Syndrome	Major phenotype
GLUT-1 deficiency syndrome	Reduced glucose transport across brain-blood barrier causing infantile seizures, delayed development, and acquired microcephaly
Fanconi-Bickel syndrome	Fasting hypoglycaemia, fed hyperglycemia hypercholesterolemia, and hyperlipidemia hepatorenal glycogen accumulation leading to hepatomegaly, proximal renal tubular dysfunction, dwarfism
Renal hypouricemia, (RHUC2)	Hypouricemia
Arterial tortuosity syndrome	Connective tissue disorder with elongation and tortuosity of the major arteries (incl. Aorta); skin and joint abnormalities (hyperextensibility, hyperlaxity); micrognathia; elongated face

DISORDERS OF GLYCOLYSIS
Some of them manifest as „glycogenoses"

Hereditary - congenital

- Phosphofructokinase deficiency – muscle fatigue
- Haemolytic anemias – red cell enzymopathies

Acquired?

- Lactate acidosis: Hypoxia, pyruvatdehydrogenase deficiency, thiamin deficiency (alcoholics), As, F, Hg intoxication, sometimes in diabetes mellitus
- Randl cycle. Increased fatty acid oxidation (obesity, diabetes) ⇒ NADH and acetylcoenzyme A overproduction. **Block of** glycolysis and glycogen synthesis ⇒ **Increased** gluconeogenesis in liver…

