Symptoms and signs of chronic kidney disease (CKD)

Block 11

Prof G van Biljon

Definition of CKD in children

Chronic kidney disease (CKD) is defined as :

"evidence of structural or functional kidney abnormalities (abnormal urinalysis, imaging studies or histology) that persist for at least 3 months, with or without a decreased glomerular filtration rate (GFR), as defined by a GFR of less than 60 mL/min per 1.73 m^2" (1)

1. KDOQI clinical practice guidelines for chronic kidney disease: evaluation, classification and stratification. Kidney Disease Outcome Quality Initiative. Am J Kidney Dis 2002;39: S1-S246

National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (NKF-K/DOQI) stages of chronic kidney disease

Stage	Description	GFR(mL/min/1.73m^2)
1	Kidney damage with normal/increased GFR	>90
2	Kidney damage with mild decrease in GFR	60–89
3	Moderate decrease in GFR	30–59
4	Severe decrease in GFR	15–29
5	Kidney failure	<15 or dialysis

Pediatr Nephrol. 2007 December; 22(12): 1999–2009

Epidemiology and prevalence of CKD

- CKD is a common disorder of varying severity
- Merits attention of general practitioners and also needs public health approach for
  - Prevention
  - Recognition / early detection
  - Management
- CKD should not only be recognised as “life threatening disorder “ affecting a few children who need the care a nephrologist

Epidemiology of CKD

- There is limited information on the epidemiology of CKD in the paediatric population
- Most epidemiological information on CKD originates from data available on end-stage renal disease = when treatment with renal replacement therapy becomes necessary

Studies on the epidemiology of CKD stages 2–5 in Europe

Country [reference]	Italy [5]	Belgium [13]	Spain [39]	Sweden [8]	France [7]	Turkey [14]
Period	1990–2000	2001–2005	2007–2008	1986–1994	1975–1990	2005
Number of cases	1,197	143	605	118	127	282
Inclusion criteria	0–19 years GFR<75	0–19 years CKD 3-5	0–17 years CKD 2–5	0.5–15 years GFR<30 or SCr>120 (< 3 years), > 150 (3–9 years), > 180 (> 10 years)	0–15 years SCr>133 (< 2 years) or 175 (> 2 years)	0–18 years GFR<75
Pediatric population covered (millions)	16.8	2.4	11.3	1.7	0.5 (Lorraine)	24.0
Incidence (pmarp)	12.1	11.9	8.7	7.7	10.5	11.9
Prevalence (pmarp)	74.7	56	71.1	59	66	
Male/female ratio	2.0	1.3	1.9	1.6	1.4	1.3
Age at diagnosis (years)	6.9 (mean)	3.0 (median)	3.9 (mean)	3.3 and 11.3 in congenital and acquired disorders (median)	6.3 and 10.6 in congenital and acquired disorders (median)	8.0 (mean)
GFR or CKD stages at diagnosis	GFR 42 (mean)	CKD 3: 67% CKD 4: 19% CKD 5: 14%	GFR 52 (mean) CKD 2–3: 82% CKD 4–5: 18%	Pre-RRT: 57%	Pre-RRT: 76%	CKD 2–3: 38% CKD 4: 30% CKD 5: 32%

Pediatr Nephrol. 2012 March; 27(3): 363–373.

Prevalence according to age

The North American Pediatric Renal Transplant Cooperative Study (NAPRTCS) [3] chronic renal insufficiency (CRI) database: 5651 patients aged 2-17 years with an estimated GFR < 75 mL/min per 1.73 m^2

0-1 years	19%
2-5 years	33%
6-12 years	17%
>12 years	31%

3. Fivush BA et al. Pediatr Nephro 1998; 12:328-337

Treatment prospects of CKD

- Associated with high morbidity, mortality and high medical expenditures
- Limited resources – few patients will qualify for renal replacement therapy
- Early detection and optimal management can
  - Prevent development of complications
  - Delay the need for dialysis / transplantation
  - Prevent premature death

Origins of adult kidney disease

- Prenatal factors may have an impact on organogenesis and determine CVS events, hypertension and the risk for CKD at adult age
- Adverse prenatal factors e.g. hypertension, smoking, maternal infection/diabetes $\rightarrow$ IUGR
- LBW is associated with $\uparrow$ risk of CKD and with $\uparrow$ rate of progression of established renal disease

1. Barker DJ. Mechanisms of disease: in utero programming in the pathogenesis of hypertension Nat Clin Pract Nephrol 2006; 2: 700-707.

2. Brenner BM et al. Glomeruli and blood pressure. Less of one, more the other? Am J Hypertension 1988; 1:335-347.

3. Dötsch. J et al. Fetal programming of renal function. Pediatr Nephrol 2012; 27: 513-520

Progression of CKD

- Initial insult $\rightarrow$ hyperfiltration of remaining glomeruli
- $\rightarrow$self-perpetuating vicious circle of fibrosis $\rightarrow$progressive renal scarring, involving all structures of kidney
- Proteinuria develops or worsens in all forms of CKD as renal function $\downarrow$

Detection of CKD

- Serum creatinine poor marker of renal function
- >60 % of kidney function may be lost while S- creat may remain in normal range
- S-creatinine correlates with muscle bulk, age, gender
  $\rightarrow$ falsely low in children with malnutrition
- Main manifestation : development of proteinuria and hypertension

Diagnosis of kidney disease in children

- Symptoms and signs associated with either acute or chronic renal conditions often appear to be unrelated to the kidney
- Advanced renal impairment often remains undetected because of the “functional reserve” of kidneys
- Children with advanced renal failure may have only mild ↑ S-urea and creatinine – thus diagnosis overlooked

Complaints “unrelated” to kidney

- Poor growth from infancy throughout childhood
- Gastrointestinal complaints – vomiting / constipation
- Swelling / pruritis - treated for allergy
- Pale - investigated for anaemia
- Bone disease – treated by physiotherapist /orthopod
- Cardiomegaly - referred to cardiologist
- Shortness of breath “pneumonia”
- “Convulsions /coma

Golden rules to diagnose kidney disease

To increase diagnostic yield of kidney disease (allowing diagnosis in > 90% of cases):

- Obtain a comprehensive medical and family history
- Do thorough physical examination, including growth standards and measure blood pressure
- Do urine dipstick test

- History
  - Antenatal and perinatal history
  - Current problem
  - Growth and development
  - Previous illnesses, investigations & hospitalisation
- Family history – with particular reference to
  - Conditions associated with inherited kidney diseases e.g. deafness
  - Congenital abnormalities of UGT
  - Hypertension
  - Relatives with chronic kidney or cardiovascular disease

Symptoms & signs of underlying kidney disease

- Poor growth
  - Stunting > wasting (Waterloo criteria)
  - Crossing growth standard lines
- Feeding problems: poor appetite, vomiting
- Polydipsia with specific preference for cold water/ice
- Constipation

Clinical examination

- Age taken into consideration
- General examination – in neonate look for
  - Dysmorphic features
  - Features of recognizable syndromes
  - Potter facies
    - Flat facial profile, beaked nose, small chin
    - Low set ears
    - Contractures / hip dislocation / club feet
- Respiratory distress
  - Pulmonary hypoplasia
  - Spontaneous pneumothorax

