

# GASTROINTESTINAL WATER AND ELECTROLYTES. III. THE EQUILIBRATION OF RADIOBROMIDE IN GASTROINTESTINAL CONTENTS AND THE PROPORTION OF EXCHANGEABLE CHLORIDE ( $Cl_e$ ) IN THE GASTROINTESTINAL TRACT<sup>1</sup>

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Although chloride is distributed chiefly in the extracellular fluid, it is also found in intracellular water in as yet poorly defined quantities. The extracellular distribution includes plasma, free interstitial fluid, the interstitial fluid of dense connective tissue and bone, and transcellular fluid. The latter has been proposed as that portion of extracellular fluid formed, at least in part, as a result of active cellular transport mechanisms (1). The chemical composition of gastrointestinal contents differs in many ways from a simple ultrafiltrate of plasma. There is good evidence that chloride flux across the gastrointestinal mucosa, either directly or indirectly, involves active transport mechanisms (2, 3).

The physiologic significance of the chloride in transcellular fluid depends on its quantity and on the extent and rate of its equilibration with total exchangeable chloride, as well as other factors. The large volume of chloride-containing fluid in the gastrointestinal tract (4, 5) is one reason for the quantitative and functional definition of this moiety in relation to total body chloride.

Radiobromide ( $Br^{82}$ ) was used as the tracer material in this study because of some disadvantageous physical characteristics of chloride<sup>36</sup> and chloride<sup>38</sup>. The half-life of  $Cl^{36}$  is  $4 \times 10^5$  years (6), making it a potential hazard in terms of laboratory contamination and disposal.  $Cl^{38}$  has a half-life of only 37 minutes, which limits its value

in studies requiring an equilibration period of more than a few hours (6).

The bromide: chloride ratio has been shown to be the same in tissues as in plasma after distribution equilibrium in animals, except for brain and cerebrospinal fluid (7-9). On the basis of these observations stable and isotopic bromide has been used extensively for *in vivo* estimations of total exchangeable chloride ( $Cl_e$ ) (7, 10-15).

This communication presents observation on a) the fraction of total exchangeable chloride ( $Cl_e$ ) in the lumen of the gastrointestinal tract of normal rabbits, b) the exchangeability of this chloride fraction based on bromide partition, and c) the amount of chloride in the gastrointestinal tract of man at post-mortem examination.

## METHODS

### A. Rabbits

Thirty-eight adult albino rabbits were studied in pairs, consisting of a male and a non-gravid female. The animals were allowed *ad libitum* ingestion of water, but food was withheld from the time of isotope injection until sacrifice. The fasting periods varied from 21 to 65 hours.

Each animal was injected intraperitoneally with 15 to 25 microcuries of  $KBr^{82}$  from calibrated syringes.<sup>4</sup> The injected material was made up as a neutral, sterile isotonic solution with saline. Observations on half-lives of decay on aliquots of the injected material fell within the reported values for  $Br^{82}$  (6), indicating that any small quantities of  $K^{48}$  present were not contributing significantly to radioassay.

<sup>4</sup>  $KBr^{82}$  was supplied by the Oak Ridge National Laboratory of the Atomic Energy Commission. On the day of shipment each unit contained 5 millicuries of  $K^{48}$  and 120 millicuries of  $Br^{82}$ . Five half-lives for  $K^{48}$  were allowed to elapse prior to use, insuring negligible contamination.  $Br^{82}$  is a  $\beta$ ,  $\gamma$  emitter with a half-life of 35.7 hours (6).

