well oriented. No edema.	

* For each 100 mg. per cent the plasma chloride is below 560 mg. per cent, give 0.5 Gm. of salt per kilo of body weight.

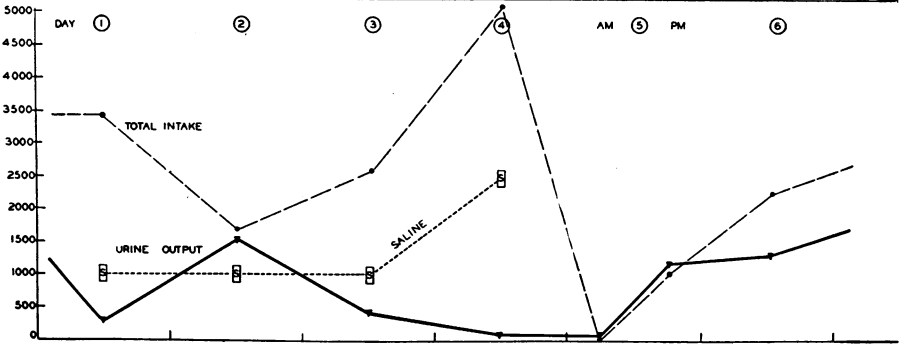
been given before the error was discovered. The patient's recovery was gradual and was associated with a negative fluid balance for seven days (Chart I).

Cases 2 and 3.—Cases 2 and 3 (consult Illustrations II and III) show that the early symptoms and signs that accompany a relatively small, acute chloride excess are not accompanied by, or due to, any gross changes in acid base equilibrium, plasma chloride, or N. P. N. This observation substantiates the conclusions of Sippel and of Evans, in that it makes it appear that the toxic symptoms may be attributable to the excess of the chloride ion in saline solution.* These three cases and many others have convinced us that the use of the "clinical rule" for chloride replacement is dangerous, especially when employed without a sound knowledge of biochemistry and physiology, and that it should not be employed.

CHART IV

A.B. 58 R.U.L. LOBECTOMY

P.O. DAY	NPN	CO2 VOL. %	PLASMA NACL	PLASMA PROTEIN	ORAL	SALINE	GLUCOSE	BLOOD	LACTATE	TOTAL INPUT	URINE OUTPUT	EMESIS	DRAIN WANG	REMARKS
1					+	1000	1900	500		3400*	300			5-HOUR ANESTHESIA — REACTED WELL
2					690	1000				1690	1535			FAIR DAY
3					600	1000	1000			2600	400		500	LARGE LIQUID STOOL VOMITING—ABDOMINAL DISTENTION
4					100	2500	2500			5100	135	1250	500	CONDITION WORSE IRRATIONAL—ABD. DISTENTION—NO FLATUS
AM 5		77			0	0	0			0	110		1760	CONDITION VERY POOR — IRRATIONAL HICCOUGHS—LUNGS WET—MUCOID SPUTUM
PM 5					0	0	0		1000	1000	1150	0	1000	STRIKING IMPROVEMENT AFTER LACTATE
6	55	87	413	4.46	500	250	1000	500		2250	1250	0	0	HUNGRY—EATING AND DRINKING RATIONAL—LUNGS DRY—RECOVERY



Case 4.—A. B., male, age 58, underwent a right upper lobe lobectomy. Ether vapor was used as the anesthetic agent. The general features of his illness, a fulminating oliguria that was associated with a rapid physical deterioration, are similar to those of the case reported by Sippel in 1910. The usual immediate temporary postoperative oliguria is apparent (Chart IV). During the forenoon of the third postoperative day he was found to be distended, he began vomiting, and he passed a large liquid stool. The urinary rate of flow began to fall after the diuresis of the second postoperative day and by the fourth day only 135 cc. of urine were excreted in the preceding 24 hours. He became irrational, and in spite of the administration of 5,000 cc. of intravenous fluids (2,500 saline) during that day, he excreted only 110 cc. of urine in 12 hours. His condition had become precarious (Chart IV). One thousand cubic centimeters of M/6 r. sodium lactate were given.† During the next 12 hours 1.150

* The chloride ion concentration in isotonic saline is greater in relation to the sodium ion than it is in plasma.