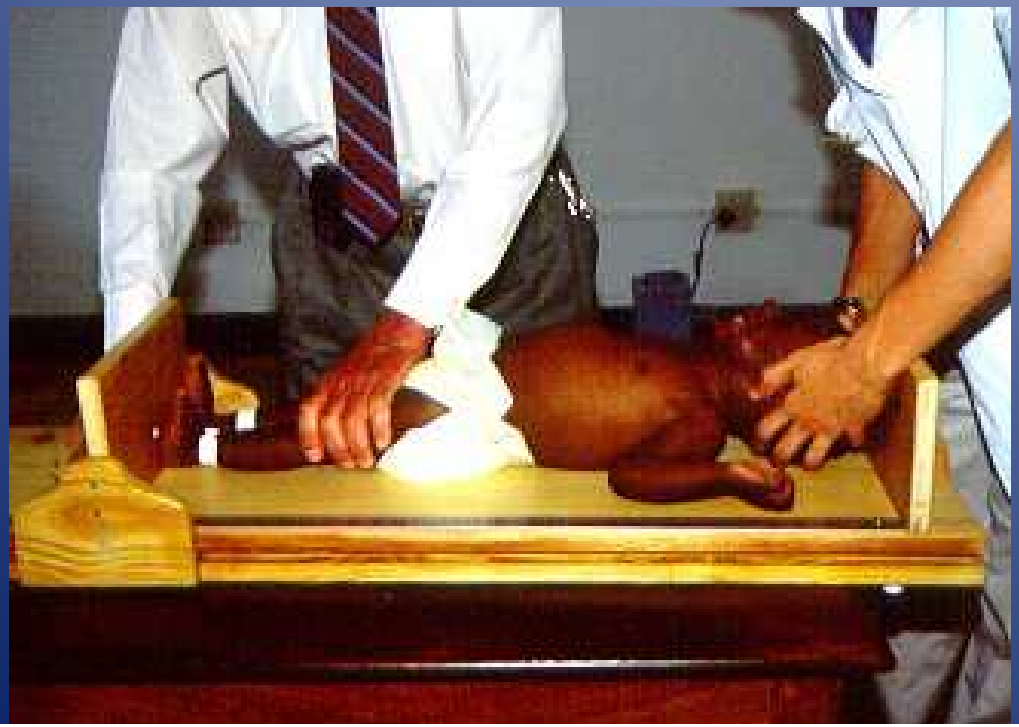
Clinical examination

- General examination – growth parameters
- JACCOL and DDD
- Vitals
- Systematic examination including
  - Skin, integument (nails and hair)
  - Musculoskeletal system
  - Abdomen, genitalia
  - All systems to be examined completely

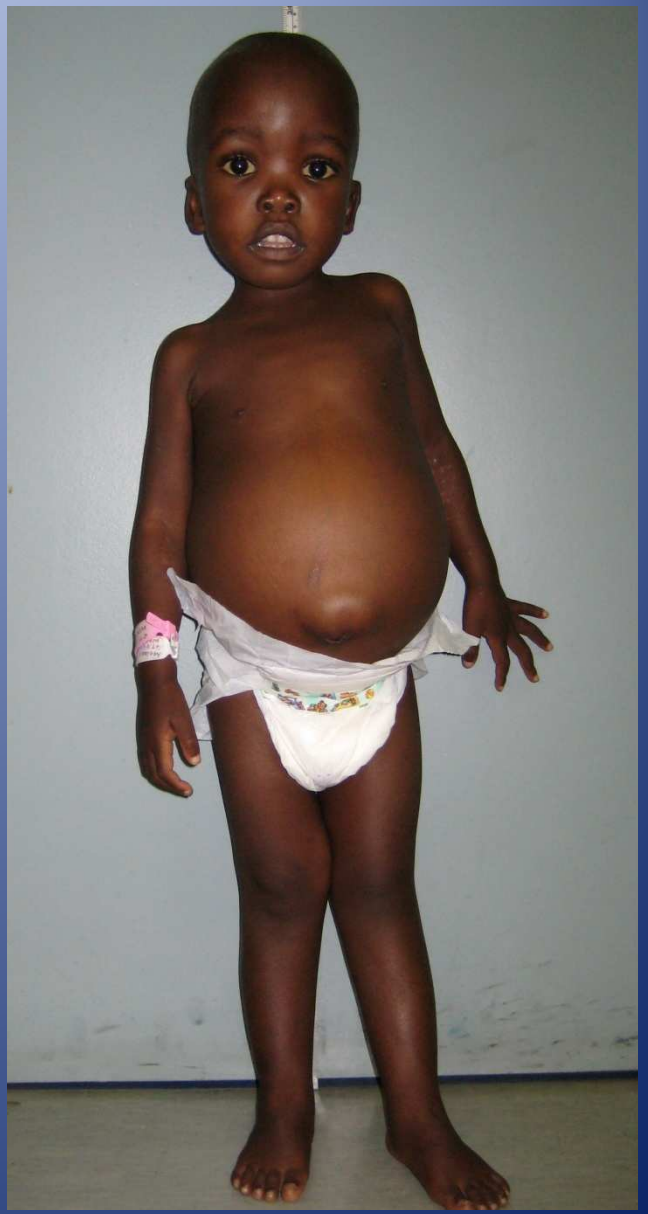
Measure height /length

Height is measured erect from the age of 3 years

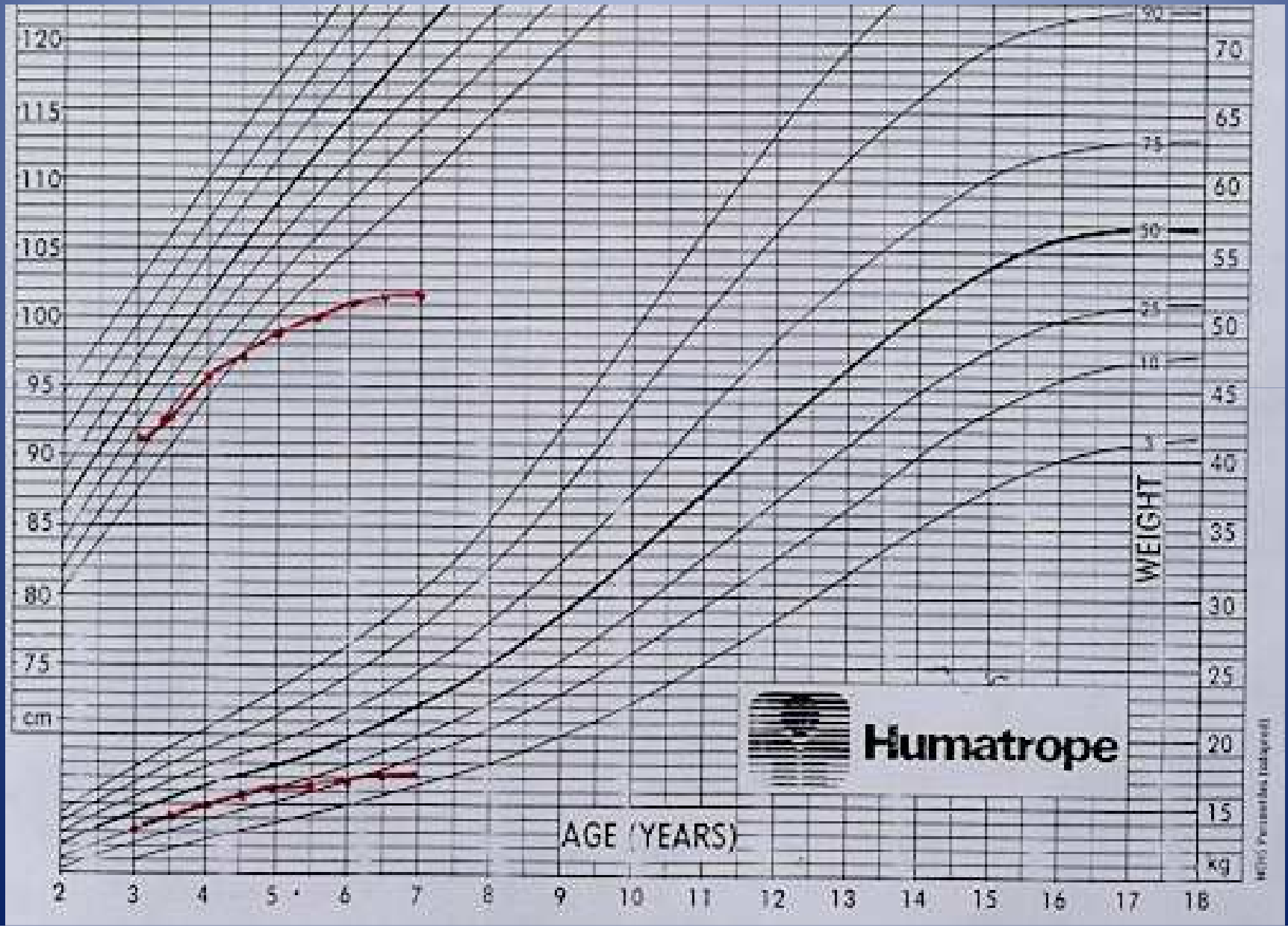
Length is measured supine from birth – 3 yrs