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The techniques of collection of blood, bladder urine, stool and gastrointestinal contents were described in previous communications (1, 16). Urine and stool passed during the period of isotope equilibration were collected quantitatively in metabolism cages. In eight instances erythrocytes were aspirated from below the plasma layer of centrifuged heparinized blood obtained by cardiac puncture. The erythrocytes were hemolyzed in four times their volume of distilled water, and the hemolysates were filtered through double thickness paper. No attempt was made to remove trapped plasma, since the error due to plasma contamination in the specific activity of erythrocyte chloride would not exceed 10 per cent. Excreted stool and fecal contents of the distal portion of the large bowel were homogenized in a Waring blender with measured volumes of distilled water, and filtrates collected after passage through glass-wool. Aliquots of plasma, lysed erythrocytes, bladder urine, cage urine, excreted stool, stool in the descending colon and gastrointestinal contents were taken for assay of radioactivity and chemical analysis. No attempt was made to prevent volatilization of HBr by neutralization of gastric contents during the brief exposure to room air.

One-ml. aliquots of all samples were plated on filter paper in metal planchets in triplicate, dried under an infra-red lamp and covered with parafilm. Standards of three separate dilutions were prepared from aliquots of each of the injected solutions. Triplicate one-ml. plates were made from each dilution as above. It was found that addition of one drop of concentrated detergent solution to the standards and one or two drops of 50 per cent sucrose solution to all planchets improved the reproducibility of radioassay.

Assay of radioactivity was carried out with an end-window, thallium-activated sodium-iodide scintillation counter. Coincidence and self-absorption losses were found to be negligible. Consequently, these corrections were not applied. Corrections for background radiation and decay were applied to each assay.

Serum, urine, stool and gastrointestinal contents were analyzed for chloride content in triplicate by the Wilson and Ball method (17). Iced containers were used to sharpen the end-points.

#### B. Human subjects

Thirteen human subjects were studied at the time of post-mortem examination. The age, sex, weight and height of each subject was recorded. The criteria for patient selection and the post-mortem pathologic findings were described in the first report in this series (1). Direct collections were achieved by emptying each segment of the gastrointestinal tract. The details of collection and processing of these samples have been reported previously (1). A thin layer of mucus invariably clung to the mucosal wall of each segment. Quantitative emptying of each segment was not attempted to avoid contamination of the samples with gastrointestinal epithelium or blood.

Triplicate chloride analyses were carried out on aliquots of the diluted contents collected from each seg-

ment of the gastrointestinal tract by the Wilson and Ball method (17).

#### CALCULATIONS

##### A. Rabbits

Bromide is, for the most part, partitioned in direct proportion to chloride in body fluids (7-9). The application of radiobromide ( $\text{Br}^{82}$ ) dilution to the measurement of total exchangeable body chloride content is justified on the same grounds as the use of bromide ( $\text{Br}^{79/81}$ ) for this purpose, and yields results which closely approximate those obtained with radiochloride ( $\text{Cl}^{36/38}$ ) (7, 14, 15).

The total exchangeable body chloride content ( $\text{Cl}_e$ ) was calculated with the conventional dilution formula (1), corrected for urinary losses. Cardiac blood samples were drawn 21 to 65 hours after injection of  $\text{Br}^{82}$ . Urinary loss of  $\text{Br}^{82}$  was extremely variable in spite of the fact that the animals were matched for age, sex and body weight and kept on identical diets prior to fasting. In 14 rabbits fasted for 21 to 27 hours the cumulative urinary  $\text{Br}^{82}$  excretion rate averaged 8.1 per cent of the injected amount per day, with a range of 1.0 to 15.2 per cent per day; in 17 rabbits fasted for 41 to 48 hours the cumulative urinary  $\text{Br}^{82}$  excretion rate averaged 9.4 per cent of the injected amount per day, with a range of 5.1 to 22.2 per cent per day, while the two rabbits subjected to 64- and 65-hour fasts excreted  $\text{Br}^{82}$  at a rate of 4.7 and 3.6 per cent of the injected amount per day, respectively.

The partition of  $\text{Br}^{82}$  in proportion to chloride in gastrointestinal contents and erythrocytes was evaluated by relating the  $\text{Br}^{82}$ :chloride concentration of these samples to the  $\text{Br}^{82}$ :chloride concentration in serum and expressed as the specific activity ratio (S.A.R.). The S.A.R. is indicative of the fractional exchange of the bromide tracer relative to chloride, and exchange equilibrium is assumed to be complete when a value of 1.00 is obtained consistently (1, 18).

