Galactose Metabolism : Phenotypic Differences among Tissues of a Patient with Congenital Galactosæmia

It has recently been reported that two patients who had the characteristic syndrome of congenital galactosæmia as infants, and who lack gal-1-P uridyl transferase in their red blood cells, are nevertheless able to oxidize galactose-1-^{14}C to $^{14}CO_2$ *in vivo* in a near-normal fashion[1]. It is therefore apparent that some tissues within these individuals must be capable of metabolizing galactose. Further studies on one of those subjects (T. B.), a 30-year-old Negro who was the first case of galactosæmia reported in the American literature[2], have inquired into possible tissue differences with respect to the presence or absence of the metabolic derangement typical of galactosæmia.

Five different tissues derived from T. B. have been examined *in vitro* for their ability to metabolize galactose. The results obtained with white blood cells[3] and skin cells in tissue culture[4] have been reported previously. These results, together with those obtained for hæmolysates, intestinal mucosa and liver, are presented in Table 1. Of the tissues studied, only liver compares favourably with the normal in its ability to oxidize galactose-1-^{14}C to $^{14}CO_2$. Thus it would appear that this case represents a situation in which marked differences exist among tissues of a galactosæmic subject with respect to their galactose-oxidizing capacity relative to that of their normal counterparts. The implications of these observations in relation to galactose metabolism *in vivo* are not immediately apparent and deserve further study.

The pathway by which the liver of this galactosæmic patient is able to oxidize galactose deserves further consideration. Anderson *et al.*[5] reported that liver obtained by needle biopsy from the same patient had about 5 per cent of the normal ability to incorporate ^{14}C-galactose-1-phosphate into uridine nucleotide in the presence of uridine diphosphoglucose and uridine triphosphate, a finding which indicated a marked reduction of transferase activity as well as of any related alternative pathway. However, the subject was capable of forming glucosiduronic acid from galactose at a normal rate[6], an observation which is consistent with the present results obtained on the patient's liver and the *in vivo* results reported previously[1]. These findings can be explained on the basis that either the low activity detected by Anderson *et al.* is sufficient to account for the results of the *in vivo* and present *in vitro* studies, or that the pathway of galactose metabolism in the liver of this subject differs from that of the normal.

Table 1. Oxidation of Galactose-1-^{14}C to $^{14}CO_2$ by Various Tissues

Tissue	Subjects: Non-galactosæmic (*A*)	Subject T. B. (*B*)	*B*/*A*
	mμM $^{14}CO_2$/10^7 cells/h		
White blood cells*	2·0 ± 0·2† (6)	0·09	0·045
Skin‡	1·6 [0·7–2·8] (3)	0	0
	mμM $^{14}CO_2$/ml. packed R.B.C./h		
Hæmolysate§	5·9 (1)	0	0
	mμM $^{14}CO_2$/100 mg tissue/h		
Intestinal mucosa¶	60 (1)	1·7	0·023
	89 (1)		
Liver‖	1·5 (1)	0·9	0·75
	0·9 (1)		

Nos. in parentheses refer to the No. of subjects.
* Data calculated from the paper by Weinberg (ref. 3).
† *S.E.*
‡ Data calculated from the report of Krooth and Weinberg (ref. 4).
§ A 20 per cent hæmolysate was prepared by freezing and thawing R.B.C. suspended in Krebs phosphate buffer, *p*H 7·4, after removal of W.B.C. by centrifugation. The incubation medium contained 2 ml. of hæmolysate, 0·1 μc. galactose-1-^{14}C (4·72 μc./mg), 1·1 μM ATP and 0·54 μM TPN. $^{14}CO_2$ was collected as described previously (ref. 7).
¶ Suction biopsy of the small intestine mucosa was performed perorally with the instrument described by Brandborg *et al.* (ref. 8), and comparisons between normal and T. B. were made using tissue from the upper jejunum. 5 mg pieces of tissue were incubated in 3 ml. of Krebs bicarbonate buffer, *p*H 7·4, containing 0·15 μc. of radioactive galactose. Each value represents the average of duplicate determinations.
‖ Liver biopsy of T. B. was performed with a Menghini needle. The 15 mg of tissue were cut into four segments and incubated as described for intestinal mucosa. One piece of tissue was boiled for 2 min before incubation and served as a blank. Liver biopsy of controls was obtained at surgery from two individuals suffering from gall bladder disease. The surgical specimen was cut into 5–10 mg segments for incubation. Incubations were performed in triplicate.

The finding of definite phenotypic differences among several tissues from a single galactosæmic patient when studied for their ability to oxidize galactose *in vitro* indicates that galactosæmia is a more complex disease entity than has been appreciated hitherto.

Yale J. Topper
Leonard Laster
Stanton Segal

National Institutes of Health,
Bethesda, Maryland.

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Metaplasia of Aortic Connective Tissue to Cartilage and Bone induced by the Intravenous Injection of Papain

The effect of intravenous papain on the cartilage matrix has been reported by L. Thomas[1]. Recently we have been investigating the acute lipæmia induced by the injection of papain solution in adult rabbits[2]. At the end of each experiment, the animals were killed by air embolism and autopsies were performed. Several of these experimental animals showed lesions in the ascending aorta and the arch, and to a lesser extent in the upper portion of the descending aorta. This communication deals with the description of these lesions and of the conditions under which they were developed.

Grossly, the lesions appeared well delineated by a halo of raised tissue with irregular surface and edges

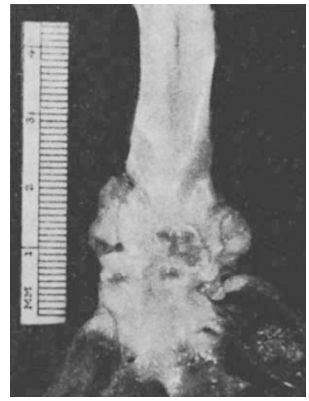

Fig. 1. Aorta of rabbit No. 89, male, 5,670 g, injected once with 15 mg papain/kg body-weight