In older child with CKD stunting is > common than wasting



Growth chart depicting growth failure



General Examination

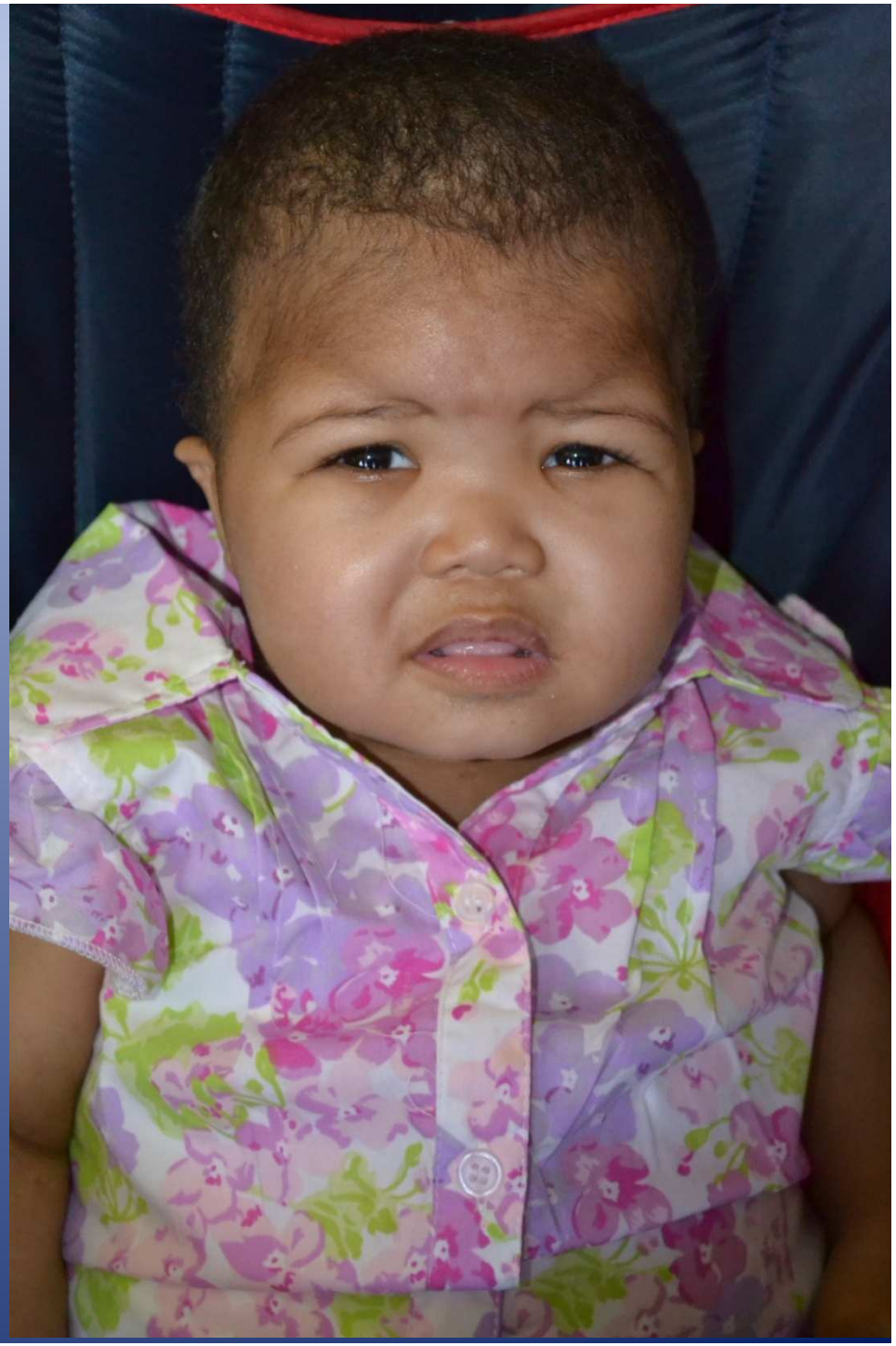
Look for:

- Dehydration in absence of excessive extrarenal fluid losses
- Circulation; peripheral pulses
- Fever (recurring without identified site of infection)
- Anaemia
- Nails: leuconychia / porcelain nails
- Oedema
- Jaundice (? haemolysis / ± liver disease)

