Carbohydrate training day

Galactose, fructose etc

Mary Anne Preece

Consultant Biochemist

Birmingham Children's Hospital

Galactose

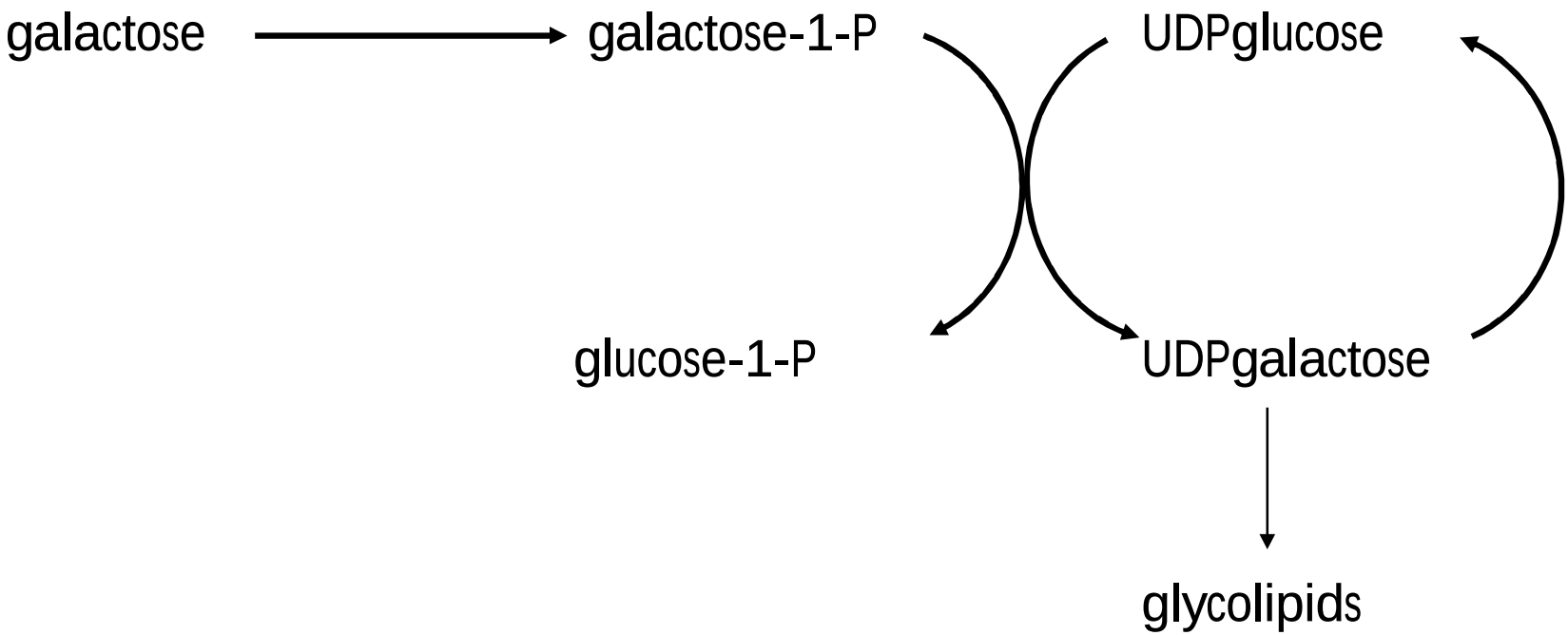
- lactose (glucose-galactose)
- primary CHO source in milk
- provides 40% of energy in neonates
- symptoms appear early in life

- metabolism
  - formation of glucose-1-phosphate ie acts as energy source especially in infants
  - formation of galactosides via UDPgal
  - minor pathways
    - formation of galactitol
    - formation of galacturonic acid

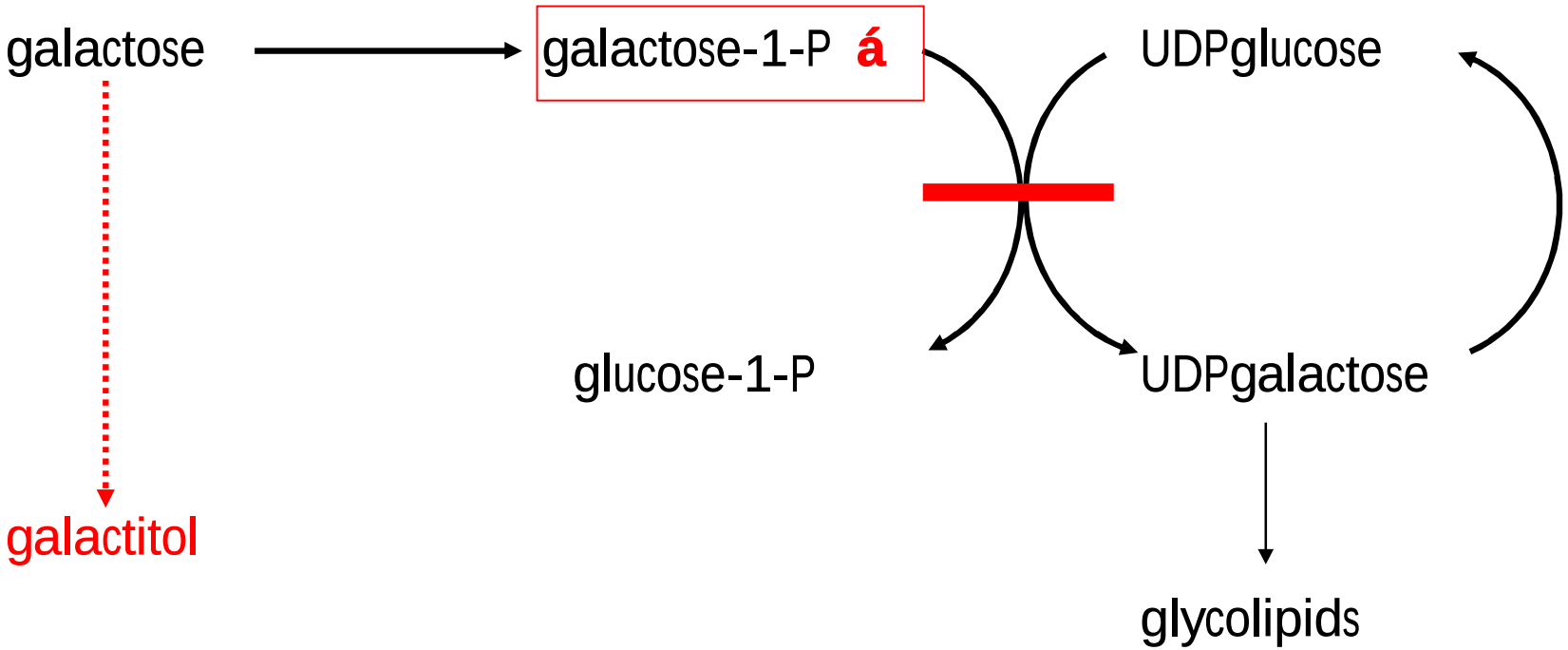
Inborn errors of galactose metabolism

- galactose-1-phosphate uridyl transferase deficiency (classical galactosaemia)
- galactokinase deficiency
- epimerase deficiency
- all autosomal recessive

Galactose metabolism



Galactose-1-phosphate uridyl transferase



Classical galactosaemia

- normal birth weight
- failure to regain birth weight
- symptoms in second half of 1st week
  - refusal to feed
  - vomiting
  - jaundice
  - lethargy
  - hepatomegaly
  - oedema
  - ascites
  - death due to liver/kidney failure, sepsis (E coli)
- cataracts within days or weeks

Classical galactosaemia

- biochemical abnormalities
  - hypoglycaemia
  - conjugated hyperbilirubinaemia (initially unconj)
  - abnormal liver enzymes
  - coagulopathy
  - hypophosphataemia
  - reducing substances
  - aminoaciduria
  - hyperphenylalaninaemia

BPSU 3 year study (1998-1990) conclusions

- incidence (UK) 1 in 44000
- diagnosis
  - clinical features/biochem 25
  - clinical features 12
  - family history 6
  - biochemical tests 3
- commencement of treatment
  - 90% by 1 month
  - 75% by 3 weeks
  - 67% by 2 weeks

Classical galactosaemia - incidence

UK	1 in 44000
Eire	1 in 26000
Australia	1 in 33000
USA	1 in 62000
Japan	1 in 667000

Diagnosis of classical galactosaemia – the practicalities

- urine sugars
- erythrocyte galactosaemia screen (Beutler)
- quantitative galactose-1-phosphate uridyl transferase (erythrocyte / fibroblast)
- erythrocyte galactose-1-phosphate
- mutation analysis
- urine galactitol

Urine sugars

- Clinistix
  - specific for glucose
- Benedict's
  - reacts with reducing substances including reducing sugars
  - glucose, galactose, fructose, lactose – POSITIVE
  - sucrose - NEGATIVE