##### B. Human subjects

The intraluminal gastrointestinal chloride content has been expressed as an absolute quantity (mEq.), as the amount per unit of body weight (mEq. per kgm.) and as a percentage of the predicted total exchangeable chloride content (per cent of  $\text{Cl}_e$ ) (cf. Table IX). The total exchangeable chloride content was predicted from previously published normal values (11, 12, 19). The available data on  $\text{Cl}_e$  in normal human subjects are too few in number to permit predictions corrected for age or body habitus. We have, therefore, applied single standards, taking into account only sex and body weight. It was assumed that the  $\text{Cl}_e$  was 29.0 mEq. per kgm. and 30.9 mEq. per kgm. of body weight in female and male subjects, respectively. There is abundant evidence from chloride balance data in humans to indicate that these predictions probably do not involve errors in excess of a factor of two. The need to establish some estimate of gastrointestinal chloride pool-size in terms of total amount of chloride in the body in humans justifies these crude approximations.

TABLE I

*Plasma versus erythrocyte specific activity in the rabbit 21 to 24 hours after injection of radiobromide\**

Rabbits	Specific Activity of Plasma	Specific Activity of Erythrocytes	Specific Activity Erythrocytes Specific Activity Plasma
	cts/min/mEq X 10 <sup>3</sup>	cts/min/mEq X 10 <sup>3</sup>	ratio
3	441.5	449.6	1.02
4	436.3	439.1	1.01
5	443.9	444.8	1.01
6	165.3	160.1	0.97
7	63.19	67.26	1.06
8	58.86	57.70	0.98
9	81.60	78.45	0.96
10	71.47	72.89	1.02

Mean = 1.00

s.d.\*\* = ±0.03

\* Specific activity refers to the activity of radiobromide per mEq. of chloride ion.

$$** \text{ s.d.} = \sqrt{\frac{\sum (x - \bar{x})^2}{n - 1}}$$

## RESULTS

### A. Rabbits

The partition of Br<sup>82</sup> between plasma and erythrocytes was evaluated by determining the S.A.R. of these samples in 8 rabbits 21 to 24 hours after the injection of Br<sup>82</sup> (cf. Table I). The mean S.A.R. of 1.00 ± 0.03 indicates that Br<sup>82</sup> is distributed in direct proportion to chloride across the red cell membrane. These data corroborate previ-

ous observations on bromide penetration into red cells (8, 14).

Sex-linked differences in body composition have been noted in human subjects in previous studies (10-12, 20). Sixteen male-female pairs were studied to evaluate the possibility of sex-linked differences in either Cl<sub>e</sub> or gut chloride content. Each pair was matched for weight and age and subjected to identical periods of fasting and isotope equilibration. Although the Cl<sub>e</sub> content of the

TABLE II

*The exchangeable chloride (Cl<sub>e</sub>) and gastrointestinal chloride content of male versus female rabbits\**

	Male	Female	t	P
Number	16	16		
Body weight in Kg. ± s.d.	2.032 ± 0.145	2.030 ± 0.277	0.003	>0.9
Cl <sub>e</sub> in mEq. ± s.d.	72.3 ± 8.7	69.0 ± 7.5	1.15	>0.2
Cl <sub>e</sub> /body weight in mEq./Kg. ± s.d.	35.5 ± 3.2	34.2 ± 3.5	1.19	>0.2
"Total" G-I chloride as % of Cl <sub>e</sub> ± s.d.**	17.6 ± 5.4	17.7 ± 5.4	0.052	>0.9

\* Each pair of animals was matched for weight and studied after identical equilibration and fasting periods. Equilibration periods varied from 21 to 65 hours.

\*\* "Total" G-I Cl<sub>e</sub> refers to the intraluminal chloride content of the gastrointestinal tract from the cardia of the stomach to the mid-transverse colon.