Peri-orbital oedema

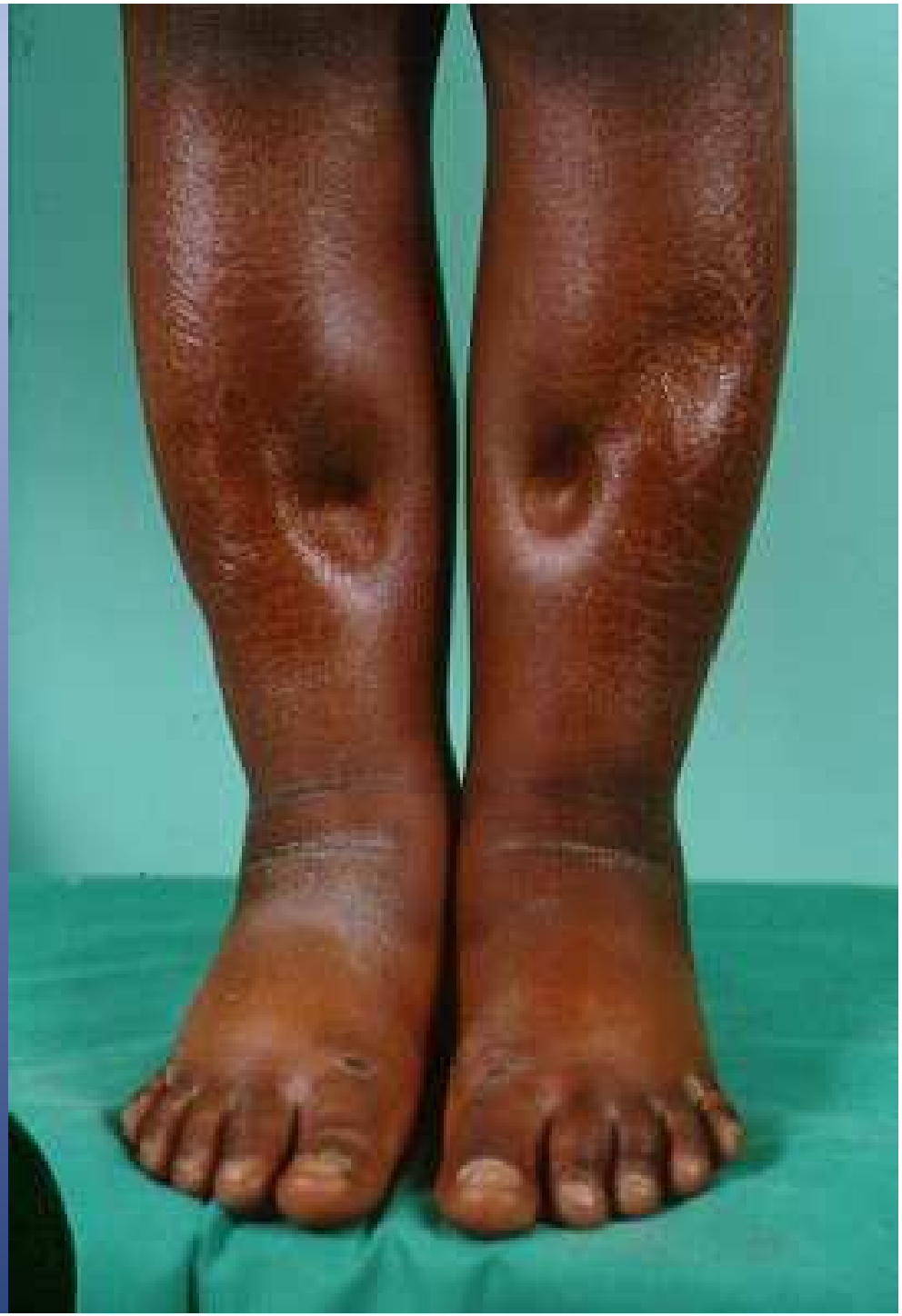
>In mornings after getting up

Often treated for “allergy”