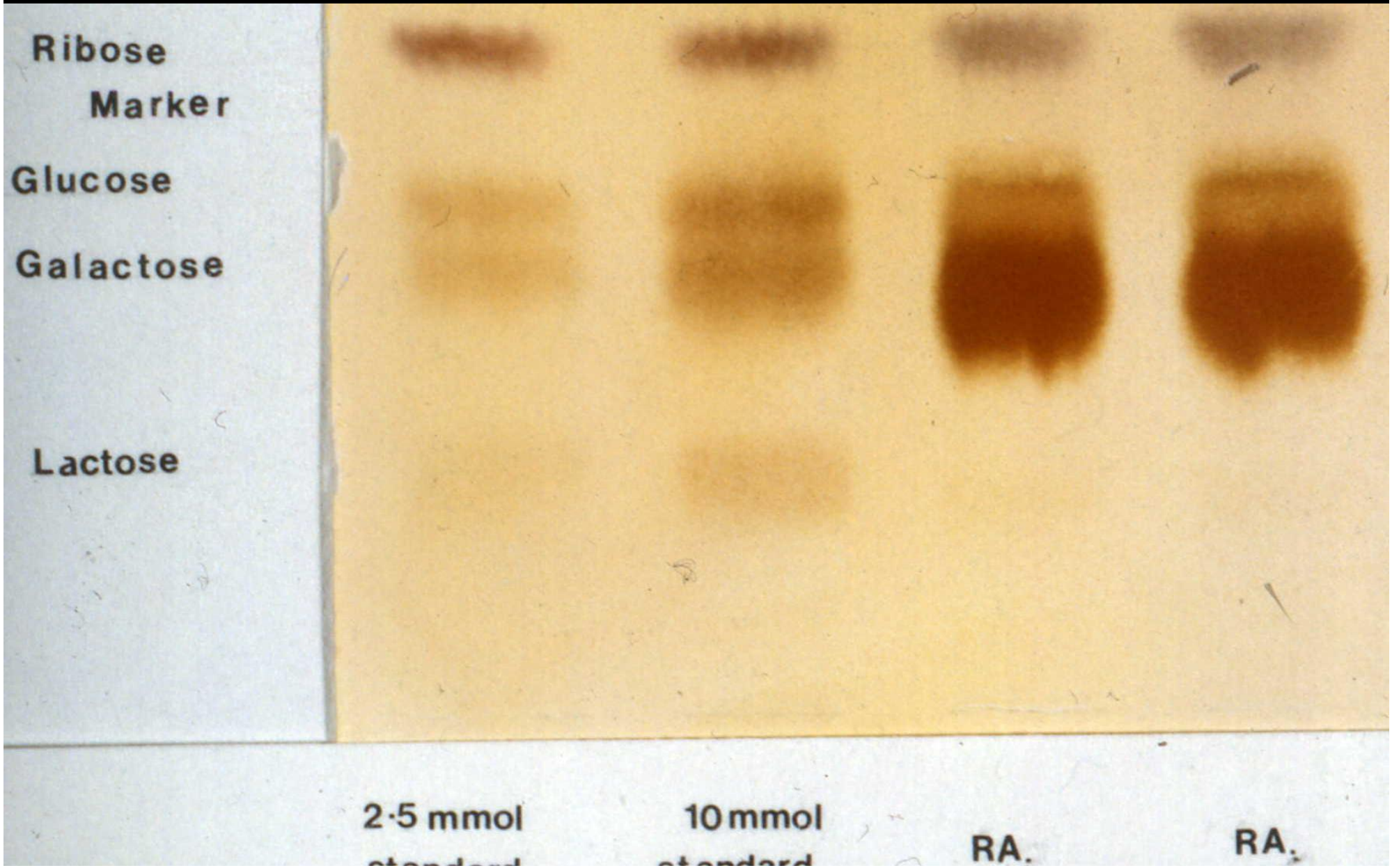
Clinistix & Benedict's

Clinistix	Benedict's	Sugars present
Positive	Negative	Glucose only
Negative	Positive	Non glucose reducing substance(s)
Positive	Positive	Glucose +/- other non glucose reducing substance(s)

Urine sugars - pitfalls

- rely on dietary intake
- Clinistix and Clinitest are confused
- can have positive Clinistix in galactosaemia
- galactosuria may be secondary to liver failure