TABLE III

The effect of varying equilibration periods of 21 to 65 hours on the estimated total exchangeable chloride ( $Cl_e$ ) content in rabbits

Equilibration Period Hours	Number of Animals	$Cl_e$ /Body Weight mEq./Kg. (mean $\pm$ s.d.)	t	P
21 - 24	14	33.8 $\pm$ 2.92	1.74	>0.10
40 - 48	17	35.7 $\pm$ 3.14		
64 - 65	2	36.3*		

\* The two values averaged are 35.9 and 36.7 mEq./Kg. of body weight. Both values fall within one standard deviation of the mean value after either 21 - 24 or 40 - 48 hours of equilibration.

male ( $35.5 \pm 3.2$  mEq. per kgm. of body weight) is slightly higher than that of the female ( $34.2 \pm 3.5$  mEq. per kgm. of body weight), neither the differences in  $Cl_e$  nor in the "total" gastrointestinal chloride achieves statistical significance (cf. Table II). In view of these findings subsequent calculations were made without regard to the sex of the individual animals.

To evaluate the possibility of slow penetration of bromide into tissues beyond the accepted 24 hours required for distribution equilibrium, studies on the effect of varying equilibration periods from 21 to 65 hours on the estimated  $Cl_e$  were carried out in 33 rabbits. These data are summarized in Table III. Although the  $Cl_e$  per kgm. of body weight is slightly higher in the group where 40 to 48 hours were allowed for equilibration, this difference, 1.9 mEq. of chloride per kgm., is not statistically significant ( $p > 0.10$ ). These

data confirm and extend those reported on the equilibration of bromide and radiochloride (8, 9, 21).

The data tabulated in Tables II and III indicate that sex or prolongation of the period of isotope equilibration may not influence significantly the  $Cl_e$  per kgm. of body weight. The data on these groups have been combined, and the serum chloride and  $Cl_e$  are listed in Table IV. The serum chloride averaged  $98.4 \pm 6.4$  mEq. per liter and the  $Cl_e$  averaged  $71.0 \pm 8.7$  mEq., or  $34.9 \pm 3.5$  mEq. per kgm. of body weight. Weir (7) reported a mean  $Cl_e$  of 30.2 mEq. per kgm. of body weight in 10 rabbits estimated by bromide dilution after 1 to 1.5 hours of equilibration, which indicates that 80 to 90 per cent of distribution equilibrium is reached in the first 1 to 2 hours.

The penetration of  $Br^{82}$  into the gastrointestinal tract has been evaluated by measurements of the

TABLE IV

The exchangeable chloride ( $Cl_e$ ) content in the rabbit\*

	Body Weight Kg.	Serum Chloride mEq./L	Exchangeable Chloride	
			mEq.	mEq./Kg.
Mean	2.038	98.4	71.0	34.9
s.d.	$\pm 0.221$	$\pm 6.4$	$\pm 8.7$	$\pm 3.5$
Coefficient of variation	10.8%	6.5%	8.2%	10.0%
Number of animals	33	33	33	

\* Equilibration period 21 - 65 hours.

TABLE V  
The equilibration of  $Br^{82}$  with intraluminal gastrointestinal chloride in the rabbit

	No. of Animals	Equilibration Period	No. of Animals	Equilibration Period	t	P
		21-24 hours		41-48 hours		
Stomach S.A.R. (mean $\pm$ s.d.) <sup>*</sup>	6	0.86 $\pm$ 0.03	19	0.90 $\pm$ 0.02	2.96	<0.01
Small intestine S.A.R. (mean $\pm$ s.d.) <sup>*</sup>	6	0.92 $\pm$ 0.05	19	1.00 $\pm$ 0.04	3.65	<0.01
Cecum & proximal half of transverse colon S.A.R. (mean $\pm$ s.d.) <sup>*</sup>	6	0.95 $\pm$ 0.04	19	0.94 $\pm$ 0.06	0	1.00
"Total" gastrointestinal contents <sup>**</sup> S.A.R. (mean $\pm$ s.d.)	14	0.94 $\pm$ 0.06	19	0.94 $\pm$ 0.03	0	1.00

\* S.A.R. = specific activity ratio.