Pitting peripheral oedema -

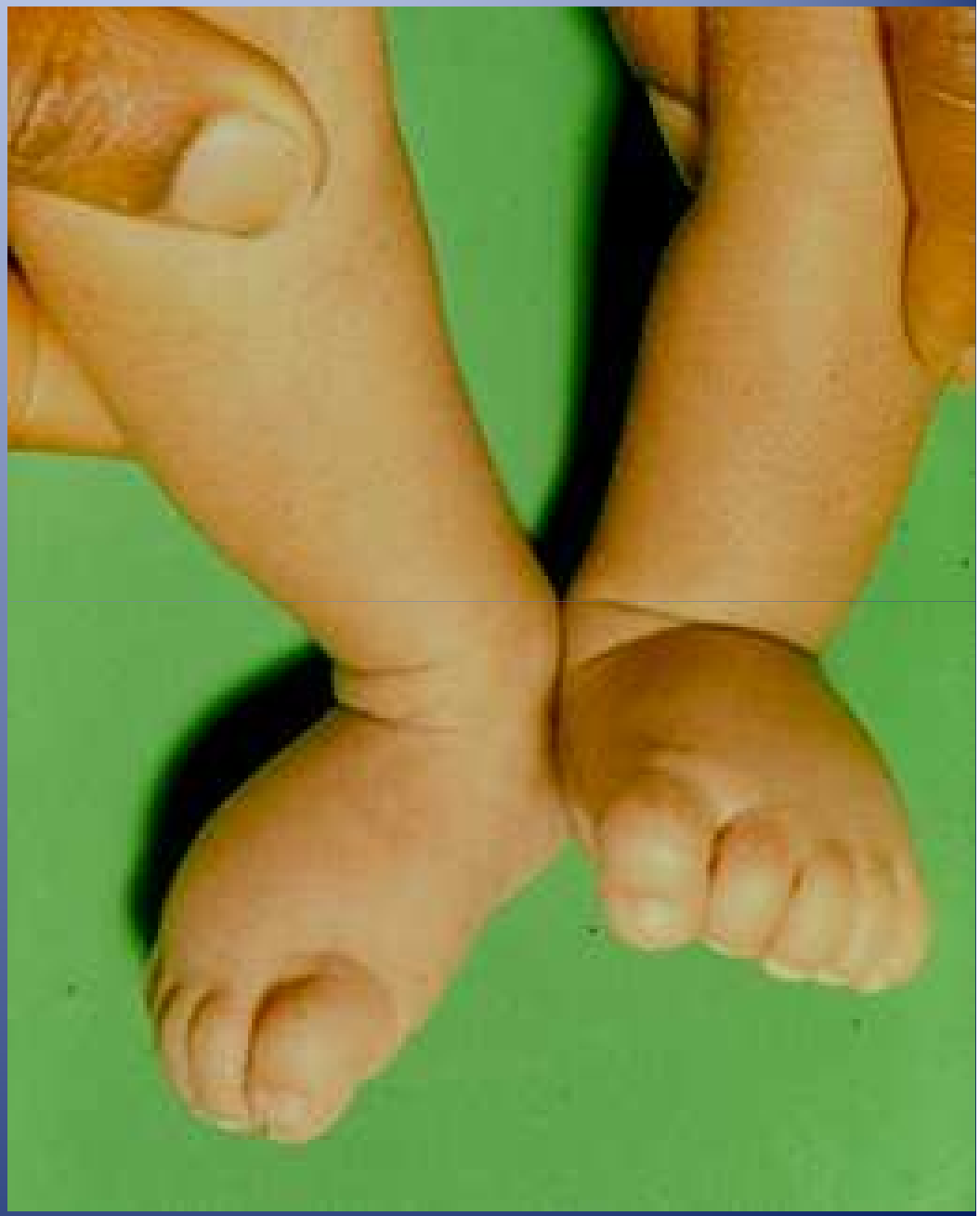
Underlying nephrotic syndrome



Oedema

Differentiate between generalised and localised oedema

Here: oedema is localised over dorsal aspects of the feet



Nephrotic syndrome

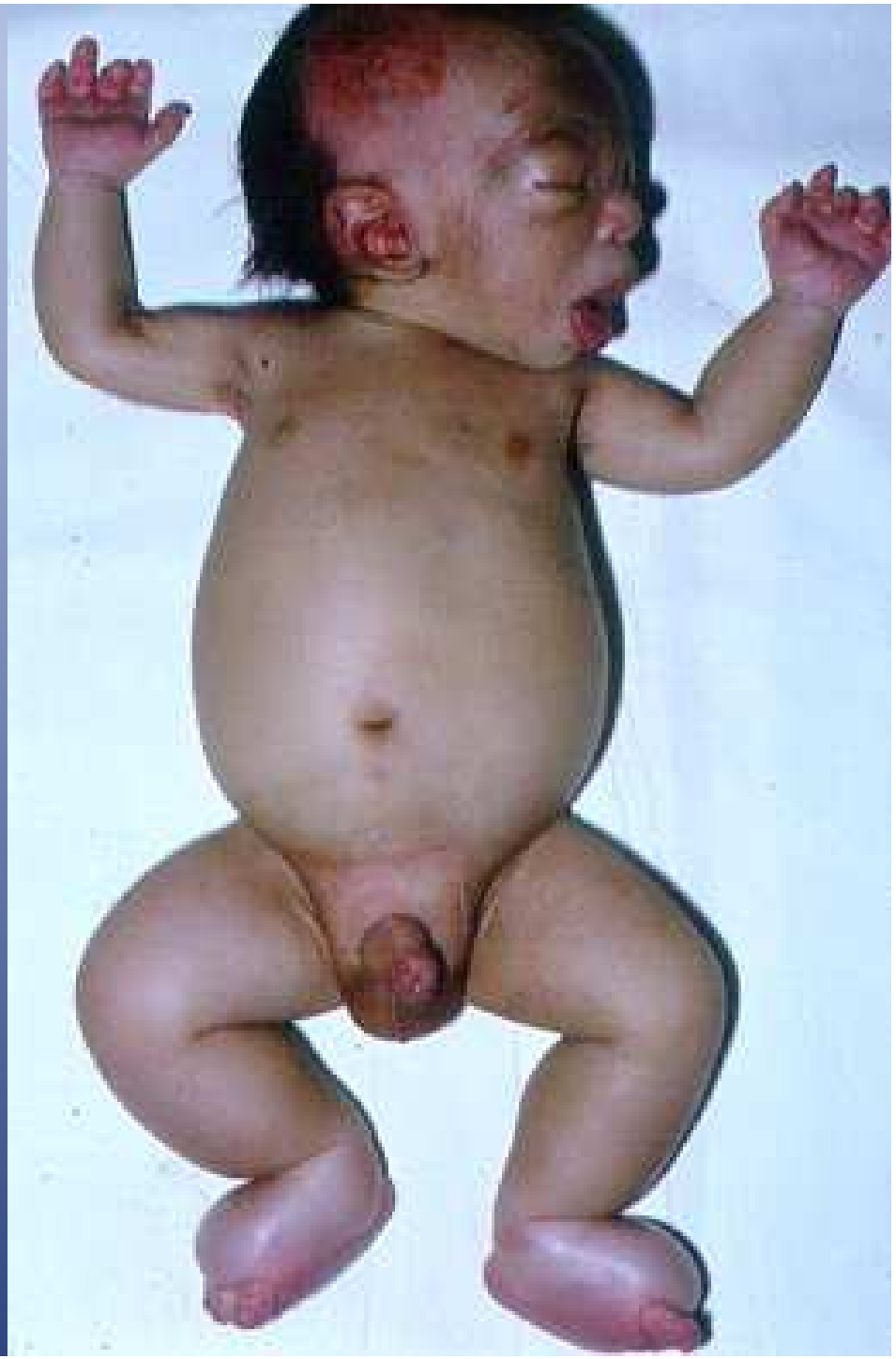
Anasarka =

Generalised oedema plus

fluid collections in body

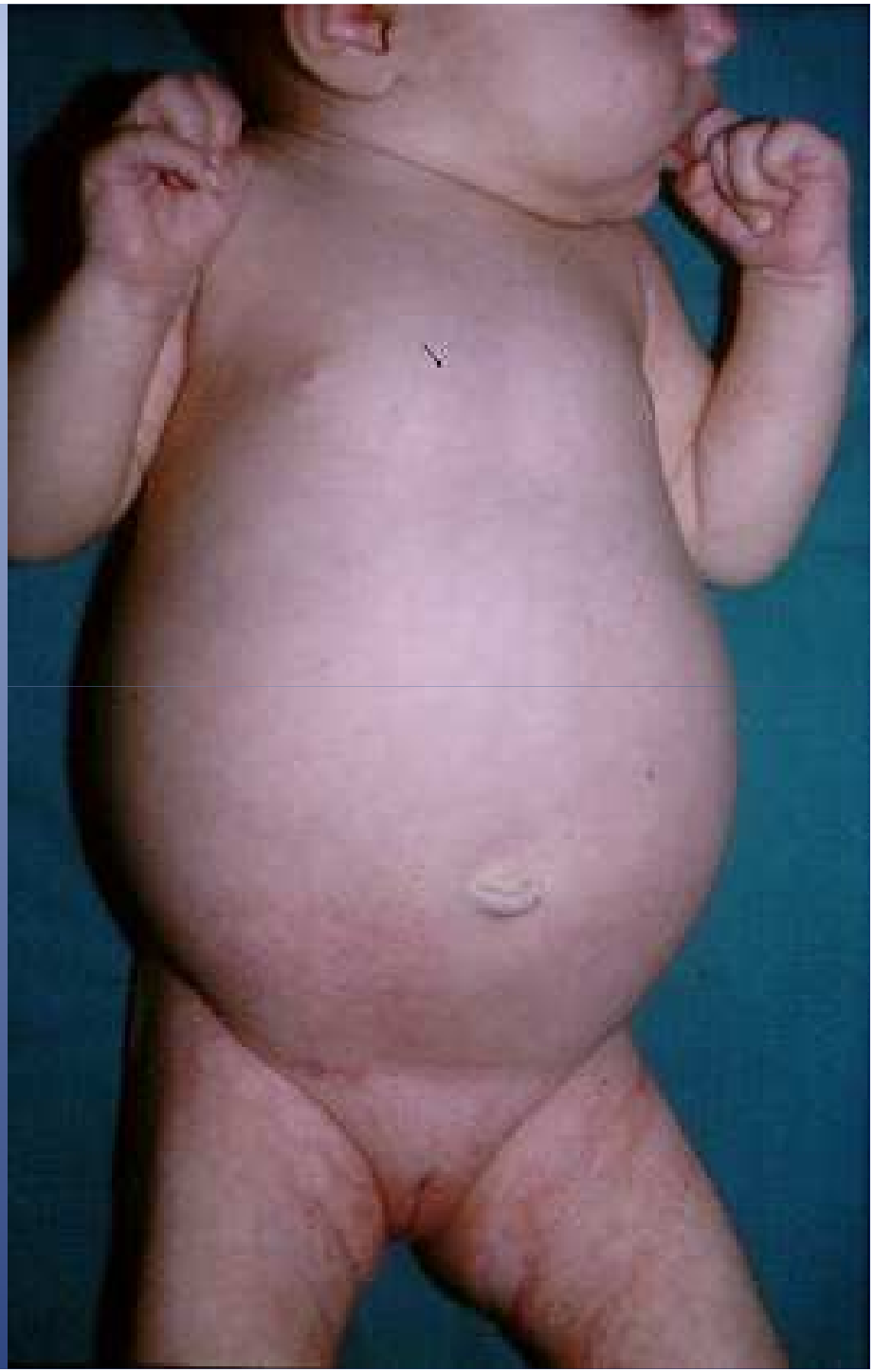
spaces, e.g. pleural and

peritoneal cavities



Neonate with

- Abdominal distention
- Fullness in the flanks
- Percussion is necessary to differentiate between fluid, solid organ/mass and air

