10 hours after the experiment has been started. This seems to indicate that the worm does not require anything in the erythrocytes to maintain normal esophageal contractions, at least for relatively short periods.

Potassium ions markedly modify the esophagogram. If plasma to which 50 meq of potassium per liter has been added is placed in the anterior chamber, the β deflection begins to rise within 15 to 20 minutes until it reaches a plateau, interrupted brusquely by the deflection. The EG returns to normal in 30 to 60 minutes if the head of the worm is placed again in a normal dog's plasma or blood.

With the system described above, it is possible to observe the worm for many hours and to make continuous graphic recordings. This same arrangement may also prove suitable for the study of drugs and of various conditions affecting the esophageal musculature and its metabolism. This method may presumably be applied to other organisms that are similar to hookworm (*2*).

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Oxidation of Carbon-14 Labeled Galactose by Subjects with Congenital Galactosemia

Abstract. Galactose-1-C^{14} oxidation was studied in eight individuals with congenital galactosemia. Although two of these subjects fulfilled the usual diagnostic criteria for this disorder, they oxidized the intravenously administered sugar to $C^{14}O_2$ in a nearly normal fashion.

Congenital galactosemia is an inherited metabolic disease characterized by mental retardation, cataracts, hepatosplenomegaly, and severe malnutrition in infants fed diets containing galactose. This clinical syndrome has been associated with elevated galactose levels in the blood, increased erythrocyte galactose-1-phosphate, and galactosuria. Kalckar and his associates (*1*) have established that the metabolic defect is an absence of galactose-1-phosphate uridyltransferase, and the assay for this enzyme in hemolysates has become a widely used diagnostic procedure. Hemolysates from galactosemic individuals are unable to oxidize galactose-1-C^{14} to $C^{14}O_2$, an observation also proposed as a basis for a diagnostic test (*2*).

Several investigators have attempted to assess the ability of galactosemic individuals to metabolize galactose by determining the fraction of ingested galactose excreted in the urine (*3*, *4*). Whereas normal individuals excrete none of the ingested galactose, galactosemics excrete 15 to 60 percent of the sugar in the urine over a 24-hour period, and it was assumed the remainder was either stored in the body or metabolized. In order to obtain a more accurate assessment of galactose metabolism by galactosemic subjects, we have assayed the oxidation of intravenously administered C^{14}-labeled galactose to $C^{14}O_2$ in expired air for a 5-hour period after injection. Our results follow.

Experiments were performed with eight galactosemic subjects ranging in age from 6 to 30 years (Table 1). All but two of the subjects had a typical history of the galactosemic syndrome which was noted shortly after birth and which subsided upon institution of a galactose-free diet. The other two, E.W. and P.R., were discovered in childhood because of the clinical findings of mental retardation and cataracts. The manifestations of the disease in infancy have been reported for subjects T.B. (*5*), J.D. (*3*), and L.J. (*6*). All of the subjects were mentally retarded and had cataracts when our study was made. All of them lacked detectable transferase in their red cells, and the corresponding hemolysates were unable to oxidize C^{14}-galactose to $C^{14}O_2$.

Table 1. The oxidation of C^{14}-labeled galactose by galactosemic subjects. After an overnight fast galactose-1-C^{14} (4.72 μc/mg) obtained from the National Bureau of Standards was given intravenously either in normal saline (1 μc/ml) or mixed with a 20-percent solution of unlabeled galactose. Expired air was collected, and $C^{14}O_2$ was analyzed as previously described (*9*). Abbreviations: M, male; F, female; W, white; N, Negro. The studies of galactose metabolism in normal subjects have been reported previously (*10*).

Subjects	Age	Sex	Race	Galactose-1-C^{14}		Administered C^{14} in expired air after 5 hr (%)
				Grams	μc	
Galactosemic						
J.O'D.	6	M	W	0.00042	2	1
B.A.	7	M	W	1.0	2	8
E.W.	9	M	W	0.00042	2	0
P.R.	9	F	W	0.00042	2	3
	11			1.0	1	7
L.J.	11	M	W	0.00042	2	1
L.Br.	11	M	N	0.00042	2	35
				1.0	3	35
J.D.	17	M	W	0.00053	2.5	3
				1.0	2.5	5
T.B.	30	M	N	0.00053	2.5	19
				1.0	2.5	26
				2.0	2.5	28
				10.0	2.5	19
Normal (No.)						
4	18–21	M	W	0.00106	5	30–35
1	18	M	W	10.0	5	29
2	18–21	M	W	20.0	5	25–27

Table 1 shows the percentage of the administered C^{14} in expired air after 5 hours. The amount metabolized to $C^{14}O_2$ varied from 0 to 8 percent in six of the patients when either 1 mg or 1 g of galactose was given. In two of the subjects, L.Br. and T.B., normal or near-normal conversion of these quantities of galactose to $C^{14}O_2$ took place during the period of study. It should be noted (Table 1) that normal subjects become saturated with respect to their galactose oxidizing capacity when about 20 g are given, whereas saturation occurred in subject T.B. when 10 g were given.

Subject L.Br., like the other 11-year-olds, was prepubertal, while T.B. was postpubertal. J.D. was also postpubertal but metabolized galactose as poorly as the younger children. Thus it appears that the ability of certain galactosemic subjects to metabolize galactose at a near normal level is not specifically related to onset of puberty or to chronological age by itself. It is interesting to note that both L.Br. and T.B. are Negroes.

