composition if one type of structure within the organ develops to a disproportionate extent at some stage. Such a change occurs in the brain during myelination.

During the first 2 weeks accumulation of plasmalogen parallels that of other phospholipids so that the ratio (Fig. 2) is relatively constant (0.09 ± 0.02). This result agrees with the idea that more material of the same type is being formed. After 12 to 16 days, however, ratio increases, indicating a differential accumulation of plasmalogen. During the following 4 weeks the total phospholipids in the brain develop increasingly larger amounts of plasmalogen until a fairly constant composition (about 0.24) characteristic for adult mammalian brain tissue(1.2.11) is reached in the seventh week.

This shift in phospholipid composition to higher levels of plasmalogen does not occur in developing adipose tissue or liver. In these organs the per cent of plasmalogen in phospholipids actually decreases during the first 3 weeks(3). Although the plasmalogen-phospholipid ratio in brains of 1- to 14-day-old rats is similar to that found in a variety of other animal organs(11), ratios as high as those found in brain after 40 days have been found in only a few other sources of lipid, *viz.* ram spermatozoa(12), heart and skeletal muscle, and white matter(11). There is no apparent similarity in these sources that might relate plasmalogen content of an organ with function, but whatever the functional role of this phospholipid may be, plasmalogen becomes an increasingly significant constituent during the development of the brain.

Summary. Plasmalogen content in brains of newborn rats is about 2 μmoles/g of wet tissue and represents about 10% of total phospholipid. During growth, and after major increase in brain weight, phospholipid composition shifts to one containing about 20 to 25% plasmalogen (12 μmoles/g). Maximal rate of accumulation of plasmalogen in brain occurs in 20- to 24-day-old rats.

ADDENDUM: Somewhat similar results were reported by Korey and Orchen(13) as this manuscript was being prepared for publication.

1. Wittenberg, J. B., Korey, S. R., Swenson, F. H., *J. Biol. Chem.*, 1956, v219, 39.

2. Christl, H., *Z. physiol. Chem.*, 1953, v293, 83.

3. Yarbro, C. L., Anderson, C. E., PROC. SOC. EXP. BIOL. AND MED., 1956, v91, 408.

4. Folch, J., *Biochemistry of the Developing Nervous System.*, 1955, Academic Press Inc., New York.

5. Folch, J., Ascoli, I., Lees, M., Meath, J. A., LeBaron, F. N., *J. Biol. Chem.*, 1951, v191, 833.

6. Fiske, C. H., Subbarow, Y., *ibid.*, 1925, v66, 375.

7. Rapport, M. M., Alonzo, N., *ibid.*, 1955, v217, 199.

8. Burton, R. M., Sodd, M. A., Brady, R. O., *ibid.*, 1958, v233, 1053.

9. Geren, B. B., *Exp. Cell. Res.*, 1959, v7, 558.

10. Brante, G., *Acta Physiol. Scand.*, 1949, v18, Suppl. 63.

11. Rapport, M. M., Lerner, B., *Biochim. et Biophys. Acta*, 1959, v33, 319.

12. Hartree, E. F., Mann, T., *Biochem. J.*, 1959, v71, 423.

13. Korey, S. R., Orchen, M., *Arch. Biochem. and Biophys.*, 1959, v83, 381.

Received September 14, 1959. P.S.E.B.M., 1959, v102.

Progress and Rate of Absorption of Radiostrontium Through Intestinal Tracts of Rats.* (25301)

C. F. CRAMER AND D. H. COPP

Physiology Dept., University of British Columbia, Vancouver, B.C.