Sugar chromatography



Beutler test

UDPgluc*

gal-1-P*

NADP*

Beutler test

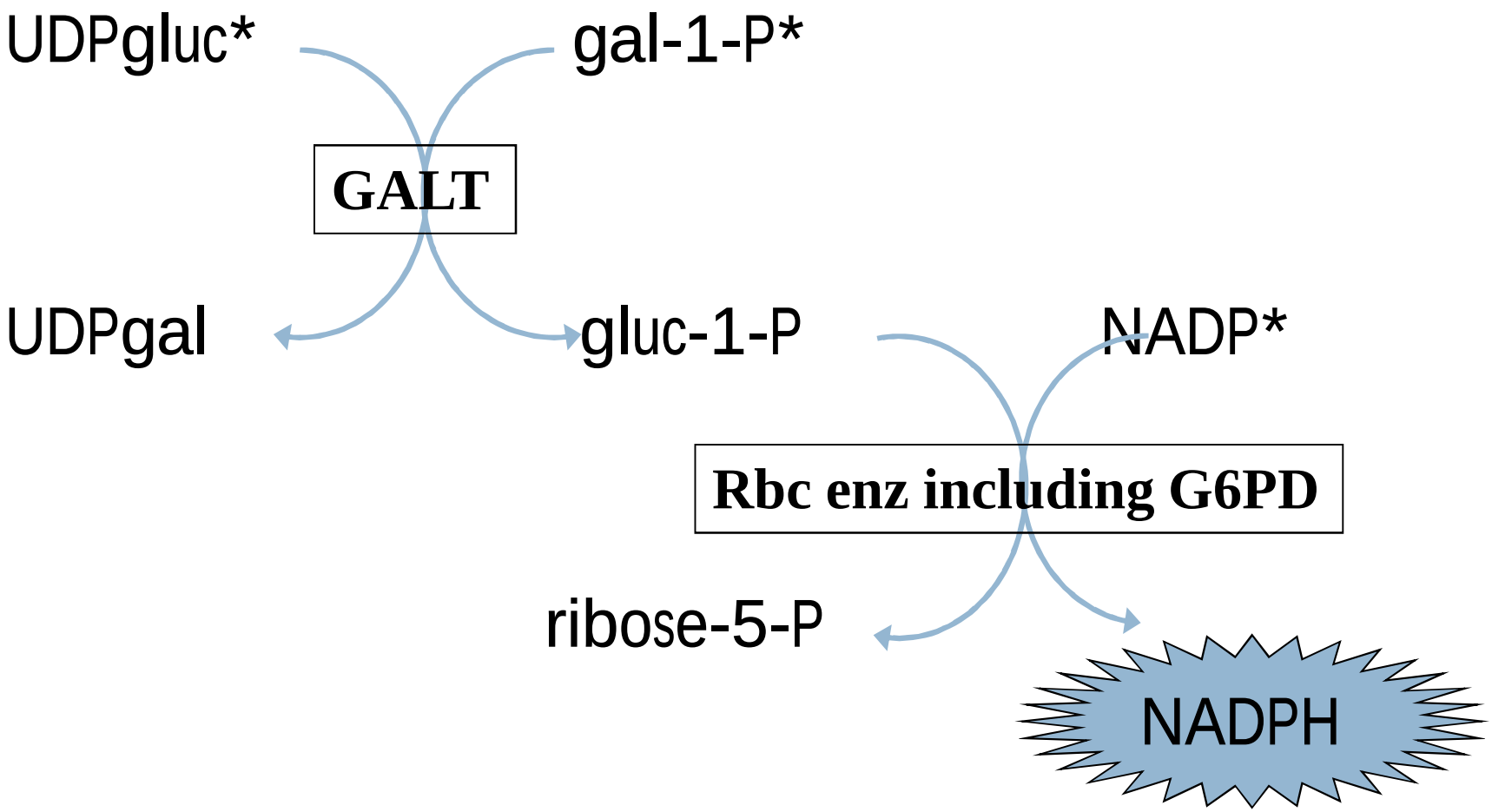
UDPgluc* gal-1-P*

GALT

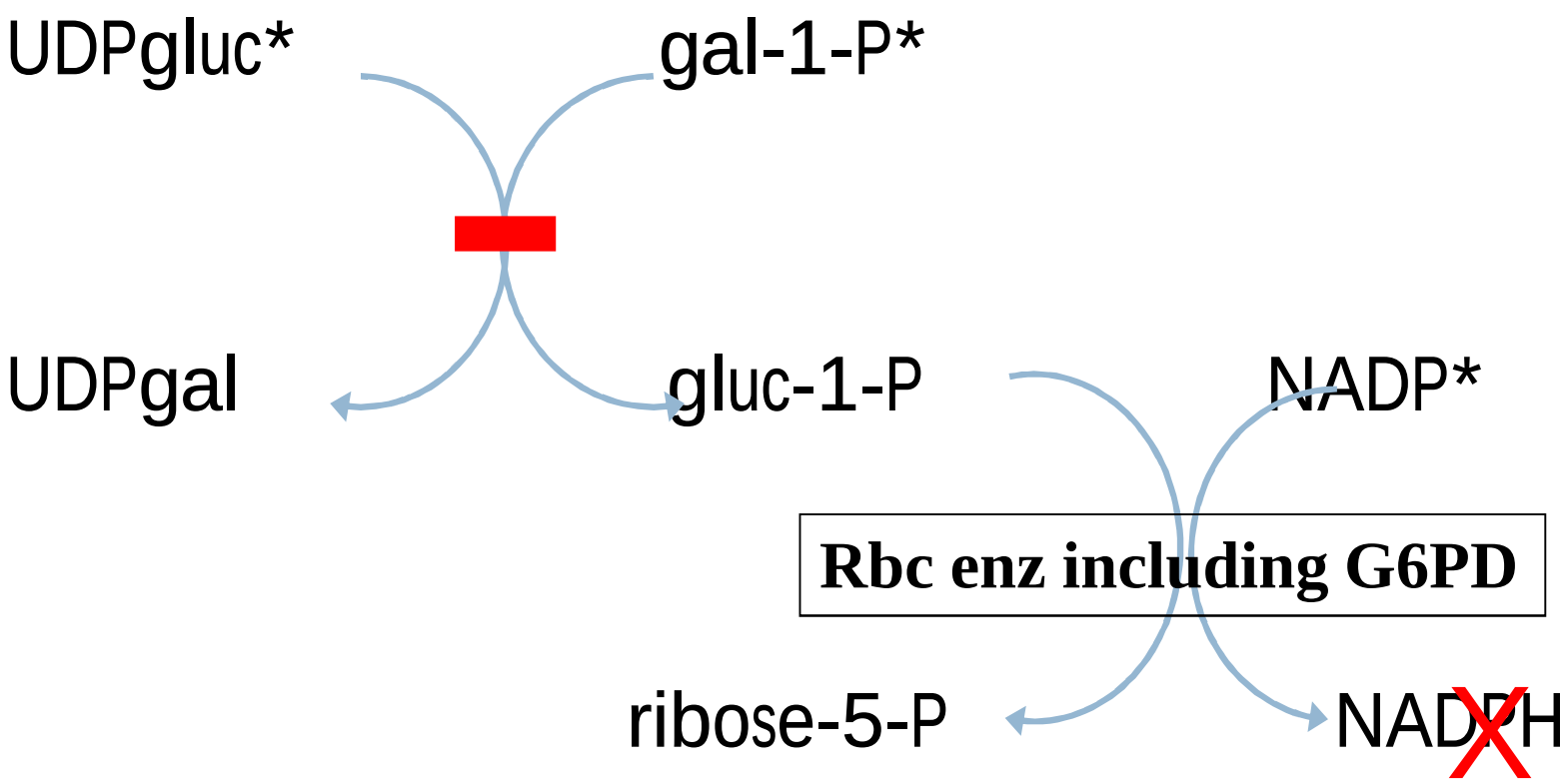
NADP*

Rbc enz including G6PD

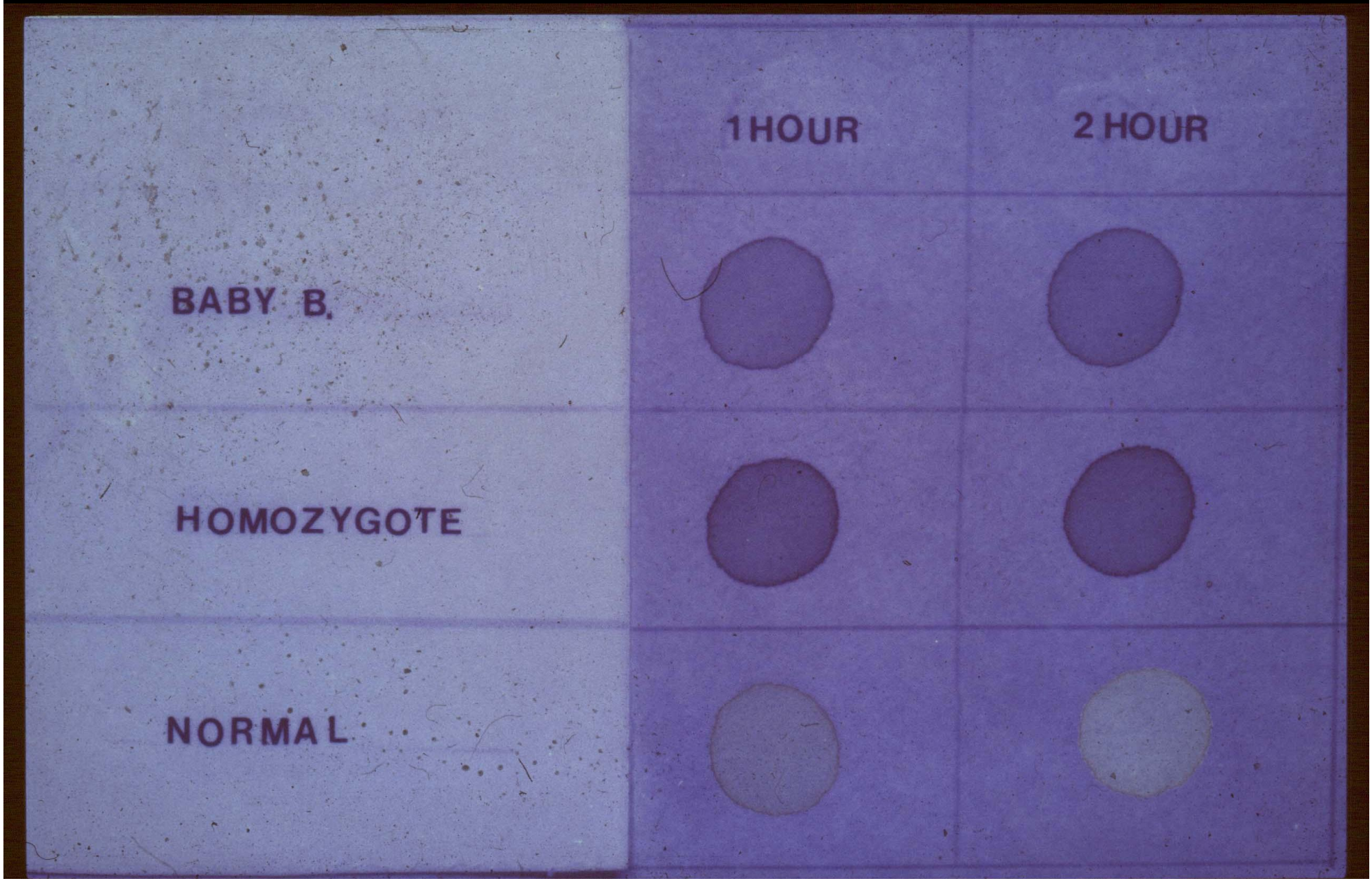
Beutler test



Beutler test in galactosaemia



Beutler test



Galactosaemia screen

- Beutler test
- pitfalls
  - false positive (false abnormal)
    - wrong anti-coagulant
    - old specimen
    - G6PD deficiency
  - false negative (false normal)
    - transfused blood
- pitfalls also apply to quantitative enzyme assay
- allelic variants eg Duarte

Erythrocyte galactose-1-phosphate

- not usually first line test for diagnosis
- remains high after blood transfusion

DNA analysis

- Q188R is common mutation
  - 70% of cases
- can be tested in transfused patients
- only diagnostic if homozygous

Urine galactitol

- may be helpful in transfused patients

Classical galactosaemia - antenatal diagnosis

- DNA in CVS or amniotic fluid cells
- enzyme activity in CVS cells or cultured amniotic fluid cells
- galactitol in amniotic fluid supernatant

Newborn screening for galactosaemia

- How?
  - Paigen microbiological method
    - galactose
    - galactose-1 phosphate
- Why?
  - to prevent mortality
  - to start treatment as early as possible
  - to improve outcome
- BUT
  - early presentation
  - variants detected

