histologically inapparent damage to liver cells. The regenerative response on the part of liver cells begins 40 to 48 hours after common duct obstruction; in time of onset, it is thus different from the regeneration that occurs after partial hepatectomy, which is advanced at 24 hours. Further, there is an early, brief interference of biliary obstruction with regeneration after partial hepatectomy, and there is a long interval of 48 hours between obstruction of the bile ducts and appearance of increased DNA synthesis and mitoses in liver cells, during which time injury, and response to injury, may occur. Substances such as serotonin(9) and thiourea(10) have been shown to cause increased liver cell mitoses in the absence of necrosis, probably due to sublethal damage to cells which is followed by proliferation.

Summary. DNA synthesis and mitosis in liver cells are partially inhibited 24 hours after operation in rats subjected to both partial hepatectomy and bile duct obstruction; at 48 hours regeneration is greater than after partial hepatectomy alone, although not as marked as that seen at 24 hours after partial hepatectomy. Liver cell proliferation occurs 40 to 48 hours after obstruction of the common bile duct, and is presumably the result of histologically inapparent injury to liver cells.

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Lens Sodium and Potassium Concentrations During Galactose Induced Cataractogenesis.* (26484)

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The electrolyte composition of the ocular lens of the rat is greatly modified during formation of galactose-induced cataracts. Of particular interest is a reduction in potassium and elevations in sodium and calcium concentration(1,2). The relationship between the changes in these cations and lens opacification is not known. Certain biochemical studies suggest that cataractogenesis is the consequence of an inhibition of lens metabolism by galactose(3,4). It has also been demonstrated that maintenance of the lens content of sodium and potassium is energy dependent(5) and the changes observed in these cations during cataractogenesis may reflect the effect of galactose on lenticular metabolism. The proposal has been made that the concentration of these cations in the lens during cataractogenesis could serve as an index to the progression of the lesion(6).

The present studies were made to determine the time course of the modification of lens sodium and potassium in relation to development of galactose-induced lens opacification. Large differences are known to exist in susceptibility of several strains of albino rats to the cataractogenic property of galac-

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tose(7,8). The degree to which susceptibility to cataractogenesis influences the magnitude and time course of the cation changes was studied by using 3 strains of albino animals known to differ markedly in this regard (8). Animals of the Carworth Farm Nelson strain fed a 60% galactose diet develop cataracts after 32 days. Total time to lens opacification in weanling rats of Rochester ex Wistar and Holtzman strain animals is 20 and 13 days respectively.

Method. Weanling male rats of Carworth Farm Nelson (CFN), Rochester ex Wistar (RW) and Holtzman (H) strains were housed in a room maintained at constant temperature. Food and water were available *ad libitum*. The diet contained 60% carbohydrate, 21% casein, 15% fat (Crisco), 4% salt mixture plus a complete vitamin supplement. Control diets contained 60% glucose; experimental diets contained 30% glucose plus 30% galactose or 60% galactose. Except when specifically indicated, experimental animals were fed the 60% galactose diet. Animals were sacrificed by decapitation, lenses were removed intact, blotted, weighed and ashed at 500°C for 24 hours. The ash was dissolved in dilute HCl and potassium and sodium determined by flame photometry. Lens calcium was precipitated as oxalate and determined by a modification of the method of Diehl and Ellingboe(9). Concentrations of these cations are reported as mEq/Kg tissue.

Results. Nutritional State of Animals. Galactose fed animals had polyuria and polydipsia with weight gains significantly below that of glucose fed animals. There was no difference in rate of weight gain of galactose-fed animals of the strain most resistant (CFN) or susceptible (H) to cataractogenesis (Table I).

TABLE I. Body Weights of Carworth Farm Nelson (CFN) and Holtzman (H) Strain Rats Fed a 60% Galactose Diet.

Day	CFN strain	Holtzman strain
0	45.0 ± 1.4*	44.0 ± 1.3
3	50.3 ± 1.0	44.4 ± 2.8
6	58.5 ± .5	62.0 ± 3.0
9	68.4 ± 1.0	68.9 ± 3.7
12	76.7 ± 1.5	78.4 ± 3.9
15	87.0 ± 3.2	87.1 ± 4.4
18	100.7 ± 3.7	99.0 ± 2.4

* Mean ± S.E. of 9 animals.