In the following study a method was developed for estimating the effective absorption of radiostrontium from different parts of intestinal tract. This involves not only rate of absorption in each part, but also amount available for absorption. Since strontium is very similar to calcium in its behavior (despite biological discrimination factors) it is

* Supported in part by extramural grant from Defense Research Board of Canada.

possible to use it as a qualitative indicator for the latter. The study also has some practical implications, since intestinal absorption is a principal route of entry of the hazardous isotope Sr^{90}. Bergeim(1) using inert indicators, found calcium absorption greatest in the small intestine of rats. Fournier(2) and Nicolaysen(3) found that calcium absorption rates were highest in first section of small intestine of rats. Moore and Tyler(4) obtained similar results in the pig. Jones and Coid(5), using ligated gut segments, found greatest absorption of Sr^{89}, during the first hour, in the duodenum. It was our purpose to evaluate the contribution of various parts of intestinal tract to strontium absorption. This was made possible by combining the use of 2 methods which measured rate of absorption and quantity of tracer continuously available for absorption in each division of the intestinal tract(6,7).

Methods. Adult female rats of Sprague-Dawley strain weighing 200-220 g were fasted overnight and anesthetized with nembutal-urethane mixture. The gut loop to be studied was tied above and below at any 2 of the following points; pylorus, duodeno-jejunal ligament, mid-point between this ligament and cecum, ileo-cecal juncture, and anal sphincter. Lengths of segments in centimeters averaged: duodenum 12, jejunum 42, ileum 42 and colon 14. Fifteen microcuries of carrier-free Sr^{89} in 1 ml saline were injected into the lumen of each loop. The fluid was injected slowly to avoid distention of gut. The rat was then placed in position such that radioactivity accumulating in the tail could be counted continuously, using a shielded Geiger counting tube, a ratemeter, and recording milliammeter. After 5 hours, little increase in tail radioactivity was observed. Rats were killed at 6 hours. Since the external tail count showed a constant ratio to the body content (6), the net absorption curve was derived from the curve of *in vivo* tail counts. The ratio was determined in each rat from final *in vivo* tail count and total carcass radioactivity after removal of gut contents. Passage of Sr^{89} along intestinal tract was measured by methods previously described(7).

Results. Fig. 1 shows *in vivo* absorption from each isolated gut segment. Each curve represents the average of 8 rats, all measured continuously. Standard errors are indicated by vertical lines. Absorption in the cecum is not shown in the Figure because it is almost negligible. The actual amount was 2.6 ± 0.2% dose in 24 hours.

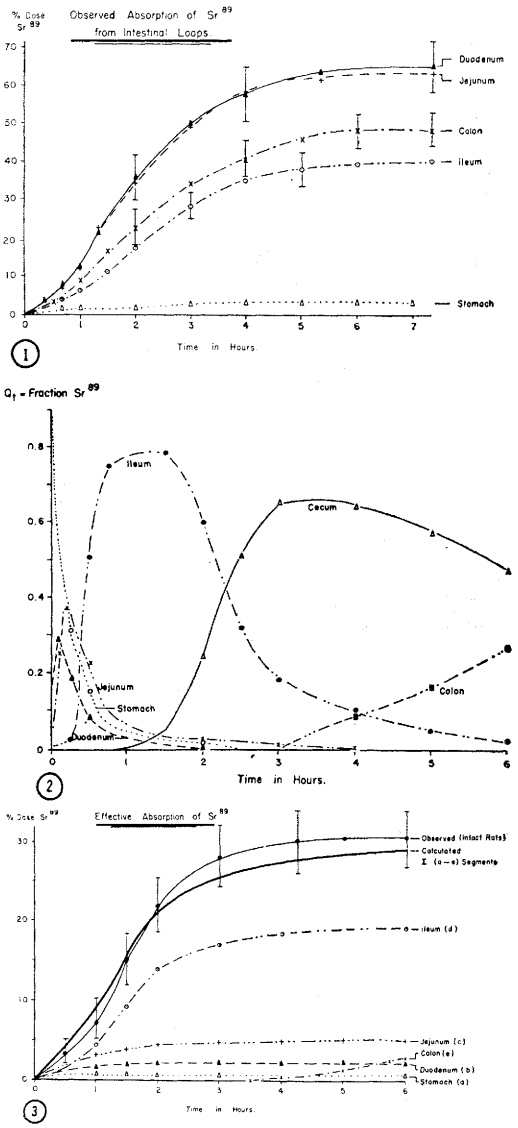

FIG. 1. *In vivo* absorption of Sr^{89} from isolated segments of intestinal tract. Stand. errors are shown.