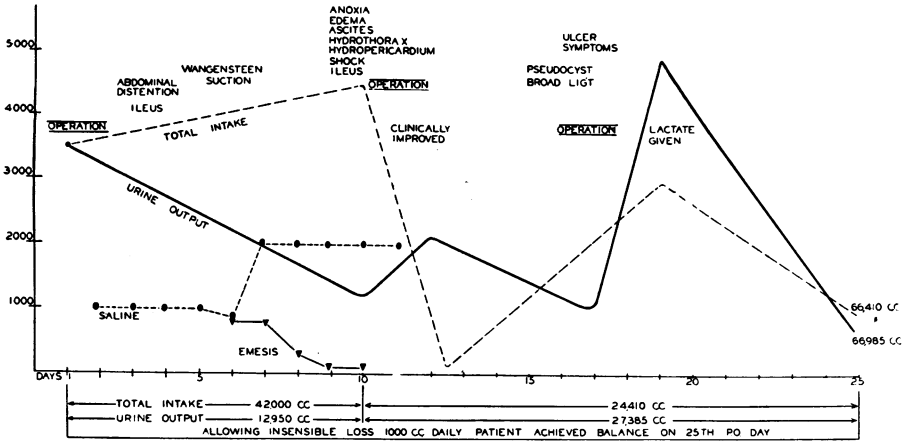
† Unpublished work indicates that the oliguria accompanying "salt intolerance" is best relieved by the administration of sodium that is not in combination with chlorine or the anions of other strong acids.

cc. of urine were excreted and thereafter his improvement was rapid. This man had had frequent examinations of urine made preoperatively and no red blood cells, casts, or albumin had been found.

The fifth case (Chart V) demonstrates an extreme accumulation of fluid in serous cavities as a result of a relatively prolonged, though a slightly excessive, administration of sodium chloride.

Case 5.—G. B., female, age 40, underwent a subtotal hysterectomy under ether anesthesia. She was given daily 1000 cc. of isotonic salt solution in addition to 2000 to 2500 cc. of 5 per cent glucose. On the fourth postoperative day she became

CHART V



DATE	SOURCE FLUID	NPN	TOTAL N	ALBUMIN NIT	GLOBULIN NIT	A/G RATIO	TOTAL PROTEIN	CHLORIDE	SODIUM	POTASSIUM	REMARKS
8-28	ABDOMEN	35.2	481.9	288.3	158.4	1.71	2.79 GM%	98.5 MEQ/L	133.8	4.66	4-5 LITERS RECOVERED
9-1	ABDOMEN		232.7	++++	+		1.45				PARACENTESIS
9-2	TUMOR	151.9	280.0	++++	0		0.80	88.75	133.8	6.62	COLPOTOMY

DATE	GLOMERULAR FILTRATION RATE C_1	EFFECTIVE RENAL BLOOD FLOW C_D	FILTRATION FRACTION $\frac{C_F}{C_D}$	REMARKS
8-28	101 CC/MIN	398 CC/MIN	0.364	10 DAYS PO.
9-4	74.7	305	0.397	
9-18	44.7	300	0.223	RT. HYDRONEPHROSIS

distended, on the fifth day she began to vomit, on the sixth day gastric suction was begun and the parenteral fluids were stepped up to 2000 cc. of saline and 2000 cc. of 5 per cent glucose *per diem.*

