culation shows that if this surface existed in the lungs, it would more than account for the diffusion resistance at rest. Measurement of the relationship between surface pressure and diffusion resistance of lung-derived films is indicated.

Summary. Saline-extractable surface-active material has been found in the lungs of rat, cat, and dog. This material, probably mucoprotein, imparts large hysteresis and characteristic elasticity to the fluid surface. Its effect on lung mechanics has been studied. Its possible influence on diffusion across the alveolar barrier remains to be elucidated.

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^{14}C Studies on Ketogenicity of Metabolites in Lactating Dairy Cows.*† (23157)

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Recent studies upon the intermediary precursors of B-hydroxybutyric acid, acetoacetic acid and acetone in the intact dairy cow have been mainly concerned with ability of the administered compound to elevate the serum and urinary ketones(1-6). Extensive investigations have been made by Kleiber *et al.* (7-10) concerning transfer of carbon-14 of intravenously injected metabolites into milk casein, lactose and fat. In these trials ^{14}C-labeled carbonate, the lower fatty acids from formate to caproate, norleucine, and glucose were injected into normal lactating dairy cows and efficiency of transfer(11) to milk products calculated. Since up to 85% of milk lactose may originate from the plasma glucose(12), incorporation of relatively large numbers of carbon-14 atoms from a metabolite into lactose should indicate glucogenicity. Entrance of carbon-14 atoms into milk fat from an injected metabolite is a measure of its role in lipogenesis and not necessarily its ketogenicity. The present study was undertaken to measure relative transfer of carbon-14 atoms of injected compounds into the urinary ketone bodies.

Materials and methods. Mature lactating dairy cows were injected intravenously with glycine-1-^{14}C, butyrate-2-^{14}C, norvaline-3-^{14}C, carbonate-^{14}C, glucose-1-^{14}C, and propionate-2-^{14}C by methods previously reported by Kleiber(11). The urine was voided at the time of administering the isotope and then collected for the first hour following the injection for preparation of the ketone bodies. Two hundred fifty ml of urine was first treated with 58 ml of a solution containing 1.5% $K_2Cr_2O_7$ in 15.6N H_2SO_4 to convert the B-hydroxybutyric and acetoacetic acid to acetone(13). Another 50 ml of 5% $K_2Cr_2O_7$ was added after boiling had commenced to insure complete oxidation(14). The carboxyl carbon of B-hydroxybutyric and acetoacetic acid was not recovered. The mixture was next doubly distilled first into cold distilled water and secondly into 150 ml of Deninges' solution(15), adding 1 g Na_2O_2 per 100 ml of distillate prior to the second distillation to insure complete oxidation of

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TABLE I. Summary of Data from Trials.

Metabolites inj. intrav.	μc inj./kg body wt	g-atoms of acetone carbon* per 100 ml urine	μc/g atom acetone carbon	Stand. specific activity† of acetone carbon	Relative ketogenicity‡
Propionate-2-^{14}C	8.83	1.62×10^{-4}	3.77	6.92×10^{-5}	1.00
Carbonate-^{14}C	9.01	7.36×10^{-4}	.87	7.12×10^{-5}	1.03
Glucose-1-^{14}C	1.78	6.18×10^{-4}	.92	3.20×10^{-4}	1.80
Glycine-1-^{14}C	6.94	1.77×10^{-3}	.51	1.30×10^{-4}	1.88
Butyrate-2-^{14}C	9.02	3.53×10^{-4}	126.0	4.93×10^{-3}	71.3
Norvaline-3-^{14}C	4.12	1.88×10^{-4}	224.2	1.02×10^{-2}	148.0

* Acetone carbon includes only carbon originating from the 2, 3, 4 carbon atoms of urinary B-hydroxybutyric and acetoacetic acid in addition to urinary acetone carbon.

† μc/100 ml urine/μc inj./kilo body wt.