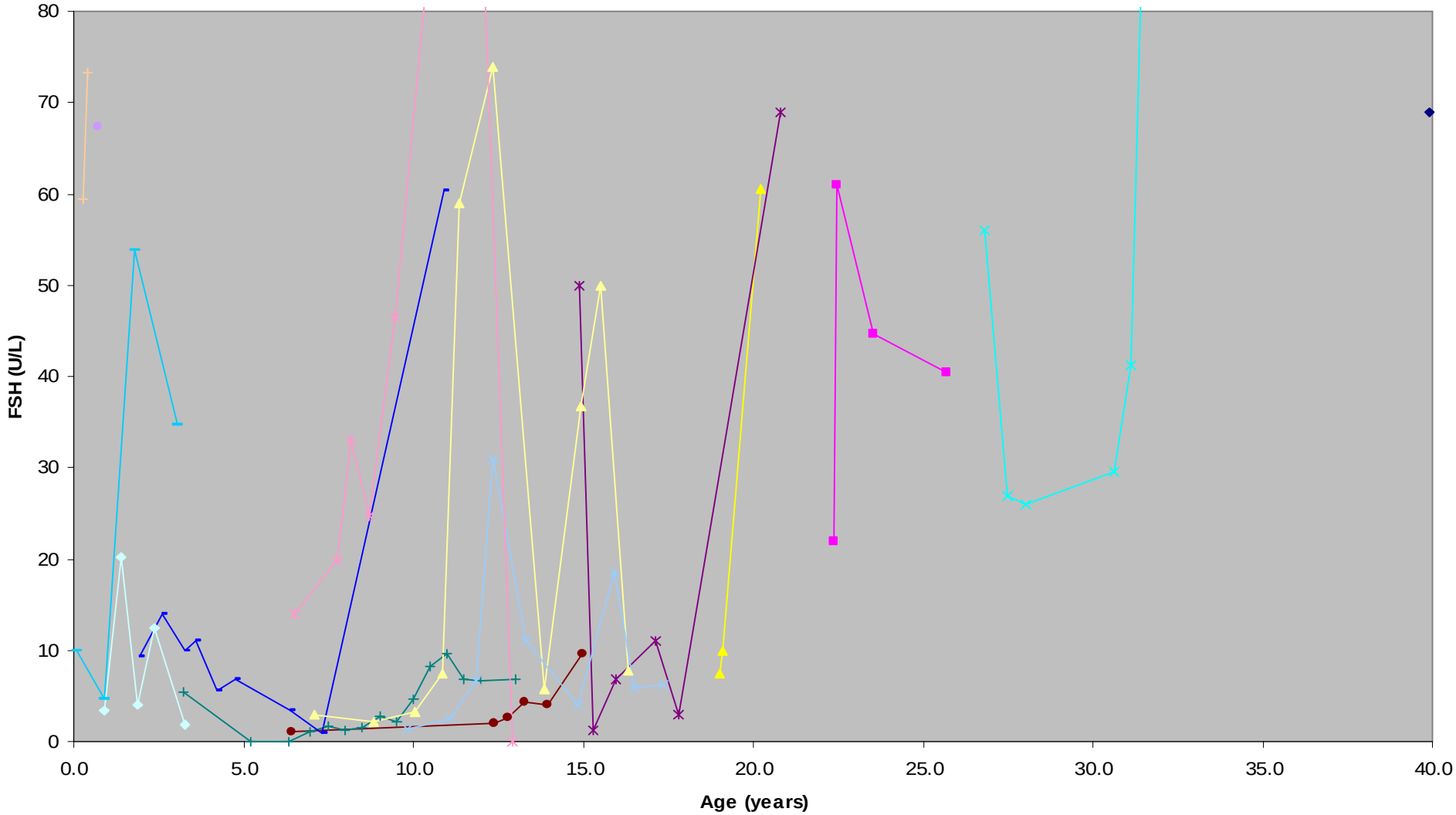
Classical galactosaemia - treatment

- restriction of galactose and lactose
- neonate
  - soya milk
- older child
  - avoid hidden sources
  - milk powder, milk solids, hydrolysed whey
  - drugs in tablet form, toothpaste, baking additives, fillers in sausages
  - some cheeses are allowed (Emmenthal, Gruyère, mature Cheddar)
- vegetables
  - galactolipids, polysaccharides, disaccharides, oligosaccharides
  - need (bacterial) α-galactosidase to be broken down

Classical galactosaemia - long term outcome

- poor intellectual function
  - falling IQ with age
- delayed speech development
- introverted personalities
- mild growth retardation
- ovarian dysfunction
  - loss of bone mineral content
  - HRT may be required

FSH in female galactosaemics



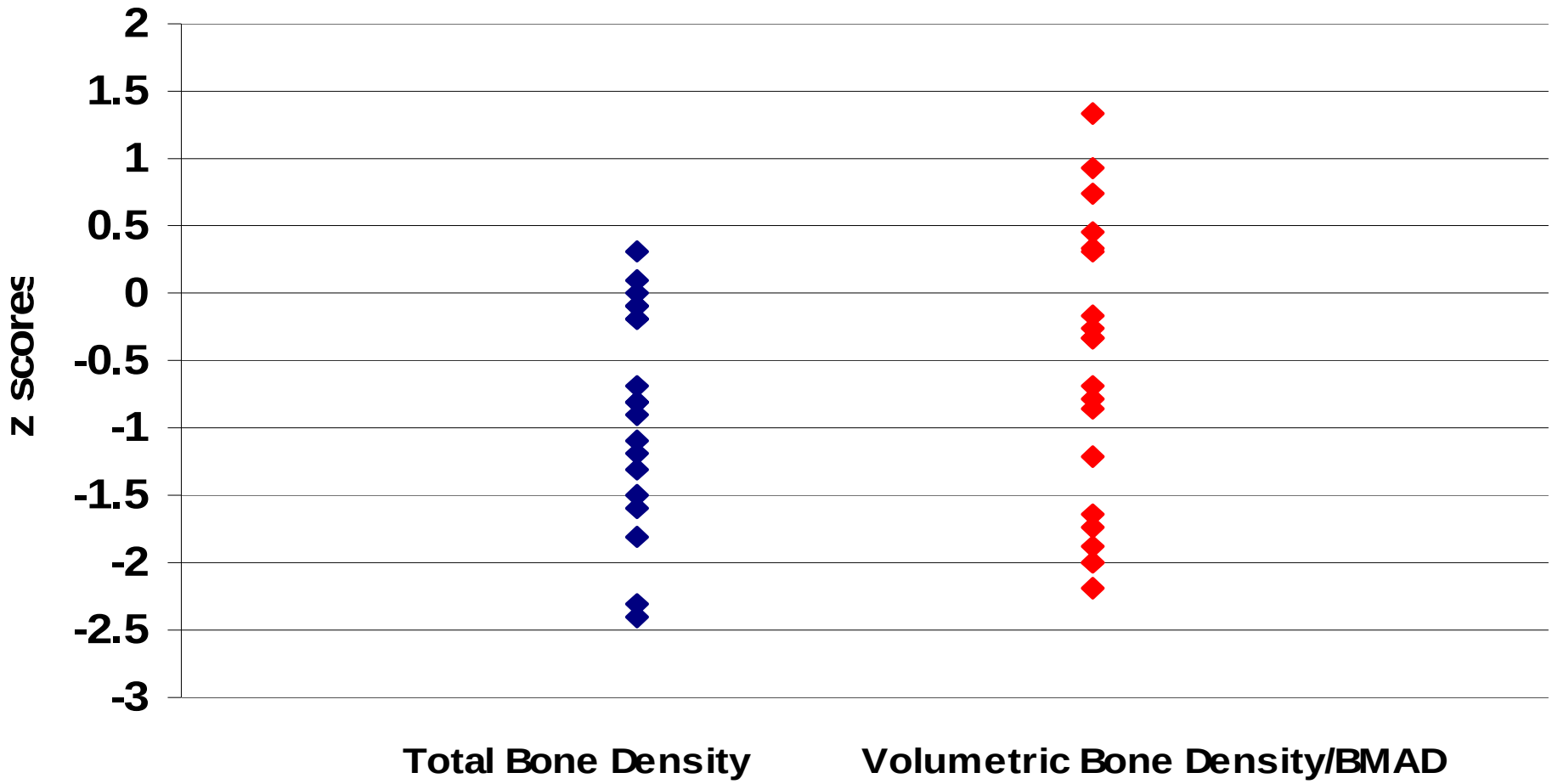
Bone density in galactosaemia

- calcium intake
  - diet inherently deficient in calcium
  - calcium supplements are unpalatable
- hormonal factors
  - females at risk of hypergonadotrophic hypogonadism
- role of galactosides
  - galactose residues normally form part of collagen matrix

Cross sectional study of bone density in galactosaemia

- 20 patients, age 5-22 years (11 M, 9 F)
  - 10 pre pubertal, 4 early puberty, 6 late/post pubertal
- Areal bone density is significantly reduced compared to normal
- Volumetric bone density in the majority falls within the normal range for age.
- Growth in galactosaemia may be compromised compared with the normal population.