\*\* "Total" gastrointestinal contents refers to the intraluminal chloride content from the cardia of the stomach to the mid-transverse colon. The gastrointestinal contents were pooled and analyzed as a single sample in 8 animals after 21-24 hours of equilibration.

S.A.R. of gastric, small bowel and proximal large bowel contents after 21 to 24 hours and 41 to 48 hours of equilibration. These data are listed in Table V. Equilibration is almost complete in 24 hours, but there appears to be some increase in equilibration during the second day in both gastric and small bowel contents ( $p < 0.01$ ). The S.A.R. for stomach may seem to be somewhat less than 100 per cent equilibrated at 48 hours because of volatilization of small amounts of HBr at the time of sample collection. Gamble, Robertson, Hannigan, Foster, and Farr (15) noted more rapid penetration of radiobromide compared with radiochloride into gastric juice of man during the first 2 hours of equilibration. Their data cannot be directly compared with ours because of differences in species and time of sampling. Proportional distribution of bromide to chloride between serum and gastric juice has, however, been found in patients after chronic bromide ingestion (22).

Data on the effect of short fasting periods on the quantity of intraluminal gastrointestinal chloride relative to  $Cl_0$  have been summarized in Table VI. There appears to be some decline in intraluminal chloride content during the second fasting day, *i.e.*, total gut chloride of  $20.0 \pm 5.6$  per cent of  $Cl_0$  after 24 hours of fasting versus a value of  $16.0 \pm 4.5$  per cent of  $Cl_0$  after 48 hours of fasting ( $0.05 > p > 0.02$ ). To be certain of this effect would require more prolonged periods of observation. Since there may also be some small gain in distribution equilibrium during the second 24 hours of fasting, a 48-hour equilibration and fasting period was used as the basis for measuring intraluminal chloride content.

The amount and distribution of intraluminal chloride after 48-hour equilibration and fasting periods are summarized in Table VII. The "total" gut chloride is quite significant in quantity, averaging  $16.0 \pm 4.5$  per cent of  $Cl_0$ . Gastric

TABLE VI  
The effect of short fasting periods on intraluminal gastrointestinal chloride content \*

	Fasting Periods		t	P
	21 - 27 hours	41 - 48 hours		
"Total" G-I chloride % $Cl_0$ (mean $\pm$ s.d.)	20.0 $\pm$ 5.6	16.0 $\pm$ 4.5	2.16	<0.05 >0.02
Number of animals	14	17		

\* Isotope equilibration period was the same as the fasting period in each case.

TABLE VII  
*Intraluminal gastrointestinal chloride content in the rabbit\**

	Stomach		Small Intestine		Cecum & Proximal Transverse Colon		"Total" G-I	
	mEq.	% of Cl <sub>e</sub>	mEq.	% of Cl <sub>e</sub>	mEq.	% of Cl <sub>e</sub>	mEq.	% of Cl <sub>e</sub>
Mean	8.7	11.7	1.8	2.5	1.2	1.7	11.8	16.0
s.d.	±3.4	±4.4	±0.4	±0.7	±0.3	±0.4	±3.6	±4.5
Coefficient of variation	39%	38%	22%	28%	25%	24%	31%	28%
Number of animals	17		17		17		17	

\* Equilibration and fasting intervals of 41-48 hours, water allowed *ad libitum*.

chloride provides the bulk of this quantity, with a mean of  $11.7 \pm 4.4$  per cent of the Cl<sub>e</sub>, which is equivalent to 73 per cent of the total gastrointestinal chloride content. This is in direct contrast to the distribution of gut sodium and potassium in rabbits, where 72 per cent of gut sodium and 63 per cent of gut potassium are in the cecum and proximal half of the transverse colon (1, 16). The small amount of chloride in the proximal segment of the large bowel,  $1.7 \pm 0.4$  per cent of the Cl<sub>e</sub>, suggests efficient cecal conservation of chloride. This is borne out by the studies on distal large bowel chloride and the small daily fecal losses of chloride.