‡ Relative entrance of carbon-14 atoms from a given precursor into urinary acetone carbon* as compared with propionate-2-^{14}C.

acetaldehyde and other related compounds (14). To insure absence of any extraneous carbon from compounds other than acetone, acetone-2-^{14}C was added to urine of known acetone concentration containing no radioactivity. No measurable extraneous carbon was present in the second acetone distillate. The acetone-mercury-sulphate-chromate precipitate was prepared according to Van Slyke (15) for quantitative urinary acetone measurements and subsequently combusted to CO_2 according to the method of Van Slyke and Folch(16). In the glycine-1-^{14}C trial, iodoform was also prepared for combustion from the acetone-mercury-sulphate-chromate salt as described by Weinhouse *et al.*(17); in this method only the 1 and 3 carbon atoms of acetone are converted to iodoform. $BaCO_3$ planchets were prepared from the combusted samples as described by Kleiber and Edick (18) and counted for radioactivity at infinite thickness with a Tracerlab windowless Geiger flow gas counter and autoscaler.

Results. Standard specific activities were calculated to compare the ketogenicity of the injected metabolites. These results are presented in Table I. Both norvaline-3-^{14}C and butyrate-2-^{14}C are highly ketogenic as contrasted to propionate-2-^{14}C, glucose-1-^{14}C, glycine-1-^{14}C and carbonate-^{14}C. The relative ketogenicity of one carbon-14 atom in a metabolite need not reflect ketogenicity of other carbon atoms in the same molecule. In the glycine-1-^{14}C trial, all of the measurable radioactivity was confined to carbon-2 of the acetone since the iodoform containing the methyl carbon atoms exhibited only background levels of activity upon combustion.

Discussion. Kleiber *et al.*(7-10) have shown that propionate and glucose contribute greatly to lactose synthesis. Since the majority of the lactose originates from plasma glucose(12), entrance of carbon atoms into lactose from these precursors may be used as an index for their relative contribution to glucose formation, their "glucogenicity." Lardy *et al.*(19), using soluble enzymes from beef liver mitochondria, have recently explained the glucogenicity of propionate and bicarbonate by showing the synthesis of succinate from these two metabolites. The glucogenicity of succinate as a TCA intermediate is well known. The metabolism of glycine to the intermediate serine (20,21) and subsequently to pyruvate also leads to glucose formation. Compounds metabolized mainly to glucose generally contribute little to the formation of ketone bodies. Table I shows the relatively low ketogenicity of propionate, carbonate, glucose, and glycine but shows a relatively high ketogenicity for butyrate. Butyrate, however, also exhibits a glucogenic behavior. Blixenkrone-Möller(22) observed increases of glycogen in feline livers perfused with butyrate. This was not direct evidence for the incorporation of butyrate carbon atoms into glycogen since no tracers were used, but was conclusively a net synthesis of glycogen. After injection of butyrate-2-^{14}C into lactating cows, Kleiber *et al.*§ observed a maximum specific activity

§ Reported at International Physiol. Congress, 1956, 503.

in the plasma glucose 140 times as high as that of blood acetate and higher ^{14}C activity in the lactose than in the butterfat. Much of the acetyl-CoA produced by beta-oxidation of the butyrate-2-^{14}C could well be incorporated into glucose within the hepatic cell via the TCA cycle since glucose is withdrawn rapidly for lactose synthesis(12). After injection of norvaline-3-^{14}C, maximum specific activity of the plasma glucose was 98 times as high as that of the blood acetate.¶ Norvaline, as indicated in Table I, also has a relatively high ketogenicity. Both norvaline and butyrate exhibit glucogenic behavior in addition to showing a relatively high ketogenicity as compared with the other metabolites investigated.

Summary. The relative transfer of carbon-14 from propionate-2-^{14}C, carbonate-^{14}C, glucose-1-^{14}C, glycine-1-^{14}C, butyrate-2-^{14}C, and norvaline-3-^{14}C into the 2, 3, 4 carbon atoms of urinary B-hydroxybutyric and acetoacetic acid, and acetone has been determined. Carbon-14 atoms of norvaline-3-^{14}C and butyrate-2-^{14}C were more ketogenic than those present in the other compounds investigated.

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Effects of Low Doses of X-Rays on Embryonic Development in the Mouse. (23158)

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Irradiation of mice in various stages of pregnancy has shown that the effect observed in the young subsequently born is closely correlated with the embryonic stage at which they were irradiated. Irradiation during the first 5 days, *i.e.*, prior to the embryo's implantation in the uterus, leads to all-or-none effects: there is a high incidence of death shortly after irradiation but those embryos that survive are normal. On the other hand, irradiation during the next 8 days, the period of major organogenesis, has little effect on

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