Bone Density Results



Possible aetiology of problems

- in utero damage
- diet not restrictive enough
- endogenous “self-intoxification”
- deficiency of UDP galactose or complex galactose containing molecules

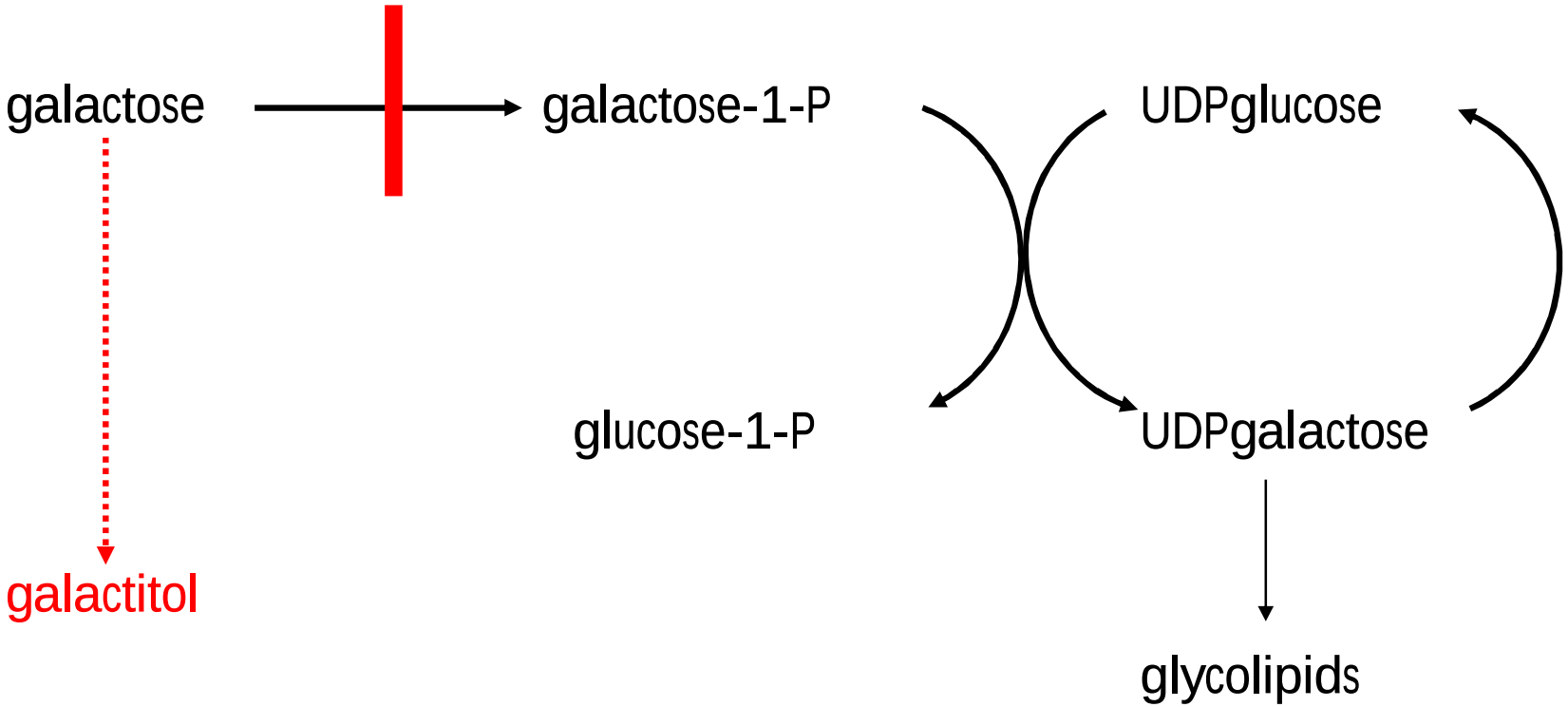
Classical galactosaemia – treatment issues

- how should we monitor?
  - galactose-1-phosphate
    - some endogenous production
    - toxic concentrations not defined
- is treatment required for life?
- how should we treat variant cases?

Classical galactosaemia - summary

- may still be under diagnosed
- REMEMBER
- urine sugars may be unhelpful
- if galactosaemia suspected always do galactosaemia screen on blood
- if baby has had a transfusion please phone to discuss investigation

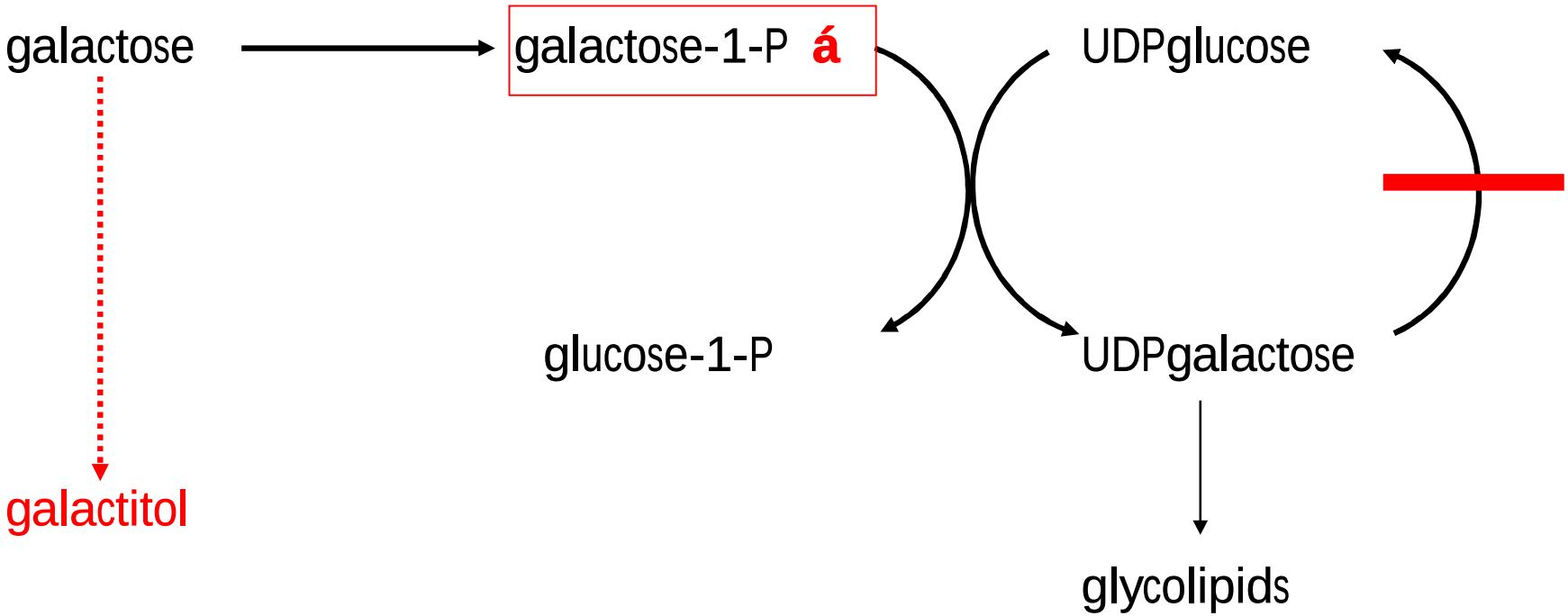
Galactokinase deficiency



Galactokinase deficiency

- bilateral nuclear cataracts in early infancy
- galactose and galactitol in urine
- enzyme defect in rbc or skin
- incidence approx 1 in 40000 (Switzerland)
- can use milk/galactose load for diagnosis

Epimerase deficiency



Epimerase

- severe form
  - present like classical galactosaemia
  - treatment difficult
    - patients are galactose dependant
- mild form
  - patients remain healthy
  - no treatment required

Fructose

- fructose - fruits, vegetables, honey
- sorbitol - fruits and vegetables
- sucrose (glucose-fructose)

- site of metabolism
  - 75% liver
  - 20% kidney
  - 10% intestine
- metabolic fate
  - phosphorylated by fructokinase
  - broken down by aldolase B to DHAP & glyceraldehyde-3-P

Inborn errors of fructose metabolism

- fructokinase deficiency (essential fructosuria)
- fructaldolase deficiency (hereditary fructose intolerance)
- fructose-1,6-bisphosphatase deficiency

Essential fructosuria

- fructokinase deficiency
- autosomal recessive
- benign and asymptomatic
- usually incidental finding (positive urine reducing substances)
- rare (approx 1 in 130000)
- liver, intestine, renal cortex

Hereditary fructose intolerance (HFI)

- aldolase B deficiency
- key enzyme in fructose metabolism
- three isoenzymes each with four identical subunits
  - A muscle
  - B liver, renal cortex, small intestine
  - C brain
- substrates
  - fructose-1-phosphate
  - fructose-1,6-bisphosphate
- aldolase B has highest V_{max} for fructose-1-P

Hereditary fructose intolerance (HFI)

- symptoms dependent on fructose intake
  - NB sucrose, sorbitol

- fructose ⟶ fructose-1-P
  - high activity of fructokinase
  - depletion of Pi and ATP

- hypoglycaemia
  - inhibition of glycogenolysis
  - inhibition of gluconeogenesis

Hereditary fructose intolerance (HFI)

- vomiting is a constant finding
- acute presentation
  - sweaty, trembling
  - nausea, vomiting
  - lethargy, coma
  - severe liver and kidney failure
  - death

Hereditary fructose intolerance (HFI)

- vomiting is a constant finding
- chronic presentation – undulating course
  - poor feeding, vomiting
  - failure to thrive
  - hepatomegaly
  - less commonly
    - drowsiness, crying, vomiting, haemorrhages, abdominal distension, irritability, diarrhoea
  - absence of dental caries

Hereditary fructose intolerance

- laboratory findings
  - abnormal liver function
  - post-prandial hypoglycaemia
  - hypophosphataemia
  - renal tubular dysfunction
- diagnosis
  - urine sugar chromatography
  - fructose load (measure glucose, PO_4, Mg, urate, HCO_3)
    DANGEROUS
  - DNA mutation analysis
  - aldolase B measurement (liver)
- treatment
  - fructose free diet
  - sub-optimal control may lead to growth retardation

HFI case 1

- 6 year old boy
- hepatomegaly discovered at routine school medical (10cm)
- PMH
  - FTND
  - thirsty, sweaty baby
  - 1 episode at 6m - difficult to arouse
  - consanguineous parents
  - diet normal but avoids fruit juices
  - stools pale and very bulky
- initial investigations
  - normal liver function tests, glucose, lactate, electrolytes
  - liver biopsy showed fatty liver and fibrosis
  - normal sweat test