Her distention increased rapidly in spite of profuse gastric drainage; by the evening of the tenth postoperative day she was practically *in extremis.* The distention was so great that the respiratory excursions were practically imperceptible. She was deeply cyanotic in spite of the fact that her hemoglobin was less than 60 per cent of normal. Her pulse was small, late, and thready, and her apex beat was very weak. A generalized one plus edema was present. During the ninth and tenth postoperative days repeated attempts had been made to pass a Miller-Abbott tube but they were not successful. Because death from respiratory embarrassment was almost certain within a matter of hours unless the distention could be reduced, it was decided that a gastrotomy should be performed and an attempt made to pass the tube directly through the pylorus. Upon entering the abdominal cavity a massive ascites was encountered, four liters of fluid were collected and another liter was estimated to have been lost.

The sodium and chloride ion concentration in this fluid was the same as it was in her

plasma. The protein content was 2.79 Gm. per cent with an A/G ratio of 1.71. Her stomach wall was approximately 2 cm. thick, her liver was enlarged and so soft that it felt like a hollow viscus. The small intestine was distended with fluid and only a small amount of gas was seen in it. There was no gross edema of the small intestine. Her omentum was a thick, amorphous, opalescent mass. After the greater part of the ascitic fluid was removed, the wound was closed. By the time she was placed in bed respirations were normal, her pulse rate had fallen, blood pressure had risen from 60/20 to 100/70, and consciousness had returned. No more "physiologic" saline was given to her and she recovered.

Cases 1, 2, 3, and 4 differ from Case 5 in that the bloods of the former contained normal amounts of hemoglobin and plasma proteins and no physical renal complications were introduced when they were operated upon. Case 5 suffered from a microcytic, hypochromic anemia and hypoproteinemia (Hb. 46 per cent and p.p. 4.26 Gm. per cent) at the time she had been operated upon* and on the sixteenth postoperative day her right ureter was found to have been obstructed at the level of the pelvic floor. This case demonstrates clearly the "washing out" effect of salt solution upon the serum proteins and the increased tendency for salt retention in hypoproteinemic states, facts which have been brought previously to our attention by Blalock.

Cases 1, 4, and 5 and nine others came to our attention during a three-month period during 1942.† Since that time no saline or Ringer's solutions have been given during the operative and immediate postoperative (48-hour) periods unless losses of extracellular fluid occurred (diarrhea, sweating, fistulous drainage, *etc.*). Extracellular fluid losses are now being replaced according to the volume for volume rule by 0.5 per cent NaCl solution to which 50 Gm. of dextrose per liter has been added. The water needs of the patients are met entirely with plain glucose solution. The practice of giving 5 Gm. of salt daily "for maintenance" has been discontinued because the salt conserving capacity of the kidneys is practically perfect.

The clinical rule (see footnote page 535) for correcting extracellular fluid deficiencies has been found to be highly inaccurate and dangerous. Its formulation and use in the University of Michigan Hospital was based upon the assumptions that the chloride level of the plasma varied directly with the extracellular fluid volume from a normal of 560 mg. per cent and that the plasma chlorides maintained a fixed relationship with the sodium ion. Both suppositions had been proven to be false, especially during illness, at the time the formula was proposed. It has been known for many years that the chloride level of the plasma could vary without a significant change in the hydration of the body. An increase of blood anions, other than chloride (bicarbonate, phosphate, citrates, acetone bodies, and lactate) is associated with a compensatory fall in chloride and need not be associated with any significant change of E. C. F.

In addition, a non-compensatory decrease of the plasma chlorides signifies that a dilution of plasma (E. C. F.) electrolytes has taken place. The

* Repeated unsuccessful attempts had been made to give her blood preoperatively.

† Cases 2 and 3 were induced during an investigation of the problem.

rate and extent of the dilution has no fixed relationship with the state of hydration, especially in different individuals. Therefore, the plasma chloride level alone cannot serve as a sufficiently accurate base for the construction of a universal hydration formula. The failure of the formula and its dangers are well illustrated in Cases 1 and 4. Earlier observations regarding the efficacy of the formula were made by Powers, *et al.*

At present, the restoration of extracellular fluid deficiencies is not being made primarily upon the basis of variations from normal of ions or molecules in blood (Cl, CO_2 combining power, plasma proteins, Hb., *etc.*) but upon the basis of the clinical status and physiologic response of the individual to test doses of parenteral fluids.