FIG. 2. Fraction of Sr^{89} in divisions of intact gut during transit. Each point represents an avg of values from at least 4 rats.

FIG. 3. Estimated effective absorption of Sr^{89} from divisions of intact gut.

Fig. 2 shows the fraction of dose of Sr^{89} found in main divisions of intestinal tract of intact rats at various times of sacrifice. Each value represents the mean of 5 animals. The differences of volume of different divisions and motility of the tract evidently determine the amount of isotope available for absorption in each segment.

The quantity of Sr^{89} available for absorption in each section (Fig. 2), can be combined with rate of absorption in that segment to estimate effective absorption. The steps are as follows: 1. Rate of absorption $\frac{dA}{dt}$ was taken as the tangent to the cumulative absorption curve (Fig. 1) of a given segment at any time t, in units of % dose/hour. 2. This rate was multiplied by $\frac{100}{100 - A_t}$ to obtain a rate in terms of amount of isotope present in the loop at time t. 3. This corrected rate is multiplied by quantity of isotope actually available for absorption (Q_t) in the segment to give the effective rate of absorption $\frac{dA_E}{dt}$. 4. Effective rates of absorption plotted against time were integrated graphically, to give cumulative effective absorption for each gut segment.

Fig. 3 shows the cumulative effective absorption in each segment, estimated as described above. This Figure also shows total effective absorption of all gut divisions added together (heavy line) compared to absorption in a separate group of intact rats given Sr^{89} by stomach tube. The calculations may be summarized by:

$$A_E = \int_0^t Q_t \left(\frac{dA}{dt} \times \frac{100}{100 - A_t} \right) dt \text{ where:}$$

A_E is net effective absorption over 6 hours.
Q is the fraction of Sr^{89} found in each gut segment of intact rats.
A is net absorption of Sr^{89}.

Discussion. Conflicting conclusions from previous studies of calcium sites of absorption may now be reassessed. Some methods of studying absorption measure only rate of absorption, and highest rates of absorption apparently occur in upper part of small intestine(2-5). High rates of absorption of Sr^{89} in upper half of small intestine are shown in Fig. 1. This confirms and extends a previous study of Jones and Coid, based on measurements covering the first hour(5).

In a ligated segment, all of administered material is available for absorption. Obviously all radioactive material in the intact animal is not confined to any one part of the gut. The actual amount of Sr^{89} available to each segment throughout the effective absorption period is shown in Fig. 2. As described above the 2 factors, *i.e.*, rate of absorption and availability of material, can be combined to estimate effective absorption in that segment in the intact animal. It is assumed that absorption rate in the ligated loop is not greatly altered from the rate in the same segment of intact animal for at least a few hours. It is significant that when the sum of effective absorption by all segments is plotted against time, the total compares very favorably with absorption curves for normal intact rats. This comparison is shown in Fig. 3. Further, if one considers size of various segments, their structure and motility, these values seem reasonable. Similar results were obtained with Sr^{85} when the experiment was repeated.

Effective absorption from the duodenum and jejunum was less than that of the ileum, principally because of their small content of Sr^{89} during period of effective absorption. The cecum and stomach were relatively ineffective due to a very low rate of absorption, and possibly prolonged storage of food in the cecum may be an important factor limiting absorption of strontium and related minerals. The part played by the colon is less easy to assess. The colon absorbed freshly administered Sr^{89} solution at a quite high rate, but little of the Sr^{89} which traveled through upper intestinal tract over 3 hours. The normal rat absorbs slowly after 3 hours. Observations indicate that more effective absorption occurs in the colon when conditions allow earlier filling of the colon. Since absorption was limited in time, both in the gut and in isolated loops, there appear to be factors in addition to movement of material through the gut which normally limit radiostrontium absorption.