HFI case 1

- Fructose load (50ml apple juice =3.5g)
  - symptomatic at 50 mins - pallor, sweatiness, decreased level of consciousness

Timemin	Gluc mM	Lact mM	PO_4 mM	Mg mM	uratemM	TCO_2mM
0	6.6	2.5	1.33	0.82	255	19.8
10	6.2	2.7	1.14	1.05	439	17.8
30	4.6	2.5	1.61	0.98	329	19.3
60	2.5	2.1	1.32	0.98	372	18.6
post	7.7	2.7	1.71	0.68	315	15.4

HFI case 1

- DNA - homozygous for the common mutation

- dietary treatment commenced
- ascorbate and folate supplements

HFI case 2

- 18 m boy
  - 8 months weaning problems
  - 9m vomiting, pallor, unconsciousness following 2 tsp fromage frais
  - diagnosis made by DNA
  - maintained on diet

- want to relax diet
- 300mg fructose load
- asymptomatic

HFI case 2 oral fructose load

Timemin	Glucmm	Lactmm	PO_4mm	Mgmm	uratemM	TCO_2mM
0	4.1	2.0	1.47	0.84	281	23.6
15	4.3	0.9	1.39	0.82	298	20.6
30	No sample					
45	4.0	2.0	1.31	0.89	333	21.3
60	3.9	1.6	1.29	0.86	340	22.4
90	4.0	1.0	1.57	0.98	333	21.4
120	3.9	1.0	1.66	0.96	324	21.6

Fructose-1,6-bisphosphatase deficiency

- symptoms not dependent on but are exacerbated by fructose ingestion
- neonatal
  - hypoglycaemia
  - metabolic acidosis and hyperventilation
  - hepatomegaly
  - hypotonia
- infancy
  - crises precipitated by fasting or infection
  - hepatomegaly
  - weakness
  - hyperventilation
  - trembling
  - lethargy

Fructose-1,6-bisphosphatase deficiency

- laboratory abnormalities due to impaired gluconeogenesis
  - hypoglycaemia
  - lactic acidaemia
  - increased pyruvate
  - increased alanine
  - increased uric acid
  - increased free fatty acids
  - glycerol and glycerol-3-P in urine
- hepatic and renal tubular dysfunction rare

Fructose-1,6-bisphosphatase deficiency

- SSIEM, 2010 Santos et al, UK cases
- 25 patients – age at presentation

Number of patients	Age at presentation
9	1- 5 days
12	5 days – 30 months
1	9 years
1	pre-symptomatic diagnosis

- all had lactic acidaemia and all but one had hypoglycaemia
- treatment
  - ER +/- uncooked cornstarch
- 2 died during acute episode

Pentose phosphate pathway

- provides ribose-5-phosphate for RNA synthesis
- reduction of NADP to NADPH

Defects of pentose phosphate pathway

- glucose-6-phosphate dehydrogenase deficiency
  - decreased NADPH production in rbc
  - rbc vulnerable to oxidative stress
    - certain drugs must be avoided
  - X-linked disorder
  - may give false positive in Beutler test

Defects of pentose phosphate pathway

- Transaldolase deficiency (TALDO)
  - progressive liver failure and cirrhosis
  - polyols
    - erythritol, arabitol, ribitol

- Ribose-5-phosphate isomerase deficiency
  - one patient, neurological phenotype
  - polyols
    - arabitol, ribitol

Glucose transporters

- enable transport of hydrophobic monosaccharides across lipophilic cell membrane
- sodium dependent glucose transporters (SGLTs)
  - active transport linked to sodium
- facilitative glucose transporters (GLUTs)
  - transport along exisiting gradients

SGLT defects

- congenital glucose/galactose malabsorption
  - SGLT1 apical membrane of enterocytes
  - neonatal presentation
    - bloating, profuse watery osmotic diarrhoea
    - severe hypertonic dehydration
    - repeated failure to reestablish oral feeds after PN
    - treat with fructose (absorbed by GLUT5)
- renal glycosuria
  - SGLT2 transports glucose but not galactose
  - glycosuria, normoglycaemia, normal renal tubular function

GLUT1

- early onset epileptic encephalopathy
- present during 1st year of life
- developmental delay, complex movement disorder
- DNA shows most cases are heterozygous *de novo* mutations
- treatment
  - ketogenic diet in childhood
  - avoid GLUT1 inhibitors
    - some AEDs, alcohol, methylxanthines (caffeine, theophylline)

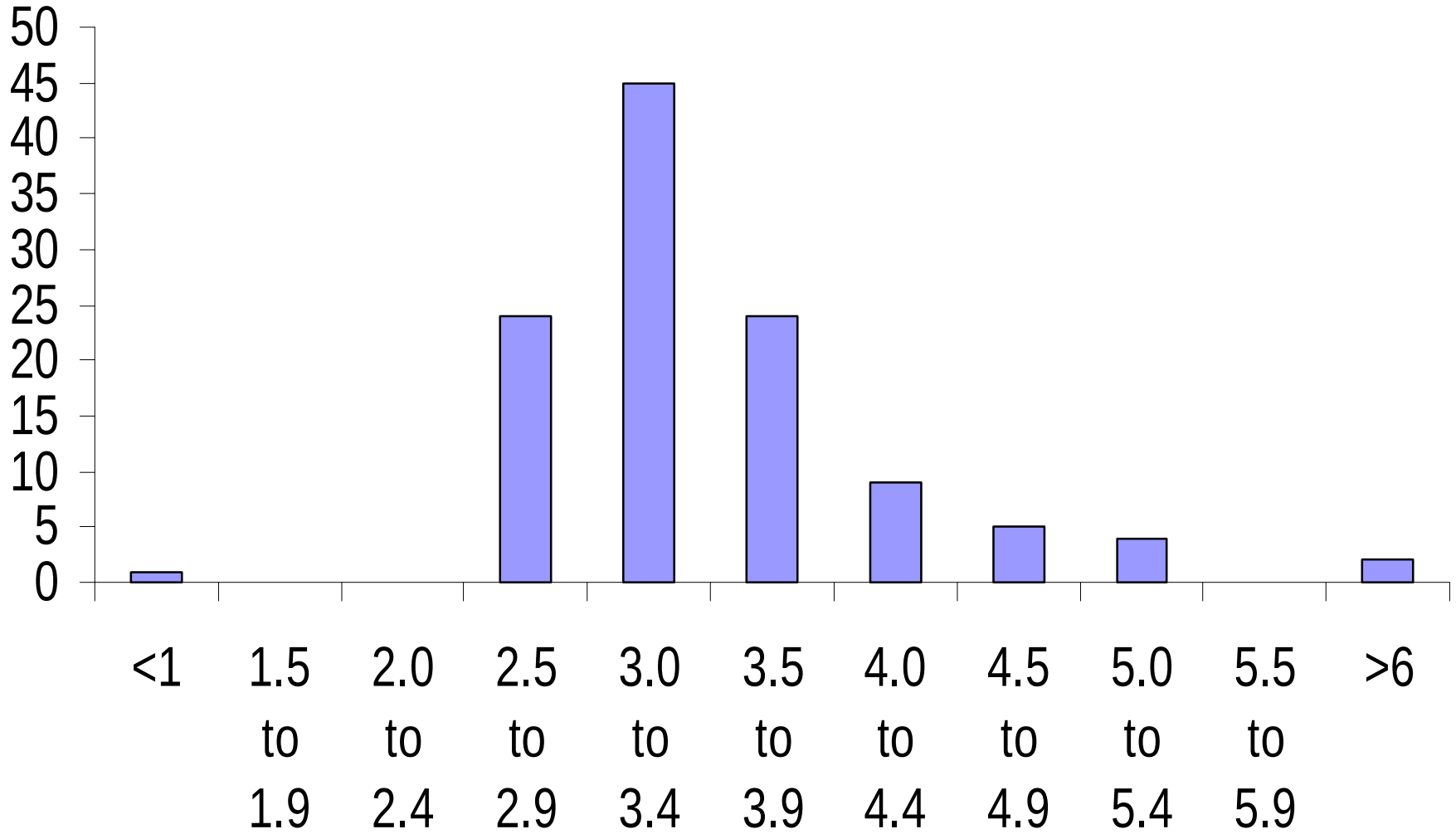
Diagnosis of GLUT1 deficiency

- low csf glucose in the presence of normoglycaemia
  - normal csf lactate
- results in 20 patients with GLUT1 deficiency (observed range)
  - blood glucose 3.4-9.4 mmol/l
  - csf glucose 0.9-2.7 mmol/l
  - csf/blood glucose ratio 0.19-0.46
  - csf lactate 0.3-1.5 mmol/l

