

Accordingly, the gastric emptying time of the solute is prolonged. The solution is further diluted during transit through the small intestine. This interrelationship between gastrointestinal water transport, gastric emptying time and rate of intestinal absorption, might be of general importance.

Ca-b.s. do not cause morphological or irreversible functional alterations in the intestine.

The implications of these findings will be discussed in relation to the results of other workers.

**66a Gesetzmässigkeiten des Strontium - Stoffwechsels und ihre Bedeutung für die Eliminierung von Strontium aus dem Skelet.** A. SCHMID (Deutschland).

Es wird über Gesetzmässigkeiten des Strontium-Stoffwechsels im Skelett, den Umsatzmechanismus *in vivo* und die Fixierung von Strontium im Knochensystem berichtet.

**66b Patterns of Strontium Metabolism and their Significance in the Elimination of Strontium from the Skeleton.** A. SCHMID (Germany).

The patterns of strontium metabolism in the skeleton, the conversion mechanism *in vivo* and fixing of strontium in the bone system are reported.

**67 On the Use of Expiratory  $^{14}\text{CO}_2$  Patterns as a Pharmacological Tool for Studying the Biochemical Effects of Drugs.** G. T. OKITA (U.S.A.).

Since all carbon containing biochemical intermediates are eventually metabolized to  $\text{CO}_2$ , alteration in their metabolism due to biochemical effects of a drug may be reflected by alteration in the rate at which labelled  $\text{CO}_2$  appears in expired air. Therefore, an apparatus which will monitor continuous expiratory  $^{14}\text{CO}_2$  patterns after the administration of  $^{14}\text{C}$ -labelled intermediates is a useful pharmacological tool for studying the mode of action of those drugs having biochemical effects as a basis for their pharmacologic response. An apparatus built in our laboratory for this purpose has been reported elsewhere.<sup>(1)</sup> Essentially, the instrument consists of a 4  $\pi$  gas phase Geiger counter, an infra-red gas analyzer for measuring  $^{12}\text{CO}_2$ , a ratio analyzer to compute specific activity ( $^{14}\text{CO}_2/^{12}\text{CO}_2$ ) of  $^{14}\text{CO}_2$ , and a ventilation meter. All measurements are recorded continuously on a 4-channel recorder after the injection of a  $^{14}\text{C}$ -labelled intermediate. Depending upon the drug under investigation such labelled intermediates as acetate, pyruvate, lactate, formate, glucose, citrate, etc. have been employed. By the use of appropriate labelled intermediates and comparison of expiration  $^{14}\text{CO}_2$  patterns between control and drug treated groups, it is possible to obtain information on the biochemical mode of action of drugs.

The effects of testosterone, oestrogen, insulin,

orinase and diamox on expiratory  $^{14}\text{CO}_2$  patterns after the administration of various  $^{14}\text{C}$ -labelled intermediates will be presented. Some of the advantages of this method for studying biochemical effects of drugs are: (1) *in vivo* condition, all experiments are conducted on intact, unanaesthetized animals and subjects; (2) simplicity, no individual  $^{14}\text{CO}_2$  samples to assay; also, 2-6 experiments may be run per day; and (3) utilization of human subjects, therefore, no need to extrapolate animal data.

1. (1960), *Int. J. Appl. Rad. Iso.*, **7**, 273.

**68 Metabolic Studies of Carcinogenesis Using Expiratory  $^{14}\text{CO}_2$  Patterns Following Administration of  $^{14}\text{C}$ -Labelled Intermediates.** E. A. EZZ and G. T. OKITA (U.S.A.).

Using an instrument developed in our laboratory<sup>(1)</sup> we were able to measure continuously expiratory  $^{14}\text{CO}_2$  patterns in experimental animals after the administration of the following  $^{14}\text{C}$ -labelled intermediates: acetate-1- $^{14}\text{C}$ , sodium bicarbonate- $^{14}\text{C}$ , glucose-1- $^{14}\text{C}$  and glucose-6- $^{14}\text{C}$ . The effect of carcinogenesis and various hormonal states such as ovariectomy, estrogen and testosterone therapy on the expiratory  $^{14}\text{CO}_2$  specific activity patterns of  $^{14}\text{C}$ -labelled intermediates were studied in virgins, exbreeders and mammary tumour C3H mice free of the mammary tumour "milk factor". The specific activity curves as well as  $^{14}\text{C}$  levels in expiratory  $\text{CO}_2$  showed significant differences in some of the experimental conditions. The most striking biochemical change noted during the carcinogenesis process was the reduction in the percentage recovery of glucose-1- $^{14}\text{C}$ /glucose-6- $^{14}\text{C}$ . Rank order arrangement for the various experimental groups of C3H mice were as follows: factor free—1.48, virgin—1.36, exbreeders—1.00, tumour (single)—0.84, and tumour (multiple)—0.75. The decrease in the ratio is a reflection of an increase in glycolytic metabolism. Ovariectomy and testosterone therapy to tumour animals tends to return the ratios to those for virgin controls. This supports the thesis that ovariectomy and testosterone therapy tend to correct the metabolic defect produced by tumour.

1. (1960), *Int. J. Appl. Rad. Iso.*, **7**, 273.

**69 Studies on the Functions and Mode of Action of Thiamine.** C. J. GUBLER (U.S.A.).

Although the symptoms of thiamine deficiency have been well documented, the metabolic disturbances which cause these symptoms are still not well understood. In order to gain a better understanding to these metabolic disturbances, and thus of the physiological functions of thiamine, rats were made