Table VIII summarizes the data on the intraluminal chloride content of the distal colon and the rates of stool chloride excretion during 24- to 48-hour fasting periods. The chloride content of the distal segment of the large bowel is minute, and the fecal chloride excretion rate is quite low, averaging about 1.0 per cent of the Cl<sub>e</sub> per day. Although chloride exchange between plasma and

gut apparently proceeds along the full length of the gastrointestinal tract, it would appear that net flow is in the intraluminal direction at the oral end and in the direction of the blood stream at the aboral end of the gut.

#### B. Human subjects

The results obtained on post-mortem examination of gut chloride in man are enumerated in Table IX. The interval between demise and collection of samples varied from 6 to 22 hours. Inspection of these data indicates that there is no correlation between gut chloride content and the post-mortem interval. Gastric chloride averaged 14.7 mEq., or 0.9 per cent of the predicted Cl<sub>e</sub>, which is approximately 50 per cent of "total" gut chloride (31.7 mEq., or 1.9 per cent of the predicted Cl<sub>e</sub>). Most of the remainder was found in the small bowel (11.4 mEq., or 0.7 per cent of the Cl<sub>e</sub>). These data, although indicating significantly smaller gut chloride contents in man as compared to rabbits, reveal a similar pattern of

TABLE VIII  
*The intraluminal chloride content of the distal colon and the rate of stool chloride excretion in rabbits*

	Distal Colon and Rectum			Stool Chloride per 24 Hours*		
	mEq.	% "Total" G-I Chloride	% Cl <sub>e</sub>	mEq.	% "Total" G-I Chloride	% Cl <sub>e</sub>
Mean	0.06	0.5	0.09	0.73	6.2	1.03
Range	0.02 - 0.13	0.2 - 1.1	0.04 - 0.16	0 - 2.64	0 - 22.4	0 - 3.72
Number of animals	13			13		

\* Stool collections were made over a 1 to 2 day period and expressed as chloride excreted per day. All animals were fasting during the collection periods.

chloride distribution along the length of the gastrointestinal tract. It must be emphasized, however, that these data are not reliable, since agonal or post-mortem changes in intraluminal chloride content may have occurred. Species differences for intraluminal water content have been reported (23). Definitive measurements in man require access to gut contents immediately after sudden death in previously well individuals.

#### DISCUSSION

Total body chloride estimated *in vivo* in man by isotope dilution averages 31 mEq. per kgm. of body weight in adult males and 29 mEq. per kgm. of body weight in adult females (11, 12, 19). Infants have significantly more chloride, averaging 51 mEq. per kgm., which is to be expected in view of their higher body sodium and water contents (13, 24, 25). Weir (7) estimated the  $Cl_e$  in rabbits to be 30 mEq. per kgm. based on 1- to 1.5-hour bromide dilution. This figure is about 85 per cent of the values of 35.5 mEq. per kgm. and 34.2 mEq. per kgm. for male and female rabbits, respectively, with 21 or more hours of equilibration of  $Br^{82}$  (cf. Table II).

The distribution of body chloride is important in the interpretation of both metabolic balance data and the movements of water and ions across cell membranes. Chloride in the lumen of the gastrointestinal tract is obviously extracellular. In man, the concentration of chloride decreases and the concentration of bicarbonate increases progressively from stomach to colon (5, 26, 27). The chloride concentration varies from about 150 mEq. per liter in the stomach to 50 to 80 mEq. per liter in the colon. There is a similar pattern of intraluminal chloride distribution in the fasting rabbit and in man studied post mortem. The blood-to-gut partition of  $Br^{82}$  parallels chloride distribution closely, as evidenced by the S.A.R. of 0.90, 1.00 and 0.94 for stomach, small intestine and proximal large bowel contents, respectively (cf. Table V). These data support the thesis that intraluminal chloride is an integral part of the body chloride pool.