Klepper & Voit, Eur J Pediatr 161:295-304

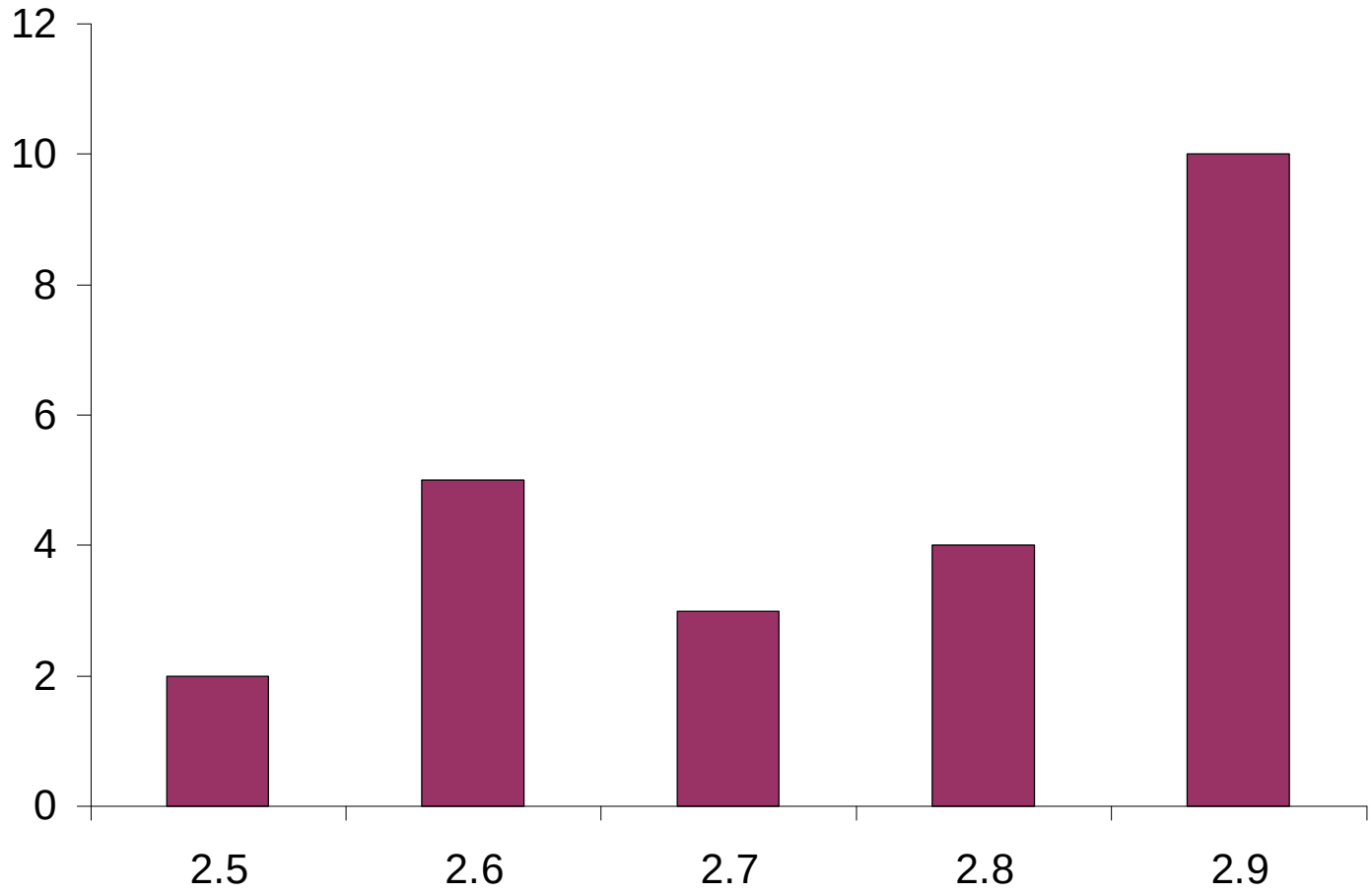
csf glucose concentrations (mM)

(GLUT1 <2.7)

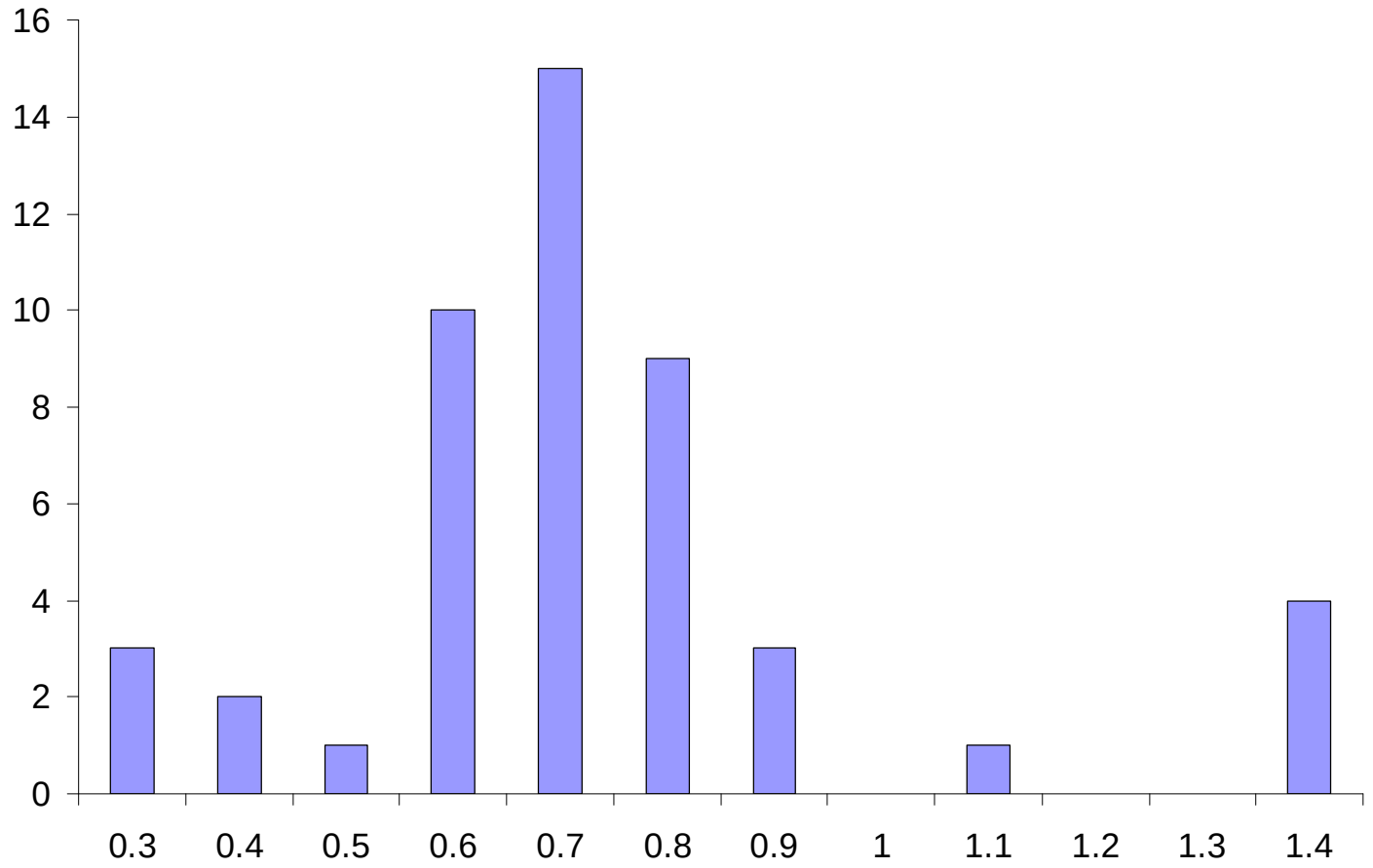


csf glucose concentrations (mM)

(GLUT1 <2.7)



csf/plasma glucose ratio
(GLUT1 <0.4)



Guidelines for csf sampling

- patient preparation
  - fast overnight
- take blood first (BEFORE LP)
  - glucose, lactate - fluoride oxalate
  - amino acids – lithium heparin
- take csf
  - glucose, lactate - fluoride oxalate
  - amino acids – plain bottle

Fanconi-Bickel syndrome (GLUT2)

- infancy (2-10m)
  - hepatomegaly
  - Fanconi-like nephropathy
  - severe glycosuria
  - fasting hypoglycaemia
  - postprandial hyperglycaemia and galactosaemia and galactosuria
- later
  - protuberant abdomen
  - moon shaped face
  - short stature
  - enlarged kidneys
  - hypophataemic rickets

Fanconi-Bickel syndrome (GLUT2)

- GLUT2
  - high K_m monosaccharide transporter (gluc/gal)
    - hepatocytes
    - proximal renal tubule
    - enterocytes
    - pancreatic β-cells
  - pathogenesis
    - impaired hepatic uptake of gluc/gal
    - impaired insulin response to hypoglycaemia
    - gluc not released from liver when hypoglycaemic
    - impaired transport in renal cells
    - glycogen storage

FBS case

- Routine biochemical abnormalities
  - slightly increased transaminases
  - increased
    - lactate
    - urate
    - lipids
  - calculated glucose reabsorption ‘zero’
- Treatment
  - symptomatic
  - UCCS
  - electrolyte replacement
- Long term outcome
  - major problem is growth

FBS case

- 12 month old boy
  - 6m – cow's milk intolerance – changed to Soy milk
  - increasing abdominal distension
  - faltering growth
    - 25^{th} to 0.4^{th} centile since 5m
- DGH
  - advanced rickets
  - renal Fanconi syndrome
    - glycosuria, phosphaturia, proteinuria, renal tubular acidosis
    - fasting hypoglycaemia
- Diagnosis confirmed by mutation analysis

FBS case

- Post-prandial hyperglycaemia
- Fasting hypoglycaemia
- Blood collected following lunch and 10g UCCS

Hours post lunch	Glucose mM	Lactate mM
1	10.0	2.9
2 ¼	3.1	1.4
2 ½	2.9	1.1
3	2.3	1.0

REAL LIFE DIAGNOSTIC ISSUES

Case examples

Urine reducing substances

- false negatives

- false positives

Urine reducing substances

- false negatives
  - lack of dietary intake
  - dilute urine?