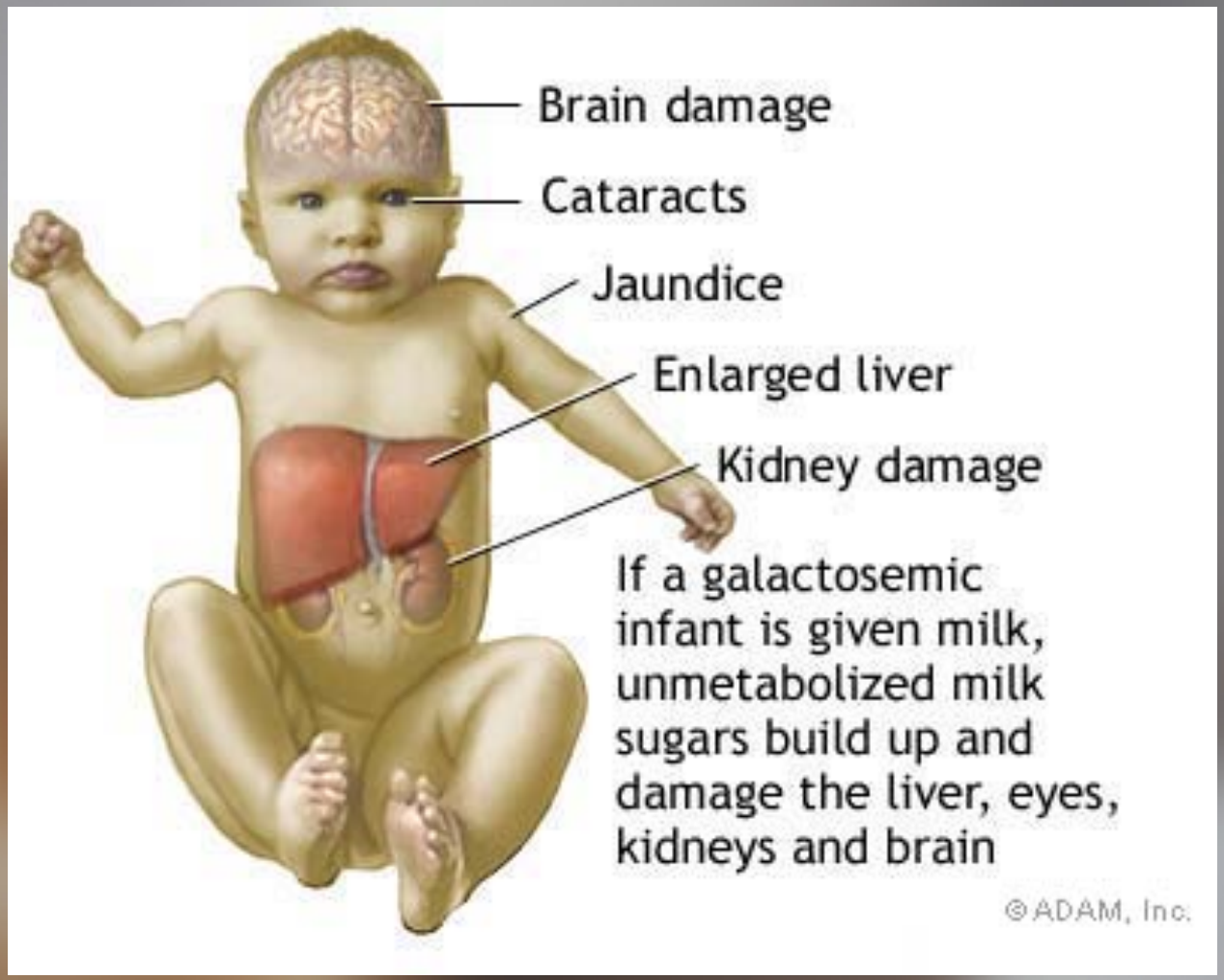
SEVERE (BUT RARE) DISORDERS OF MONOSACCHARIDE METABOLISM

- **Galactosemia AR, 1/20 000 – 60 000**
  - Accumulation of galactose, gal-1-P, galactitol ⇒ cataract, mental retardation, liver cirrhosis, haemolysis, kidney failure ⊗ diet without milk
- **Fructose intolerance AR, 1/20 000**
  - Accumulation of fructose & F-1-P ⇒ **block** of **glucose metabolism** (glycolysis, gluconeogenesis, glycogenolysis) ⇒ hypoglycaemia after sweet fruits and sweets ⊗ **omit them**

GALACTOSEMIA

Lactose = Gal-Glu

AR, 1/20 000 – 60 000, neonatal screening



LESS SEVERE (BUT RELATIVELY COMMON) DISORDERS OF SUGAR METABOLISM

- **Milk intolerance – opposite mutation**
  - Lactose is important source of energy for small children
  - The activity of **lactase** is high up to age 4 years, later **decreases**
  - Milk intolerant adult people are the *nonmutants*
  - People able consume milk in adulthood are *mutants* – **their off switch** is not working
  - Selection according to life style – hunters contra farmers
- **Fructosuria**
  - Fructose does not enter into metabolism, excretion through urine

Disorder	Primary underlying cause of the problem	Defective Nephron Segment(s)	Altered transport molecule	Nephron Segment(s) affected
Diabetes Mellitus	Lack Insulin-raises plasma [glucose]	NA	NA	PT, and all downstream segments
Nephrogenic glucosuria	Defective glucose reabsorption	Proximal Tubule	SGLUT2, SGLUT1, or GLUT2 or GLUT1	PT
Diabetes Insipidus	Lack Antidiuretic hormone ADH	NA	NA: AQP2 expression is absent due to absence of ADH	Entire collecting duct system i.e. CCD and downstream .

GLYCOGEN STORAGE DISEASES, GSD*

- Synthesis of glycogen (energy from ATP & UTP)
  - G6P ⇒ G1P no problem
  - Activation with UTP ⇒ UDP-glucose
  - primer, 1-4 polymerisation & 1-6 branching after 10
  - 20 nm particles
- Glycogenolysis
  - phosphorylase (different from amylase) makes G1P
  - debranching makes glucose

Table 21.1 Glycogen-storage diseases

Type	Defective enzyme	Organ affected	Glycogen in the affected organ	Clinical features
I Von Gierke	Glucose 6-phosphatase or transport system	Liver and kidney	Increased amount; normal structure.	Massive enlargement of the liver. Failure to thrive. Severe hypoglycemia, ketosis, hyperuricemia, hyperlipemia.
II Pompe	α-1,4-Glucosidase (lysosomal)	All organs	Massive increase in amount; normal structure.	Cardiorespiratory failure causes death, usually before age 2.
III Cori	Amylo-1,6-glucosidase (debranching enzyme)	Muscle and liver	Increased amount; short outer branches.	Like type I, but milder course.
IV Andersen	Branching enzyme (α-1,4 ⟶ α-1,6)	Liver and spleen	Normal amount; very long outer branches.	Progressive cirrhosis of the liver. Liver failure causes death, usually before age 2.
V McArdle	Phosphorylase	Muscle	Moderately increased amount; normal structure.	Limited ability to perform strenuous exercise because of painful muscle cramps. Otherwise patient is normal and well developed.
VI Hers	Phosphorylase	Liver	Increased amount.	Like type I, but milder course.
VII	Phosphofructokinase	Muscle	Increased amount; normal structure.	Like type V.
VIII	Phosphorylase kinase	Liver	Increased amount; normal structure.	Mild liver enlargement. Mild hypoglycemia.

Note: Types I through VII are inherited as autosomal recessives. Type VIII is sex linked.

Table 21.1
***Biochemistry*, Seventh Edition**

Insulin and its antagonists

- **Glucagon** – glycogen breakdown, gluconeogenesis glycolysis blockade in liver
- **Adrenaline, noradrenaline** – glycogen breakdown and gluconeogenesis in muscles, lactate ⇒ glucose in liver
- **Growth hormone** (anabolic hormone), lipolysis, proteosynthesis
- **Glucocorticoids** – gluconeogenesis, block of proteosynthesis
- **Thyroid hormones and oestrogens**

In physiological conditions synergism (counter-regulation)

Hyperglycemia = diabetes mellitus

- No insulin (type 1 dm, removal of pancreas, etc.)
- Deficient action of insulin (type 2 dm)
- Antagonists (glucocorticoids, adrenaline, growth hormone, gravidity)
- Stress (MI, stroke)