In the experimental animals of all strains studied, equatorial vacuolization, characteristic of the initial stage of cataract development, appeared between days 6 and 10. During the next 3 to 4 days, vacuoles increased in size and the extent of lens involved, then remained relatively unchanged until 24 to 48 hours prior to opacification. At this time rapid progression to complete opacification occurred.

Lens Ca Concentrations. Lens calcium concentrations were determined in control and experimental animals of the CFN strain only. No differences in calcium content between these groups developed during the first 20 days (Fig. 1). A slight increase in calcium content may develop during days 20 to 30. Other studies have indicated that the lens Ca concentration of 7 week old control animals of this strain is 1.5 ± 0.2 mEq/Kg.

Lens K. Concentration. Earlier studies have shown that in the CFN strain of rat, lens potassium on the second day of galactose feeding is not different from that of the controls (37.6 ± 3.6 mEq/Kg and 43.6 ± 2.8 mEq/Kg). The later time course of the lens potassium concentration in control and experimental animals of this strain is shown in Fig. 1. Lens potassium concentration is significantly below control values on day 4; this decreased concentration is maintained approximately 48 hours when concentration increases to a value approaching that found in control animals. Concentration of this cation is maintained at approximately 75% of control values from day 8 until day 16. At this time, 12 days before opacification, another precipitous drop occurs to a value comparable to that of the mature cataracts.

In another group of animals of the CNF strain fed the 30% galactose diet, initial opthalmologic changes were observed on day 14 and after 60 days only 50% of the animals had developed complete cataracts. On the twentieth day of feeding the 30% galactose diet, lens potassium concentration was 13.6 ± 6.1 mEq/Kg and at 60 days, in the lenses

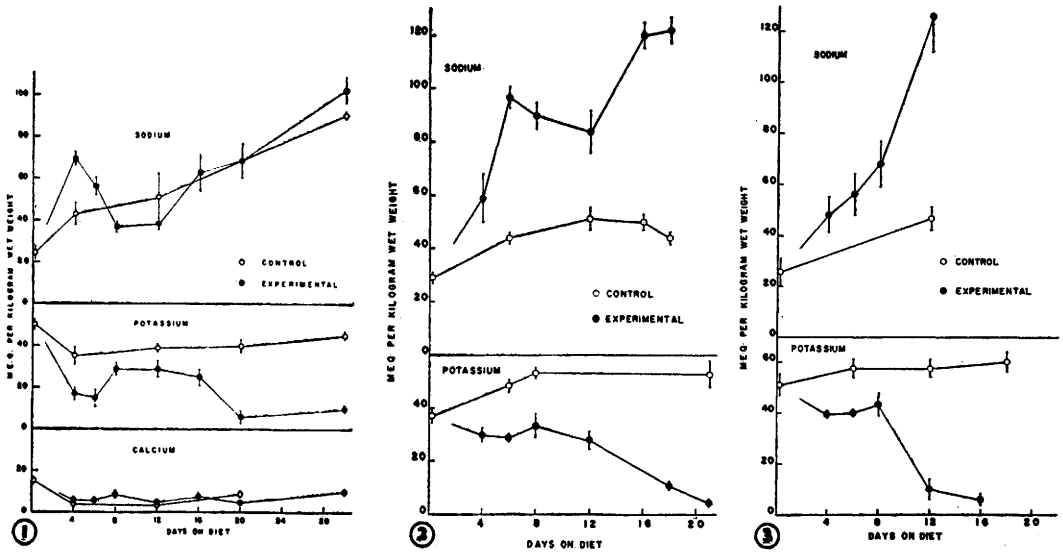

FIG. 1. Lens sodium potassium and calcium concentrations in weanling Carworth Farm Nelson strain rats fed diets containing 60% glucose or 60% galactose.

FIG. 2. Lens sodium and potassium concentrations in Rochester ex Wistar strain weanling rats fed diets containing 60% glucose or 60% galactose.