Urine reducing substances

- false positives
  - reducing substances
    - alkaptonuria
  - galactose
    - liver dysfunction
      - tyrosinaemia type 1
    - citrin deficiency
    - Fanconi-Bickel
  - fructose
    - liver dysfunction

Sugar chromatography (BCH)

- Run 2 plates

Plate 1 PABA stain	Plate 2 Naphthoresorcinol stain
Ribose marker	Fructose
Glucose	Sucrose
Galactose	Lactulose
Lactose	Raffinose

Case 1

- female
- FTND 3.2 kg
- no consanguinity
- sister 4 years - well
- 2 days
  - discharged from hospital
  - mild jaundice

Case 1

- days 3-5
  - increasing jaundice noted by midwife
  - bilirubin 452 µmol/l
- day 6
  - readmitted, weight 2.92 kg
  - O/E
    - well
    - no hepatosplenomegaly
  - commenced phototherapy

Case 1

- bilirubin 400 µmol/l
- Coombs test negative
- PT 94/13
- PTT 100/37
- treated with vitamin K
- urine
  - Clinitest 2%
  - Clinistix neg
- galactosaemia screen ABNORMAL
- commenced dietary treatment

Case 1

- 8 days
  - unwell
  - abdominal distension
  - bleeding
    - PT 120/13
    - PTT 250/39
- treated with IVI, FFP, antibiotics
- home at 17 days

Case 2

- FTND 4.24 kg

- day 3 bilirubin 295 µmol/l
  - phototherapy commenced
  - poor feeding
  - sleepy
  - ??ABO incompatability
  - Coombs and infection screen negative
  - parents unrelated
  - 5y old brother alive and well

Case 2

- day 5 bilirubin 287 µmol/l
  - poor intake of food, vomiting
- day 6 bilirubin 262 µmol/l
  - Vomiting, Dioralyte commenced
  - urine – reducing substances positive (sucrose and glucose)
- day 7 bilirubin 369 µmol/l
  - vomiting when feeds restarted
- day 8 bilirubin 371 µmol/l
  - urine result received
  - feeds restarted
  - hepatosplenomegaly noted
  - vomited
  - Bmstix 1, Dioralyte recommenced

Case 2

- Day 9
  - Ba swallow - no gastric emptying
  - ??pyloric stenosis
    - test feed
      - no vomiting
      - no palpable tumour
  - sleepy, floppy, very slow at feeding
  - large firm liver
  - nil by mouth
    - BMstix 0 SYMPTOMATIC
    - responded well to iv dextrose
  - no acidosis

Case 2

- liver function tests
  - total bilirubin 286 µmol/l
  - conj bilirubin 99 µmol/l
  - alk phos 1711 IU/L
  - Ast 212 IU/L
  - Alt 70 IU/L
  - albumin 31 g/l
  - prolonged PT and PTT

Case 2

- Day 12
  - galactosaemia screen abnormal
  - confirmed by quantitative enzyme measurement
  - commenced dietary treatment

Case 3

- A typical request form?
- Clinical details
- ‘Metabolic screen. Rule out
  - Urea cycle defects
  - Mild organic acid disorder
  - Glycogen storage disease’

Case 3

- urine screening tests
  - Clinitest 1 trace, 2 neg
  - Albustix 2 pos, 1 unsat
- amino acids
  - generally increased pattern, prominent thr in 2 specimens
- organic acids
  - 1 NAD, 2 slightly increased 4-OH-phenyllactate
- GAGS and oligos (2 specs)
  - 2 faint oligo bands in one spec
  - increased DMB in one spec
- VLCFA, acyl carnitines normal
- Transferrin electrophoresis abnormal
- amino acids suggestive of liver dysfunction

Case 3

- Follow-up of transferrin electrophoresis
  - Neuraminidase digestion
  - Repeat specimen
    - Confirmed abnormality
  - Galactosaemia screen – ABNORMAL
  - Hereditary fructose intolerance
    - Not tested for

Case 3

- FTND
- 2w – viral illness
  - abnormal LFTs, palpable liver, resolved over next 2 months
- 4m – projectile vomiting
- 5m – infected eczema
  - LFTs again abnormal, slightly increased TSH, normal fT4
  - developmental delay, failure to thrive, poor feeding
- 7m – cataracts, macrocephaly

Case 3

- galactosaemia screen
  - ABNORMAL
- urine reducing substances
  - negative
- urine sugar chromatography
  - trace amounts of galactose
  - on lactose containing feeds from birth
  - approx 50% more lactose than normal infant

Case 3

- G6PD
  - normal
- galactose-1-phosphate uridyl transferase
  - undetectable
- mutation analysis
  - Q188R hetero
- galactose-1-phosphate
  - grossly increased

Case 4

- born at 29/40 because of placental problems
- well at birth
- 1 week
  - coagulation problems
  - renal failure
  - intraventricular haemorrhage
  - breast fed for 72 hours then on 10% dextrose

Case 4

- neonatal screening results
  - increased phenylalanine, increased tyrosine
  - galactosaemia screen
    - ABNORMAL
  - tyrosinaemi screen
    - EQUIVOCAL
- had had 6 transfusions

Case 4

- no urine obtainable
- DNA analysis
  - Q188R heterozygote
- erythrocyte galactose-1-phosphate
  - grossly increased
- baby died at 23 days
- diagnosis confirmed in fibroblasts

Case 5

- FTND 39/40
- 5 days
  - not feeding well
- 6 days
  - jaundiced
  - handling poorly
  - abdominal distension
    - midwife visit
      - immediately to hospital

Case 5

- bilirubin 317 µmol/L (conj 72 µmol/L)
- INR >10
- lactate 17.2 mmol/L
- ammonia 266 µmol/L

- advanced sepsis with DIC
- high inotrope requirement
- anuric
- peritoneal dialysis
- ventilated
- died at 7 days of age

Case 5

- urine
  - amino acids grossly increased
    - renal tubular dysfunction/acute collapse
  - organic acids
    - severe liver dysfunction
  - sugar chromatography
    - galactose
- blood
  - acyl carnitines normal
  - amino acids
    - grossly abnormal (severe liver dysfunction and acute collapse)
  - galactosaemia screen normal
  - tyrosinaemia screen equivocal

Case 5

- post-mortem – cause of death
  - E. coli sepsis
  - peritonitis
- review of results
  - blood transfusion prior to blood specimen

Case 5

- review of results with consultant
  - blood transfusion prior to blood specimen
  - no blood taken for DNA
  - skin biopsy banked
- parents tested for Q188R
  - both heterozygous
- DNA extracted from fibroblasts
  - Q188R homozygote

Case 6

- born at 31/40
- urine for ‘metabolic screen’
  - amino acids - normal
  - organic acids - liver dysfunction
  - positive Clinitest, trace Clinistix
- baby transferred to hospital 2
  - had had multiple transfusions for low Hb
- arranged
  - urgent sugar chromatography
  - blood for galactose-1-phosphate

Case 6

- urine sugar chromatography
  - galactose >10 mmol/l
- erythrocyte galactose-1-phosphate
  - increased
- baby transferred to hospital 3
- DNA
  - Q188R homozygote
- baby transferred to hospital 4 for treatment

Case 7

- 3w old boy
  - prolonged jaundice bilirubin 295 µmol/l
- galactosaemia screen abnormal
- further information
  - feeding well
  - gaining weight
  - normal liver enzymes
  - no reducing substances in urine

Case 7

- repeat blood obtained
  - galactosaemia screen abnormal
  - galactose-1-phosphate undetectable
  - glucose-6-phosphate dehydrogenase undetectable

  - Filipino mum

Case 8

- baby of galactosaemic father tested at birth
  - multi-consanguineous family
  - GALT mutation + Duarte 2 mutation
  - galactosaemia screen abnormal/equivocal
  - galactose-1-phosphate grossly increased
  - commenced on diet

- over the next few months
  - galactose-1-phosphate undetectable – twice
  - DNA showed heterozygous for family mutation & Duarte 2

Case 8

- 1 year
  - galactose-1-phosphate increased
  - more DNA results
  - compound heterozygote for 2 GALT mutations
  - also has Duarte 1 and Duarte 2
  - GAL1PUT activity 2.0 µmol/h/g Hb
  - VARIANT form of galactosaemia
- maintained on diet
  - when should diet be stopped?