Both of the patients who exhibited a considerable ability to oxidize galactose had typical histories of the disease as infants. T.B. was the first reported case of galactosemia in the American literature (*5*), and his clinical picture in infancy served as the basis for the recognition of other such patients. L.Br. had malnutrition, hepatosplenomegaly, jaundice, ascites, and cataracts in the 6-month period after birth. Townsend *et al.* (*7*) pointed out that at age 7 T.B. could be given 200 ml of milk with each meal without subsequent galactosuria. This suggests that T.B. had the capacity to metabolize galactose in childhood as has L.Br.

It was pointed out above that the red cells of L.Br. and T.B., like those of the other six patients, are lacking in the transferase enzyme and are incapable of oxidizing galactose-1-C^{14} to $C^{14}O_2$. In these two patients, therefore, the results of the erythrocyte tests do not reflect the in vivo capacity to metabolize galactose to CO_2, although they are consistent with the presence of the galactosemic syndrome in infancy.

These results indicate that from a group of individuals with typical galactosemia in infancy a subgroup can be delineated in childhood, the members of which possess metabolic pathways for galactose metabolism in tissues other than red blood cells. The precise biochemical and genetic basis for this observation is not known (*8*).

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6 November 1961

Dimethylacetamide: A Hitherto Unrecognized Hallucinogenic Agent

Abstract. Dimethylacetamide in large doses was found to be a potent hallucinogenic drug in the human. Characteristic electroencephalographic changes accompanied the clinical abnormalities.

Dimethylacetamide has been found to have a significant antitumor effect in the experimental animal (*1*). During the course of a preliminary clinical trial with this drug, unusual psychological phenomena reminiscent of those described in individuals receiving hallucinogenic drugs such as lysergic acid or mescaline were encountered. In view of current interest in the psychotomimetic drugs, and because of the simplicity of the chemical structure of dimethylacetamide itself, we feel it desirable to record our observations in these cases.

Fifteen patients with advanced malignancies of various types were treated with dimethylacetamide (*2*). With the exception of one patient with seizures, none exhibited clinical signs of disease of the central nervous system prior to therapy. Two patients died within a few days of the institution of treatment; their critical state precluded adequate evaluation of mental function, and they cannot be considered further here. The remaining 13 patients all developed a distinctly abnormal mental state when the dosage of the drug reached a critical level of 400 mg per kilogram of body weight per day for 3 days or more.

Several of the patients had previously received this drug in dosages of 200 to 300 mg/kg without developing consistent untoward effects; when therapy was instituted at the higher levels, abnormal mentation was noted with predictable regularity. The earliest recognizable signs, generally noted on the 2nd or 3rd day of treatment, were depression, lethargy, and occasionally confusion and disorientation. Lethargy and confusion became very severe in four patients; in these individuals it was not possible to assess more subtle psychological abnormalities, or to determine with any accuracy the presence or absence of hallucinations. In the nine others, however, the lethargy and confusion syndrome either remained relatively mild in degree or fluctuated in such a manner as to allow of more detailed, albeit intermittent, evaluation. On the last (4th or 5th) day of therapy, or within 24 hours thereafter, striking hallucinations, perceptual distortions, and at times delusions became evident in all nine. The hallucinations were predominately visual, although auditory hallucinations were also described, and were extraordinarily well formed and vivid. With but one exception the patients developed relatively little anxiety about these experiences, an appearance of detachment, unconcern, and affective blunting being common. These phenomena persisted in severe form for an additional 24 hours, after which they gradually disappeared, the patients becoming normal several days after discontinuation of the drug. With recovery, the majority of these individuals were aware that they had experienced an altered mental state, and that their experiences had been hallucinatory in nature. At no time during the course of these psychological derangements could additional abnormalities be detected with repeated neurological examinations.

Serial electroencephalographic studies were carried out in five of these patients (Fig. 1). Four of these had normal electroencephalograms prior to therapy; one demonstrated focal activity in the right frontoparietal region. Electro-

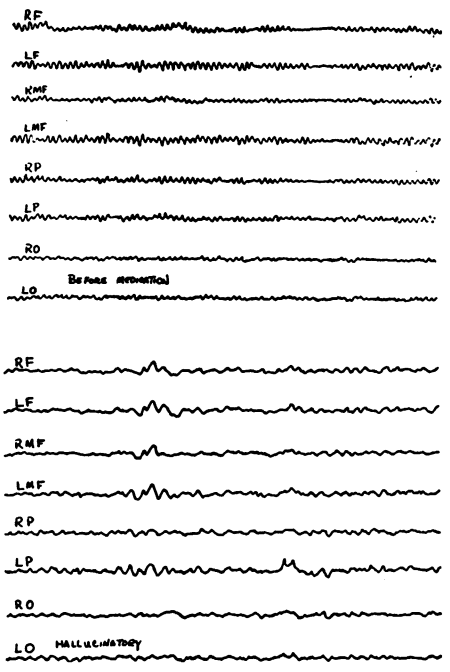

Fig. 1. Serial electroencephalograms in a patient who received dimethylacetamide. (Top) Normal tracing before therapy was begun. (Bottom) Episodic moderately high-voltage slow waves on final day of therapy during period of active hallucinations. Note absence of alpha rhythm.