Direct evidence for bidirectional flow of chloride has been obtained by Hogben (3) for the gastric mucosa of the frog and by Visscher and his associates (28-31) for the small bowel mucosa of

the dog. Gastric transport of chloride is energy dependent and oriented from serosa to mucosa (3). Intestinal transport of chloride probably has an active component as well. Bidirectional flux is highest in the jejunum and lowest in the colon (28-31). At the aboral end of the bowel, chloride movement is oriented from gut to blood. Isotonic chloride solutions placed in the ileum or proximal colon show consistent diminution in chloride concentration and a reciprocal rise in bicarbonate concentration, while the sum of the concentrations of these anions remains unchanged (27, 32, 33). Taken together, these observations justify the identification of intraluminal chloride as a distinct subdivision of total extracellular chloride.

The rabbit has an impressive amount of intraluminal chloride. After 48 hours of fasting, 16 per cent of the  $Cl_e$  is in the gut and 73 per cent of this quantity, or 11.7 per cent of the  $Cl_e$ , is in the stomach (cf. Table VII). Since chloride in the proximal colon is only about 1.5 to 2.0 per cent of the  $Cl_e$  and the fecal excretion rate is only about 1.0 per cent of the  $Cl_e$  per day under fasting conditions, intestinal conservation of chloride is clearly an efficient process.

Using multiple simultaneous dilution techniques it has been estimated that total intracellular chloride is 30 to 40 per cent of the  $Cl_e$  (11, 12, 19). Since the methods for estimating extracellular fluid exclude gut contents, intraluminal chloride is mistakenly included in these intracellular figures. In the rabbit,  $Cl_e$  averages 35 mEq. per kgm.; assuming a plasma-interstitial compartment of 20 per cent of body weight (34) and a serum chloride concentration of 100 mEq. per liter, there would be 15 mEq. of chloride per kgm. of body weight outside of this phase. At least 30 per cent of this fraction, or 6 mEq. per kgm., is intraluminal, and less than 25 per cent of the  $Cl_e$  is intracellular. This does not take into consideration other transcellular fluids so that even this figure is too high.

Although post-mortem studies on distribution of electrolytes in man are unreliable, it is of interest to note the smaller quantities of intraluminal chloride compared to those in the rabbit, averaging approximately 2 per cent of the predicted  $Cl_e$  (cf. Table IX). The pattern of distribution along the length of the gastrointestinal tract is much the same as in rabbits, about 50 per cent of "total"

TABLE IX  
*Intraluminal gastrointestinal chloride content in the human studied post mortem*