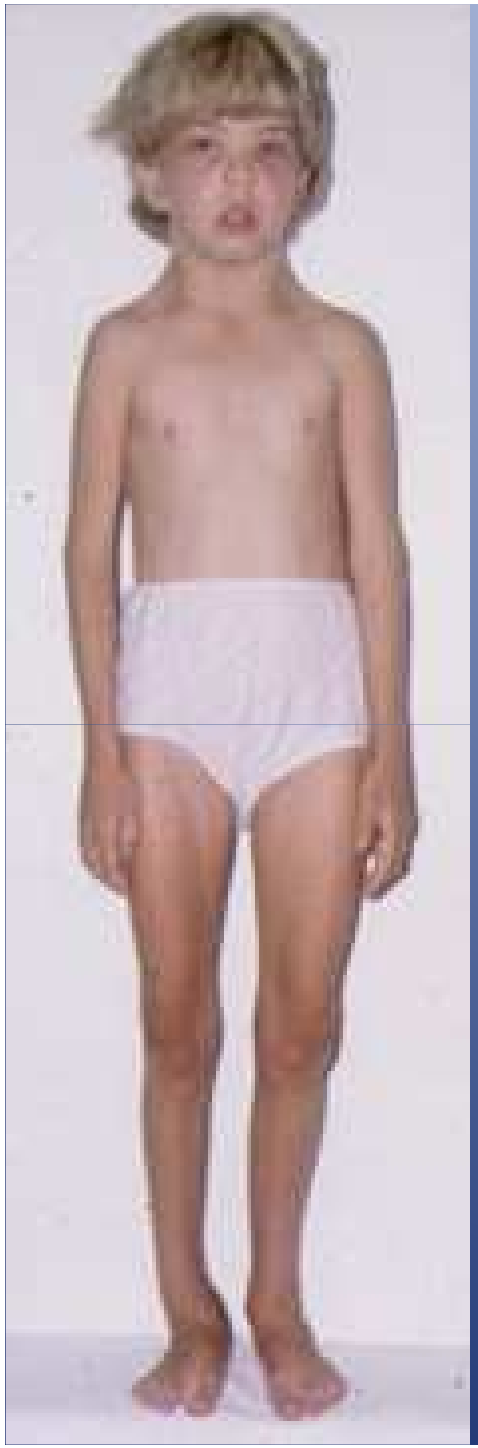


Abdominal distension

Resonant to percussion

No shifting dullness

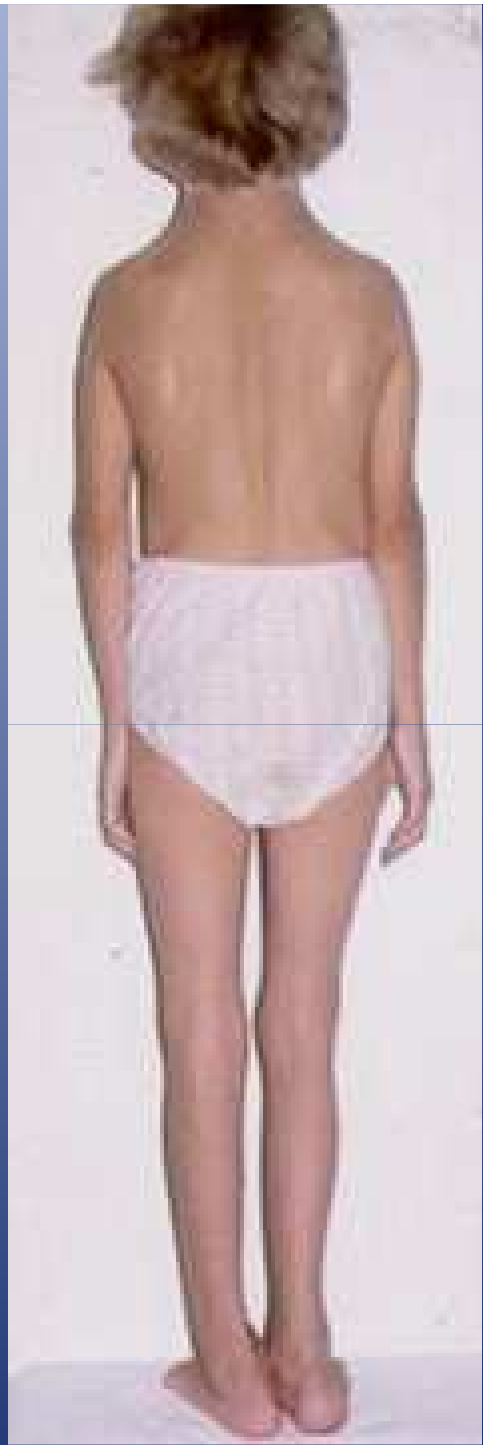
Constipation due to polyuria



Dysmorphic Features

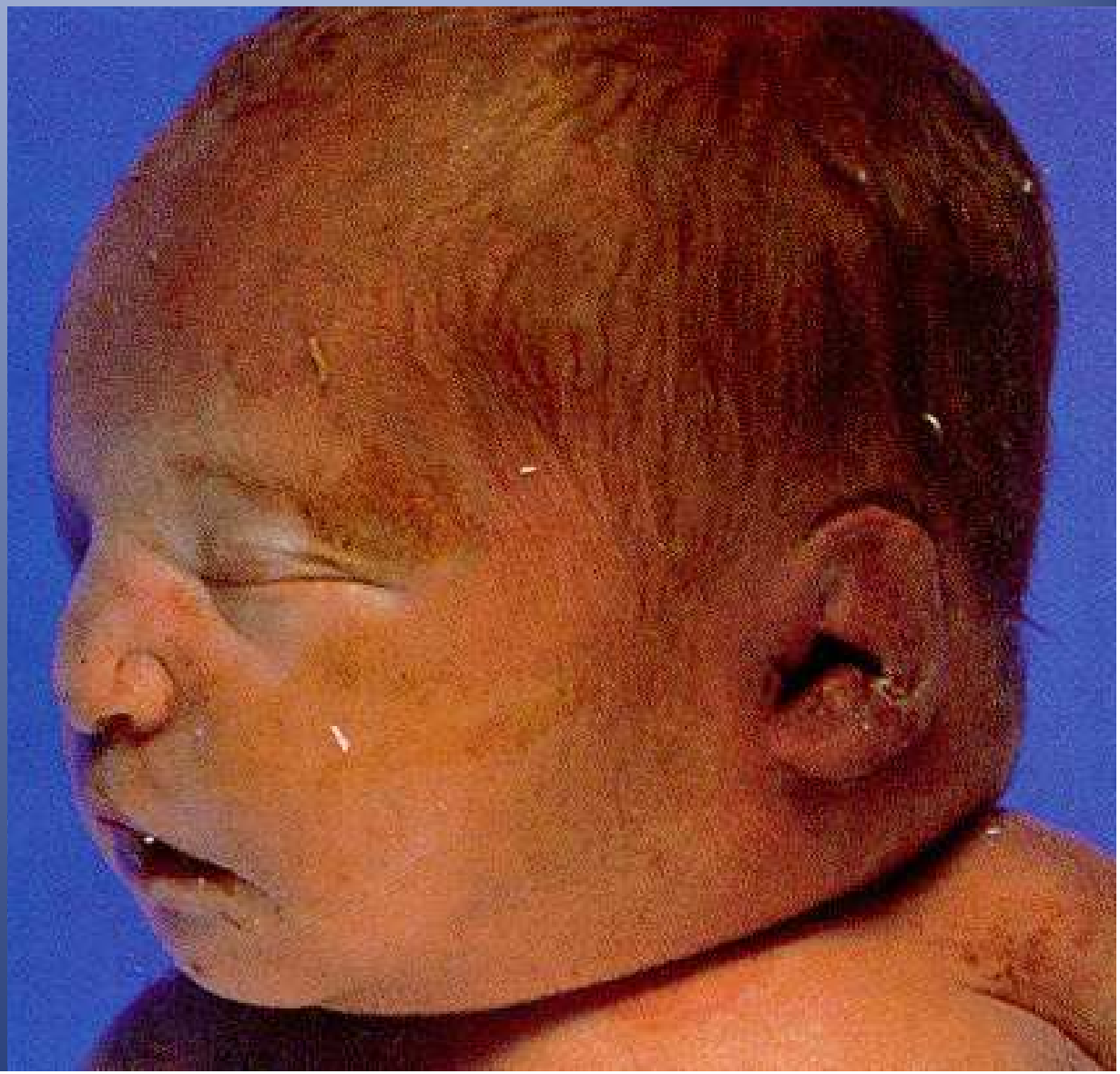
Turner Syndrome

- –Stunted girl
- –Skeletal deformity
- –Webbed neck
- –Wide spaced nippples



Potter Sequence

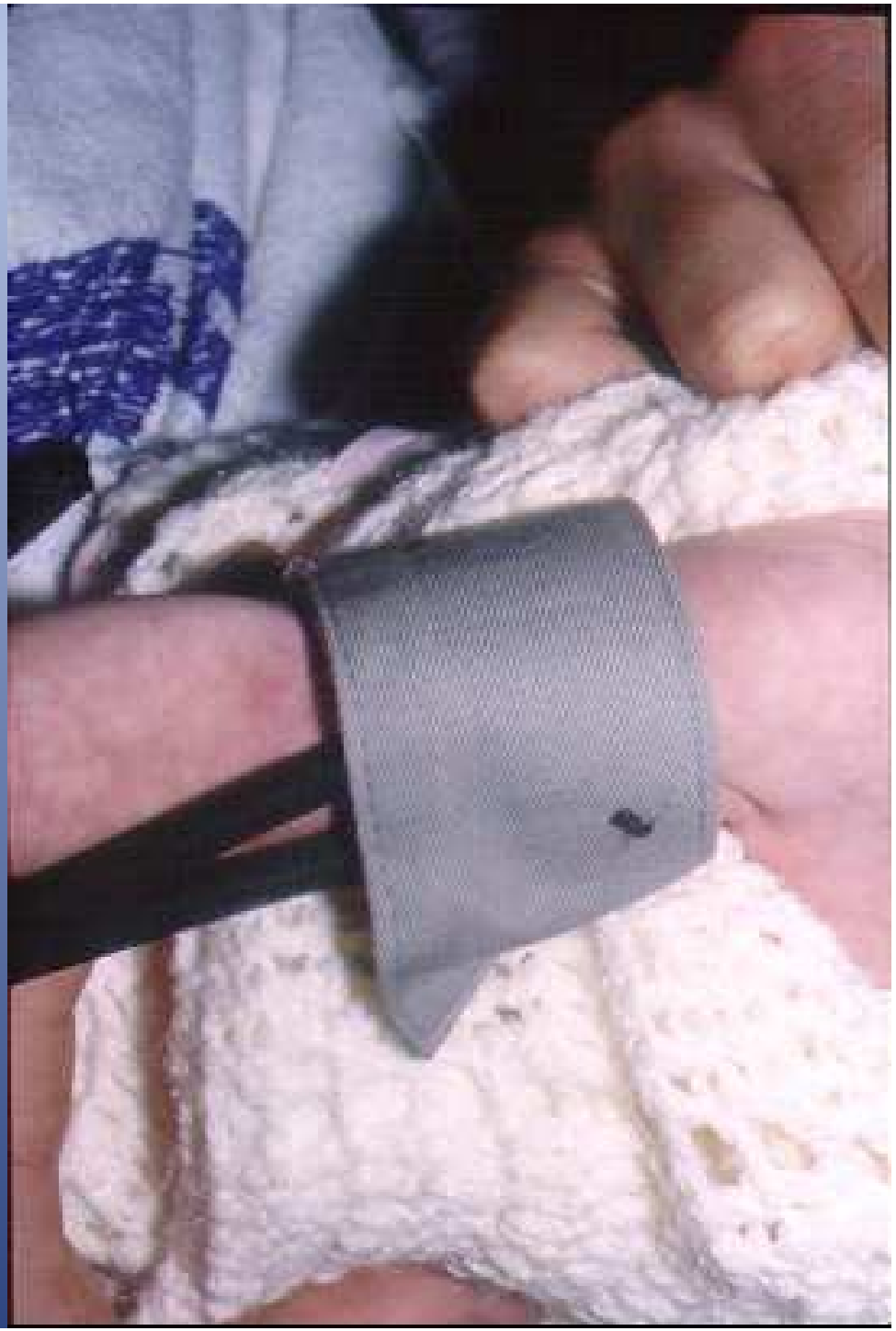
- Caused by compression of foetus due to oligohydramnios
- Abnormal facies
- Pulmonary hypoplasia



Prune Belly Syndrome

- Absence of abdominal muscles
- Cryptorchidism
- Dilated urinary tract
  - obstructed or
  - non-obstructed

Measuring the blood pressure



95th Percentiles of Blood Pressure for Boys for Age & Height Percentiles

Age	Systolic Blood Pressure by Percentile of Height, mmHg+							Diastolic Blood Pressure by Percentile of Height, mmHg+						
	5%	10%	25%	50%	75%	90%	95%	5%	10%	25%	50%	75%	90%	95%
1	98	99	101	103	104	107	106	54	54	55	56	57	58	58
2	101	102	104	106	108	108	110	59	59	60	61	62	63	63
3	104	105	107	109	110	109	113	63	63	64	65	66	67	67
4	106	107	109	111	112	111	115	66	67	68	69	70	71	71
5	108	109	110	112	114	112	116	69	70	71	72	73	74	74
6	109	110	112	114	115	114	117	72	72	73	74	75	76	76
7	110	111	113	115	117	115	119	74	74	71	76	77	78	78
8	111	112	114	116	118	117	120	75	76	72	78	79	79	80
9	113	114	116	118	119	119	121	76	77	74	79	80	81	81