Examples may serve to clarify this method:

Example 1.—A patient, age 60, enters the hospital with pyloric obstruction. He has been vomiting for three weeks. He has lost 20 pounds. He is not thirsty, the specific gravity of his urine is 1.014, his temperature is normal, his pulse is 80 and full, he answers questions readily and at length, he complains of slight lassitude. His plasma chlorides were 460 mg. per cent and the CO_2 combining power was 50 vols. per cent.

The lack of thirst and the low specific gravity of his urine indicate that he has been retaining enough water to prevent dehydration. His normal temperature, normal mental responses, and normal pulse indicate that although his extracellular fluid volume may be below his ideal normal, the reduction has been fully compensated. The low plasma chloride is not regarded as an indication for the immediate administration of over three liters of saline as would be given should the "clinical rule" be employed. Instead the low chloride level is considered to be compensatory to the "starvation acidosis" (weight loss of 20 pounds in three weeks), and only one liter of saline is given to him as a test dose. If his physiologic status does not change after receiving the saline, he is considered to be compensated and on succeeding days the gastric aspirations are replaced by equal volumes of 0.5 NaCl solution, in addition to glucose solution in sufficient amount to prevent thirst and maintain the specific gravity of the urine below 1.020.

Example 2.—A man, aged 60, suffering from pyloric obstruction enters the hospital after vomiting for three weeks. His weight has decreased 30 pounds within that period. He is thirsty, his temperature is 97° F., his pulse is 80 and soft, he answers questions in monosyllables, he goes to sleep between questions, his respirations are shallow and slow. The specific gravity of his urine is 1.028, the plasma chlorides are 400 mg. per cent, his CO_2 combining power is 90 vols. per cent.

The thirst and high urine specific gravity indicate a need for free water. The subnormal temperature, apathy, and soft pulse show that a dangerous reduction in extracellular fluid volume has occurred. The alkalosis is disregarded.

MANAGEMENT

The intravenous drip is set as follows:

1st bottle—10 per cent glucose, 1000 cc.
2nd " —Ringer's solution, 1000 cc.
3rd " —10 per cent glucose, 1000 cc.

If thirst remains or if the specific gravity of the urine is above 1.020, the fourth bottle is glucose. If not, it is Ringer's solution, and the second bottle of Ringer's is given very slowly (200 cc. per hour). Should the patient's pulse fill out, his mind become clearer and his temperature rise appreciably before the second liter of Ringer's has been given, the injection is stopped.

Upon each succeeding day glucose is given first in amounts sufficient to allay thirst completely and to keep the specific gravity of urine at least in the 1.010–1.020 range. This is followed by one liter of Ringer's solution daily (in excess of the volume-for-volume replacement of drainage by 0.5 per cent, Ringer's) until the CO_2 combining power and plasma chloride values have become constant. If the plasma Cl and CO_2 combining power reach plateaux before their arbitrary so-called normal values are reached, no attempt is made to change them further. Considerable departure from normal in Cl and CO_2 combining power can be expected in starvation, emphysema, *etc.*

The type of saline solution administered also depends upon the clinical status of the patient. In the preceding examples simple repair solutions (saline or Ringer's solution) will satisfy requirements. However, in a case such as follows, a buffered solution is considered to be indicated:

Example.—Patient age 70, weight 60 Kg., with pyloric obstruction and vomiting for three weeks, entered the hospital in semicoma. Urine, catheterized—20 cc., sp. gr. 1.035, contained albumin, casts, and red blood cells. Respiration was deep and labored, pulse weak and irregular, CO_2 combining power 30 vols. per cent, plasma chlorides, 200.