Sex	Pathological Diagnosis	Postmortem Interval hours	Age yrs.	Body Weight Kg.	Predicted Cl <sub>2</sub> mEq.	Stomach		Small Intestine		Cecum and Proximal Transverse Colon		Total* G-I mEq./Kg. % of Cl <sub>2</sub>						
						mEq./Kg. % of Cl <sub>2</sub>	mEq.	mEq./Kg. % of Cl <sub>2</sub>	mEq.	mEq./Kg. % of Cl <sub>2</sub>	mEq.							
P-1	Recent myocardial infarction	6	77	35.0	1015	5.9	0.17	0.58	6.9	0.20	0.68	1.1	0.03	0.11	13.9	0.40	1.37	
M-2	Rheumatic heart disease with mitral stenosis	11	53	51.8	1601	5.3	0.10	0.33	6.4	0.12	0.40	1.7	0.03	0.10	13.3	0.26	0.83	
M-3	Hypertensive cardiovascular disease	22	51	43.6	1347	32.5	0.75	2.42	7.6	0.18	0.57	1.9	0.04	0.14	42.0	0.96	3.12	
F-4	Pituitary tumor	9	94	58.2	1688	2.6	0.04	0.15	15.9	0.27	0.94	2.6	0.04	0.15	21.0	0.36	1.25	
M-5	Squamous cell carcinoma of lung	7	64	43.6	1264	21.7	0.50	1.72	11.6	0.27	0.93	4.1	0.09	0.32	37.6	0.86	2.97	
F-6	Cerebral arteriosclerosis with encephalomalacia	6	56	58.2	1688	14.6	0.25	0.87	5.5	0.10	0.33	10.4	0.18	0.62	30.5	0.53	1.81	
F-7	Hypertensive and arterio-sclerotic heart disease	22	68	63.4	1839	2.9	0.05	0.16	14.3	0.23	0.78	5.3	0.08	0.29	22.5	0.35	1.22	
M-8	Paralysis agitans and bronchopneumonia	16	69	63.2	1953	2.7	0.04	0.14	15.0	0.24	0.77	8.1	0.13	0.41	25.8	0.41	1.32	
F-9	Cerebral thrombosis	20	67	65.0	1855	36.4	0.59	2.04	8.7	0.13	0.46	0	0	0	47.1	0.72	2.90	
M-10	Dissecting aneurysm of ascending aorta	19	59	68.0	2101	1.9	0.03	0.09	16.2	0.24	0.77	1.2	0.02	0.06	19.3	0.28	0.92	
M-11	Recurrent myocardial infarction	16	72	64.5	1993	11.2	0.17	0.56	2.5	0.04	0.13	14.0	0.23	0.70	27.7	0.43	1.39	
M-12	Chromophobe adenoma of pituitary	7	50	70.0	2163	24.2	0.35	1.12	21.9	0.31	1.01	7.7	0.11	0.35	53.8	0.77	2.49	
M-13	Traumatic demyelination of cervical spinal cord	12	76	54.5	1684	26.8	0.49	1.59	14.9	0.27	0.88	16.0	0.29	0.95	57.7	1.06	3.43	
						Mean:	14.7	0.27	0.91	11.4	0.20	0.67	5.7	0.10	0.32	31.7	0.57	1.89
						Range:	1.9-38.4	0.03-0.75	0.09-2.42	2.5-21.9	0.04-0.31	0.13-1.01	0-16.0	0-0.29	0-0.95	13.3-57.7	0.26-1.06	0.83-3.43

gastrointestinal chloride in the stomach, 35 per cent in the small bowel, and 15 per cent in the proximal half of the large bowel. The validity of these observations is not yet established, however, for the previously stated reasons.

## SUMMARY

Intraluminal gastrointestinal chloride content was measured in rabbits and in human subjects studied post mortem. In the former, gut chloride was referred to  $Cl_e$  estimated with  $KBr^{82}$ , while in the latter gut chloride was referred to the predicted  $Cl_e$  values.

Total exchangeable chloride averaged  $34.9 \pm 3.5$  mEq. per kgm. of body weight in rabbits. Of this,  $16.0 \pm 4.5$  per cent was in the lumen of the gastrointestinal tract, with  $11.7 \pm 4.4$  per cent in the stomach,  $2.5 \pm 0.7$  per cent in the small intestine, and  $1.7 \pm 0.4$  per cent in the cecum and proximal half of the large intestine. Radiobromide exchange equilibrium was complete to within 10 per cent for all segments of the gastrointestinal tract 48 hours after injection. No significant difference in either the  $Cl_e$  or the quantity of intraluminal gastrointestinal chloride was found between male and female rabbits.

Human subjects at post-mortem examination had relatively small amounts of intraluminal gastrointestinal chloride; the mean values were 1.9 per cent of the predicted  $Cl_e$  in the "total" gastrointestinal tract, with 0.91 per cent in the stomach, 0.67 per cent in the small intestine, and 0.32 per cent in the cecum and proximal transverse colon. The quantity of intraluminal chloride in normal man cannot be reliably inferred from these data.

The implications of these data are discussed in terms of the dynamics of chloride transport across the gastrointestinal mucosa and the anatomy of body chloride.

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