Summary. Rate of absorption of Sr^{89} from ligated loops of rat intestine, and rate of passage of Sr^{89} through the intact intestinal tract were measured. Assuming only that absorption rate in ligated loops is reasonably the same as rate of absorption from that segment in the intact rat, the actual effective absorption was estimated. The highest initial rate of absorption occurred in the duodenum with jejunum, ileum, colon and stomach following in decreasing order. Since the radiostrontium passed rapidly through the duodenum and jejunum, the largest actual effective absorption occurred in the ileum (65%), with smaller contributions by the jejunum (17%), colon (8%), duodenum (7%), and stomach (2%). Two factors were found to limit Sr^{89} absorption: (1) Movement of the isotope into gut segments having slower absorption rate, and (2) decreased absorption of Sr^{89} in each gut loop with time.

The authors acknowledge the technical aid of Isabel Hewlett.

1. Bergeim, O., *J. Biol. Chem.*, 1926, v70, 51.
2. Fournier, P., *Compte Rend. Acad. Sc.*, 1950, v231, 1556.
3. Nicolaysen, R., *Acta Physiol. Scand.*, 1951, v22, 260.
4. Moore, J. H., Tyler, C., *Brit. J. Nutr.*, 1955, v9, 81.
5. Jones, H. G., Coid, C. R., *Clin. Sci.*, 1956, v15, 541.
6. Cramer, C. F., PROC. SOC. EXP. BIOL. AND MED., 1959, v100, 364.
7. Cramer, C. F., PROC. SOC. EXP. BIOL. AND MED., 1959, v102, 511.

Received September 14, 1959. P.S.E.B.M., 1959, v102.

Quantitative Measurement of Gastrointestinal Blood Loss During Ingestion of Aspirin. (25302)

KENNETH K. MATSUMOTO AND MORTON I. GROSSMAN
Wadsworth Vet. Hospital and Depts. of Medicine and Physiology, University of California Medical Center, Los Angeles

It has long been suspected that treatment with salicylates may induce gastrointestinal hemorrhage(1). Several recent studies(2-4) show that tests for occult blood in feces frequently become positive when salicylates are given. This report deals with the effect of ingestion of aspirin on gastrointestinal blood loss quantitatively assessed by measurement of fecal radioactivity in subjects whose erythrocytes were labeled with Cr^{51}.

Methods. Estimation of gastrointestinal blood loss with Cr^{51}. Twenty ml of venous blood was drawn and added to 10 ml of acid-citrate-dextrose solution containing 300 μ-curies of Cr^{51} as sodium chromate. The mixture remained at room temperature 30 minutes and then was injected intravenously. Starting 1 day later, oxalated blood samples were taken every 3 days. Serial 3-day composite stool collections in cardboard containers lined with bags of polyethylene film were begun 1 day after injection of tagged cells. Stool samples were weighed, a weighed amount of water was added, and homogenized in Waring blendor of 1 gallon capacity. Radioactivity of an aliquot of blood samples taken at beginning and end of each stool collection and of a weighed aliquot of homogenized stool was measured in a well-type scintillation detector with a gamma ray spectrometer set for Cr^{51} peak at 320 Mev. Gastrointestinal blood loss in ml/day was calculated as described by Ebaugh *et al.*(5). Subjects were adult male patients on gastroenterology wards of Wadsworth Veterans Hospital. Diagnoses, presence of upper gastrointestinal hemorrhage at time of entry to hospital, and incidence of history of gastrointestinal hemorrhage occurring while taking salicylate preparations are given in Table I. Patients who were bleeding when admitted to hospital were studied 2 or more weeks after evidences of hemorrhage had disappeared and, when study was begun, all were losing less than 2 ml of blood/day in the feces. *Administration of aspirin.* 28 subjects in Group 1 received 1 g of aspirin (3 tablets) 3 times a day