In this case urinary suppression has resulted in a retention of acid radicles of sufficient degree to counteract the tendency of chloride reduction to produce an alkalosis and instead a severe "uremic" acidosis is superimposed upon a reduction of total base from vomiting. This man obviously is in great need for a rapid replacement of extracellular fluid, but in the face of the anuria, no solution should be given which has a chloride content in relation to sodium that is greater than is present in his plasma, or the acidosis may be increased beyond tolerable limits. For that reason, normal saline and Ringer's solution (chloride, 150 m. eq. vs. 100 m. eq. in plasma) are considered to be less adequate from a physiologic standpoint than Hartmann's solution. The plan of administration is as previously outlined.

SUMMARY AND CONCLUSIONS

1. Three clinical types of "salt intolerance" are described.

2. Because of the relatively high incidence of "salt intolerance" following a general anesthesia, it is felt that no *isotonic* saline solution or Ringer's solution should be given during the day of operation and during the subsequent

first two postoperative days. The fluid requirement of the patient is met with glucose solution. If a significant loss of extracellular fluid occurs during the above period, it is replaced with 0.5 per cent sodium chloride solution to which 50 Gm. per liter of dextrose has been added. Isotonic saline solution (0.9 per cent) or Ringer's solution is used to replace extracellular fluid loss after the postoperative urinary suppression has disappeared, usually after the second postoperative day.

3. Great care must be used in administering isotonic saline and Ringer's solution to patients who are hypoproteinemic, anemic, acidotic, or oliguric.

4. It is recommended that the correction of uncompensated extracellular fluid deficiency states be made upon the basis of the physiologic response to test doses of the appropriate salt solution rather than upon the basis of the plasma chloride, the CO_2 combining power, the N. P. N., the plasma protein, or the hemoglobin levels. Three examples are given to illustrate the method.

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DISCUSSION.—DR. ROBERT L. RHODES, Augusta, Ga.: Doctor Coller referred to a paper published in 1913 by Doctor Trout, with whom I was associated at the time. I had not thought of that for a long time. I am reminded in these days of shortage of man power and woman power in hospitals of some thoughts brought out in that paper. In 1910 we began a comparative study of rectal administration of salt solution and water, on alternate cases operated upon; there were 2000 consecutive cases, 1000 of each. Out of the 1000 that had salt solution, approximately 125 or 150, 12 to 15 per cent developed edema, and when the salt solution was shifted to water the edema subsided.

It is a very simple matter to give water by drip, not the Murphy drip, but the Lawson drip, described by him in May, 1909. The original dropper was a simple medicine dropper inserted into a test tube. When first brought out the dropper was too slender, so that if not held perfectly erect the drop would span the gap between the two tubes and syphonage would result instead of drops. The larger bulb effect was designed by me, and first made by Wocher of Cincinnati upon order for us. This bulb avoided syphonage even when lying almost flat. Later someone stuck a hole in the bulb with the thought of allowing gas to escape, but what it really does is allow suction of air to come into the bulb and be carried into the rectum between the drops of the solution and produce irritation of the rectum. When this hole is sealed-off with adhesive tape and the dropper is regulated to 40 drops per minute, you have a foolproof mechanism. At this rate the fluid is absorbed about as rapidly as it is introduced and any collection of gas in the rectum is easily expelled beside the small indwelling catheter.

As he published, the amount of water a patient would take is approximately one pint more than salt solution, without producing edema. John B. Murphy was the first to suggest rectal administration of fluid, but with a large tube which produced irritation. Our studies show that a small catheter slipped into the bowel for three or four inches and strapped to the buttocks would not irritate the sphincter muscle or rectum, could be left in position for days and, at 40 drops per minute, three quarts of water, saline or glucose could be easily given in 24 hours. Many medicines may be added to the solution and given in this way.