FIG. 3. Lens sodium and potassium concentrations in Holtzman strain weanling rats fed diets containing 60% glucose or 60% galactose.

that had not opacified, 23.1 ± 1.4 mEq/kg. Lens potassium concentration in glucose fed animals on day 20 and 50 was 40.0 ± 1.5 and 51.2 ± 5.0 mEq/Kg respectively.

In the RW and H strains a initial reduction, similar to that observed in CFN animals, occurred in potassium concentration on day 4 (Figs. 2 & 3). In these strains, no subsequent partial recovery occurred. Concentration of this cation remained at approximately 60% of control value until day 8 in the most susceptible strain (H) and day 12 in the RW strain; then, at 5 and 8 days, respectively, prior to opacification, potassium concentration decreased to values characteristic of mature cataracts.

Lens Sodium Concentration. In galactose fed animals of the CFN strain, lens sodium concentration followed a pattern generally reciprocal to that of potassium (Fig. 1). A sharp initial rise was followed by a temporary restitution of control values. The time course of these changes in sodium was the same as that described for potassium.

In the RW strain of rats (Fig. 2) sodium concentration rose initially to value 200% of that found in control animals. No partial reversal occurs in this more susceptible strain and this concentration was maintained until days 12 to 16 when a further increase occurred. As with the CFN strain, changes in sodium concentration were reciprocal to, but followed the same time course as, those found for potassium.

In H strain, changes in lens sodium changes paralleled those seen in RW strain animals (Fig. 3).

Discussion. The polyuria and polydipsia of the galactose-fed animals reflect the inefficiency of utilization of this sugar. The finding of equal weight gains in animals resistant (CFN) and susceptible (H) to cataractogenesis suggests that differences in capacity to metabolize galactose are not the basis for strain differences in cataract susceptibility. Other studies(7) have indicated that the strain differences, in susceptibility to xylose-induced cataractogenesis, appear to reside in the lens itself.

In galactose fed animals of all of the 3 strains, modification of concentrations of potassium and sodium is evident on day 4, prior to appearance of initial opthalmologic changes. In only the most resistant strain (CFN) was there a partial recovery toward control values. In the 2 more susceptible strains of

rats, lens sodium concentration remains relatively unchanged until the time that potassium concentration decreased, at which time sodium concentration rose again. The finding that sodium and potassium change reciprocally in the CFN strain suggests that this partial recovery reflects a real difference between this relatively resistant and the other more susceptible strains. Length of time that potassium concentrations are maintained at 60 to 70% of control values varies directly with degree of strain resistance. In all strains a precipitous drop in lens potassium occurred prior to opacification. Again, length of time between the second fall in potassium concentration and lens opacification varies directly with strain resistance.

These findings suggest that a critical period in studies of the resistance of the CFN strain might be centered around days 6 to 8. A new energy-yielding metabolic pathway or an augmentation of those already present may permit partial recovery to the control concentrations of sodium and potassium ions. In this strain, opacification does not occur, in the presence of a depressed lens potassium concentration for 12 days while ingesting a 60% galactose diet and for 25 days when fed a 30% galactose diet.

A single sodium or potassium analysis of the lens does not provide an adequate index of the progression of cataract formation or even to the proximity of opacification. The time course and magnitude of the changes in lens sodium and potassium concentration appear to be characteristic of and dependent upon the relative susceptibility of the strain employed.

Summary. The lens concentrations of sodium and potassium were determined during galactose-induced cataractogenesis in 3 strains of albino rats. Four days after galactose feeding was initiated, lens potassium concentration decreased to 60% and sodium concentration increased to 175% of control values. In resistant, but not in susceptible, strains of animals partial return to control concentrations of both of these ions occurred. The changed lens sodium and potassium concentrations were maintained for 4-16 days depending on degree of resistance in each strain. Lens potassium then decreased and sodium concentration increased prior to actual opacification. The comparable weight gains of *ad libitum* fed animals of resistant and susceptible strains suggested that resistance or susceptibility to cataractogenesis resides in lens itself.

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