and antipyrine was used in all experiments as a reference substance. The experiments showed that compounds with a high oil–water partition coefficient disappeared most rapidly from the perfusate while compounds with low water–oil partition coefficient disappeared at a slow rate. The results thus point to a lipoid barrier between blood and liver tissue which seems to be qualitatively similar to the blood–brain barrier. In a second experiment drug penetration into the liver tissue was studied by using tissue slices. This means that drugs could enter the cells from the incubation fluid without passing through the walls of the blood vessels. In these experiments no important differences in the rate of penetration of the various compounds could be detected. This suggests that the main obstacle for the penetration of drugs is located within or in the close vicinity to the walls of blood vessels.

64 The Inhibitory Effect of Sodium Lauryl Sulphate on the Intestinal Absorption of Glucose and its Potentiation of Phloridzin. J. A. NISSIM (United Kingdom).

The inhibitory effects of cationic quaternary ammonium germicides, such as trimethylhexadecylammonium stearate, cetrimide and domiphen, on the intestinal absorption of nutrients have been described previously.(1) Striking enhancement of inhibitory activity on the intestinal absorption of both glucose and sodium butyrate was achieved in cetrimide–phloridzin combinations, which was of the order of 50–100 times for the former and 10–15 times for the latter.(2)

These studies have now been extended to sodium lauryl sulphate. This is an anionic surface-active germicide, which showed no histological injury to the intestinal mucosa when perfursed or injected. The compound was perfused into the intestine of pure strain C3H mice with 0·2 per cent glucose in normal saline (25 ml) in half-hour experiments. Values of the percentage absorption of glucose are given in Table 1, and are compared with those obtained with cetrimide.

Sodium lauryl sulphate exhibited a weak inhibitory effect as compared with cetrimide or phloridzin. The potency ratio of lauryl-phloridzin combinations to phloridzin alone, however, was 5·8 with fiducial limits at P = 0·01 of 12·3 and 2·9, while the potency ratio of cetrimide-phloridzin combinations to phloridzin was 16·2 with corresponding fiducial limits of 40·7 and 7·6. Striking reduction of glucose absorption was shown by surfactant-phloridzin combinations at concentrations of the drugs which possessed no inhibitory activity whatever when perfused along (first column). Further, in spite of poor intrinsic activity, sodium lauryl sulphate showed considerable phloridzin-potentiating effect, which was only 1/3γ1/2 that of cetrimide.

Table 1

Percentage absorption of glucose. Figures represent mean of four experiments except where number is indicated in brackets. Control percentage absorption in 27 mice = 35·4 ± 1·1

Substance	Concentration of substance in perfusion fluid					
	0·001%	0·002%	0·01%	0·02%	0·1%	0·5%
Cetrimide	46·6	30·4(10)	24·1		3·7	
Phloridzin	34·3(8)	19·6(8)	10·8(8)		−0·9(8)	
Sodium lauryl sulphate			34·9	28·3	20·8	19·0(3)
Phloridzin[1] +Cetrimide	7·0	5·1	−1·6			
Phloridzin[2] +S.L.S.	16·5	8·4	−0·4			
Phloridzin[1] +S.L.S.			2·3			

(1) Equal conc.
(2) S.L.S. conc. 10 times that of phloridzin.

1. NISSIM, J. A. (1960a), *Nature (Lond.)*, **185,** 222; (1960b), *Nature (Lond.)*, **187,** 305; (1960c), *Nature*, **187,** 308.
2. NISSIM, J. A. (1961). Submitted for publication.

65 Intestinal Absorption Influenced by Calcium-binding Substances. E. SÖGNEN (Norway).

The presence of calcium-binding substances (Ca-b.s.), EDTA, sodium fluoride and sodium oxalate, in the gastrointestinal tract reduces the effect of orally administered drugs. Thus lethal oral doses of strychnine or barbiturates leave the animals unaffected or only slightly influenced when given concomitantly with Ca-b.s. A decreased plasma level of barbiturate and sulphonamides is found in experimental animals, compared to controls as previously reported.

Further study has revealed that the decreased plasma concentration is not due to increased renal excretion. The influence of Ca-b.s. on factors determining the rate of intestinal absorption has therefore been more closely studied.

Perfusion experiments on isolated small intestine *in situ* and experiments on isolated everted loops of small intestine *in vitro* have shown that the transmucosal translocation of water, glucose and sulphonamides and the utilization of glucose, is reduced by Ca-b.s.

The retard rate of transmucosal translocation is supposed to be caused by the effect of Ca-b.s. on glucose metabolism.

In the intact animal the observed alteration in gastric and intestinal fluid transport results in a dilution of the initially administered solution.

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 inre 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 $^{14}CO_2$ 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 CO_2, alteration in their metabolism due to biochemical effects of a drug may be reflected by alteration in the rate at which labelled CO_2 appears in expired air. Therefore, an apparatus which will monitor continuous expiratory $^{14}CO_2$ patterns after the administration of ^{14}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.[1] Essentially, the instrument consists of a 4 π gas phase Geiger counter, an infra-red gas analyzer for measuring $^{12}CO_2$, a ratio analyzer to compute specific activity ($^{14}CO_2/^{12}CO_2$) of $^{14}CO_2$, and a ventilation meter. All measurements are recorded continously on a 4-channel recorder after the injection of a ^{14}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 $^{14}CO_2$ patterns between control and drug treated groups, it is possible to obtained information on the biochemical mode of action of drugs.

The effects of testosterone, oestrogen, insulin, orinase and diamox on expiratory $^{14}CO_2$ patterns after the administration of various ^{14}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 $^{14}CO_2$ 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. Appld. Rad. Iso.*, **7**, 273.

68 Metabolic Studies of Carcinogenesis Using Expiratory $^{14}CO_2$ Patterns Following Administration of ^{14}C-Labelled Intermediates. E. A. EZZ and G. T. OKITA (U.S.A.).

Using an instrument developed in our laboratory[1] we were able to measure continuously expiratory $^{14}CO_2$ patterns in experimental animals after the administration of the following ^{14}C-labelled intermediates: acetate-1-^{14}C, sodium bicarbonate-^{14}C, glucose-1-^{14}C and glucose-6-^{14}C. The effect of carcinogenesis and various hormonal states such as ovariectomy, estrogen and testosterone therapy on the expiratory $^{14}CO_2$ specific activity patterns of ^{14}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}C levels in expiratory 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}C/glucose-6-^{14}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. Appld. 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