time to state whether the step of Eq. 3, the inversion, was also absent because neither normal nor galactosemic hemolyzates showed any detectable amounts of galacto-waldenase. The problem whether galactosemia is a one-enzyme or a multi-enzyme defect, or whether a different pathway of galactose metabolism is operating as compared with normal individuals, could therefore not be sufficiently clarified at that time. Meanwhile, E. Maxwell, working in our laboratory, found that purified galacto-waldenase from calf's liver requires diphosphopyridine nucleotide (DPN) as a cofactor (*7*). This finding prompted us to add DPN to human hemolyzates in order to see whether galacto-waldenase might be present, but not yet detected because of the absence of its coenzyme (DPN) (*8*).

As shown in Table 1, it is indeed possible to demonstrate galacto-waldenase in hemolyzates from both normal and galactosemic subjects if DPN is also added. It appears that the lack of galacto-waldenase activity in crude hemolyzates is not due primarily to the destruction of DPN but mainly to a greatly increased requirement of galacto-waldenase for the coenzyme (*9*).

It can be seen from Table 1 that the activity of galacto-waldenase is of the same order of magnitude in the hemolyzates from galactosemic subjects as it is in those from normal.

Table 2 summarizes the average activities found for the various enzymes involved in the galactose metabolism of human hemolyzates. The galactokinase activity was measured according to a new sensitive and specific method that has not yet been published (*10*).

Table 1. Activity of galacto-waldenase in hemolyzates, with and without added DPN; 0.07 μmole of UDPGal are incubated with 0.5 ml hemolyzate corresponding to 0.25 ml of erythrocytes, 50 μl of 1*M* glycine at *p*H 8.7. Incubation time 15 min, at 37°C; DPN either omitted or added in amounts corresponding to 1 μmole. Total volume 0.6 ml. The activity is expressed as μmoles UDPG formed and UDPGal consumed (compare Kalckar *et al.*, *6*).

Condition of subjects	Enzyme activity (μmoles/ml hr)	
	No DPN	DPN
Normal (avg. of 3 cases)	0.002	0.32
Galactosemic (avg. of 3 cases)	0.002	0.35

Table 2. Activity of the four hemolyzate enzymes that catalyze the reactions of Eqs. 1, 2, 3, and 4 of the reaction scheme. Activity is given in micromoles of reactants converted per milliliter of lyzed erythrocytes, per hour.

Condition of subjects	Galacto-kinase		PGal-uridyl transferase		Gal-waldenase		PP-uridyl transferase	
	Sub-jects (No.)	Activity (Avg.)	Sub-jects (No.)	Activity (Avg.)	Sub-jects (No.)	Activity (Avg.)	Sub-jects (No.)	Activity (Avg.)
Normal	3	0.10	15*	0.82	3	0.32	9	1.20
Galactosemic	3	0.08	10	0.02	3	0.35	8	1.85

* This figure also includes infants that were on galactose-free diets (*5*, *6*).

The lack of PGal-uridyl transferase and the presence of galactokinase in the hemolyzates of blood from galactosemic subjects is in full accordance with the fact that galactose-1-phosphate accumulates in the erythrocytes of such patients if galactose (or milk) is administered (*4*). The presence of the freely reversible step of Eq. 3 in hemolyzates from galactosemic subjects would explain why normal development is possible (compare Mason and Turner (*11*) in these patients on galactose-free diets at an age when appreciable amounts of brain galactolipids are synthesized. These observations provide additional evidence for the fact that congenital galactosemia represents a block that is confined exclusively to a single enzyme, PGal-uridyl transferase. Genetic studies (*12*) indicate that the disease is presumably of hereditary origin and that it seems to be the result of a single recessive gene or of a more complex genetic pattern.

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References and Notes

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3. The following abbreviations are used: Gal, Galactose; Gal-l-P, galactose-1-phosphate; G-1-P, glucose-1-phosphate; UDPG, uridine diphosphoglucose; UDPGal, uridine diphosphogalactose; ATP, adenosine triphosphate; ADP, adenosine diphosphate; UTP, uridine triphosphate; PP, pyrophosphate.
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8. Bodil Waage-Jensen rendered valuable technical assistance as a trainee under the American-Scandinavian Foundation through a grant-in-aid that was generously made available to one of us (H.M.K.) by the Eli Lilly Laboratories.
9. Unpublished experiments show that hemolyzates, even after heat inactivation, bring about a marked increase in the requirements of galacto-waldenase for DPN. This applies to the enzyme present in erythrocytes as well as to purified liver galacto-waldenase. If the norite eluate (nucleotide fraction) from a hemolyzate filtrate was tested with purified liver galacto-waldenase, it was found that by this new highly sensitive assay (*7*) sufficient amounts of DPN were present to bring about an almost optimal rate of reaction. By this assay method, the amount of DPN present in filtrates of hemolyzates is estimated to be 0.05 to 0.1 μmoles/ml in accordance with Leder and Handler [in *Phosphorus Metabolism*, W. D. McElroy and B. Glass, Eds. (Johns Hopkins Univ. Press, Baltimore, 1951), vol. 1, p. 421]. However, in order for the galacto-waldenase to be activated in the presence of crude hemolyzates, a large excess of DPN must be added. In the series of experiments cited in Table 1, a 250-fold excess over the amount of DPN that gives an effect on purified galacto-waldenase was used.
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27 February 1956

Correction

In the article "Absorption and metabolism of iron" [*Science* 123, 87 (20 Jan. 1955)], the wavelength of maximum absorption of the iron-siderophilin complex was incorrectly given as 520 millimicrons. On page 89, the first sentence in the second paragraph under the heading "Iron transport" should read "The Fe^{+++}-B_1-globulin complex has a characteristic salmon-pink color with a maximum light absorption at 460 millimicrons. . . ."

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I am more and more convinced that our happiness or unhappiness depends far more on the way we meet the events of life than on the nature of those events themselves.—KARL VON HUMBOLDT.