Examine eyes and ears

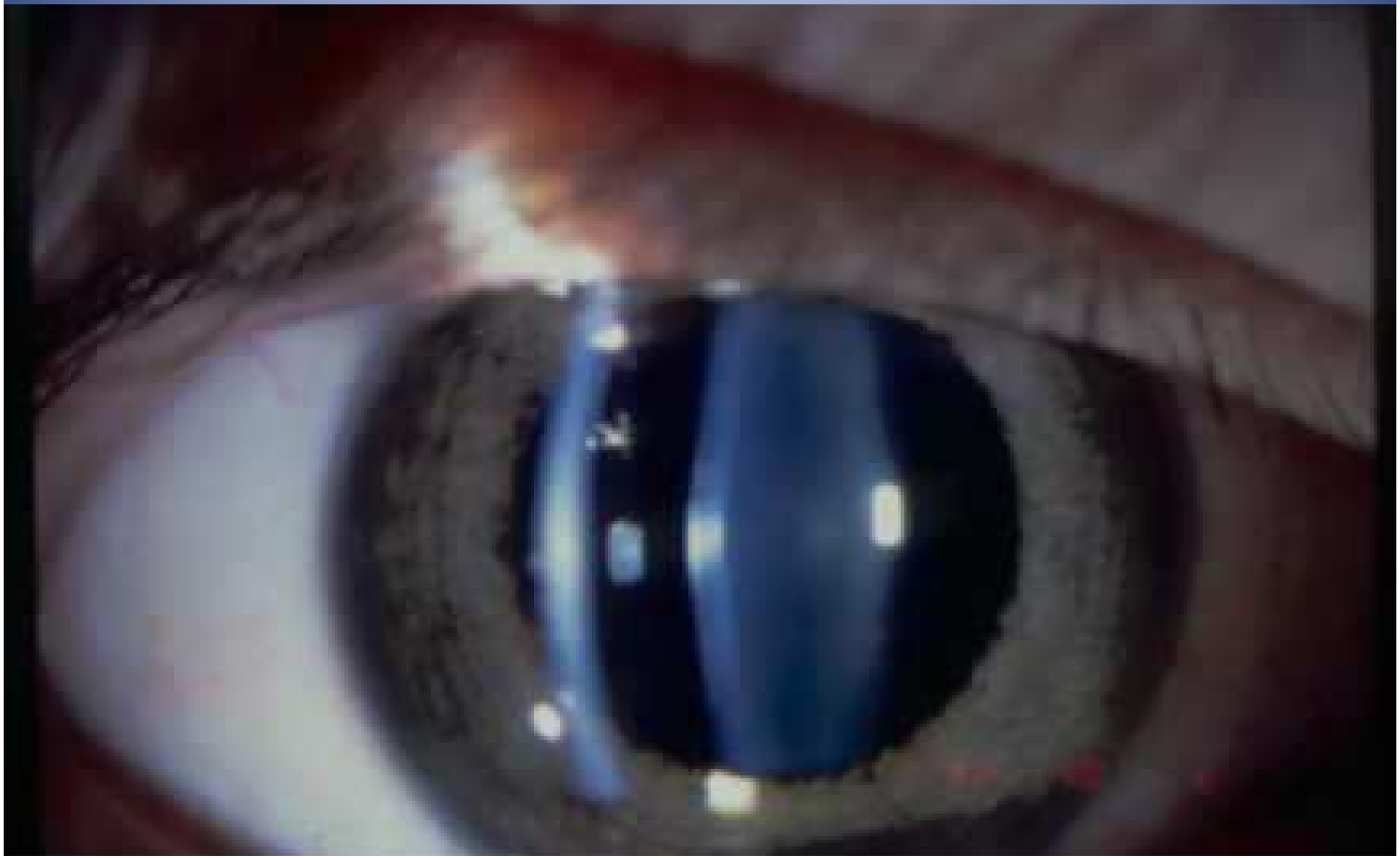
Including fundoscopy

Acquired and inherited kidney disease often associated with ear or eye pathology

- Night blindness due to Retinitis Pigmentosa
- Retinal degeneration

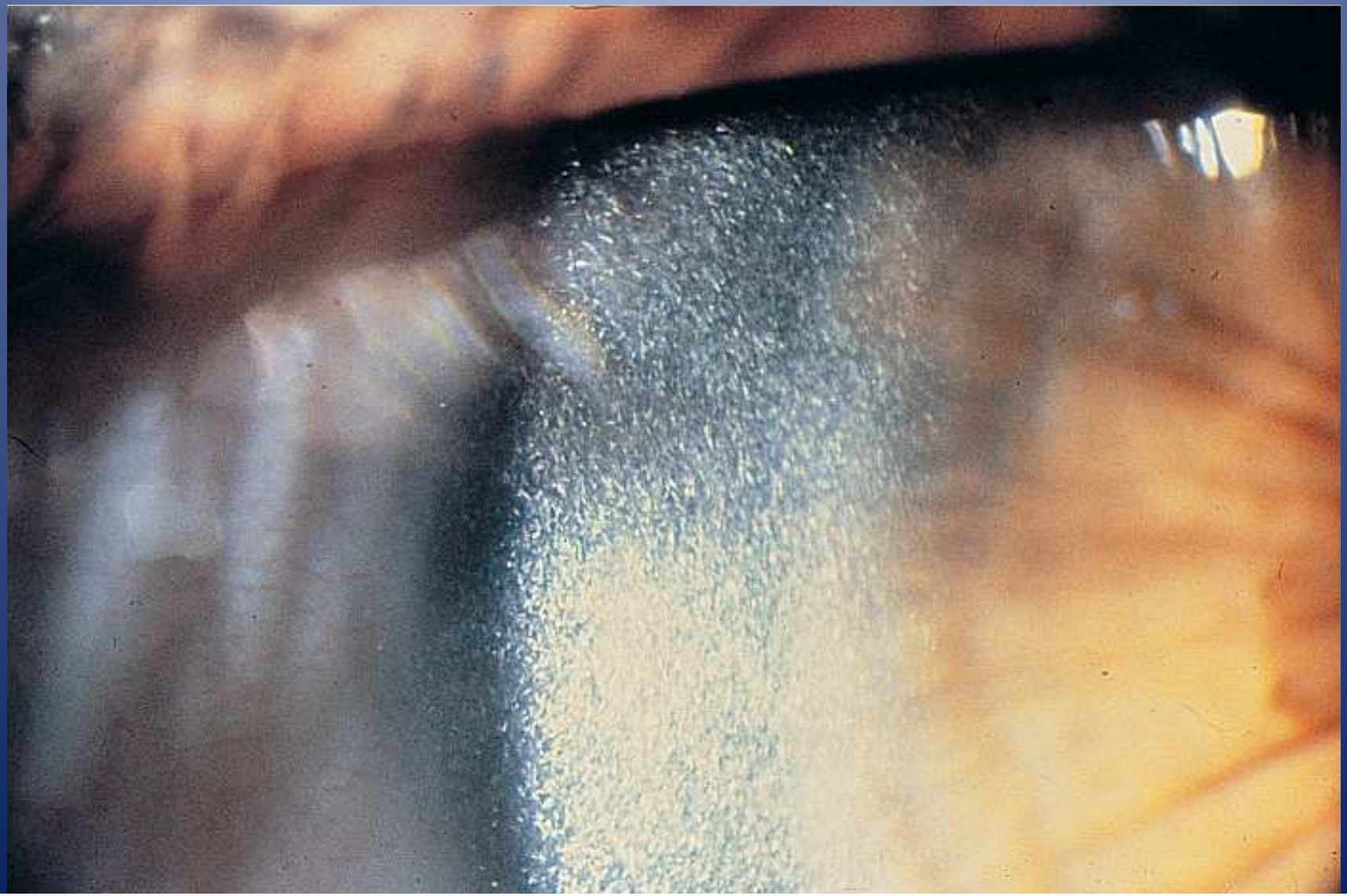
Juvenile Nephronophthysis

Keratoconus is associated with Alport Syndrome



Impaired eye sight and painful eyes

Corneal opacities in cystinosis

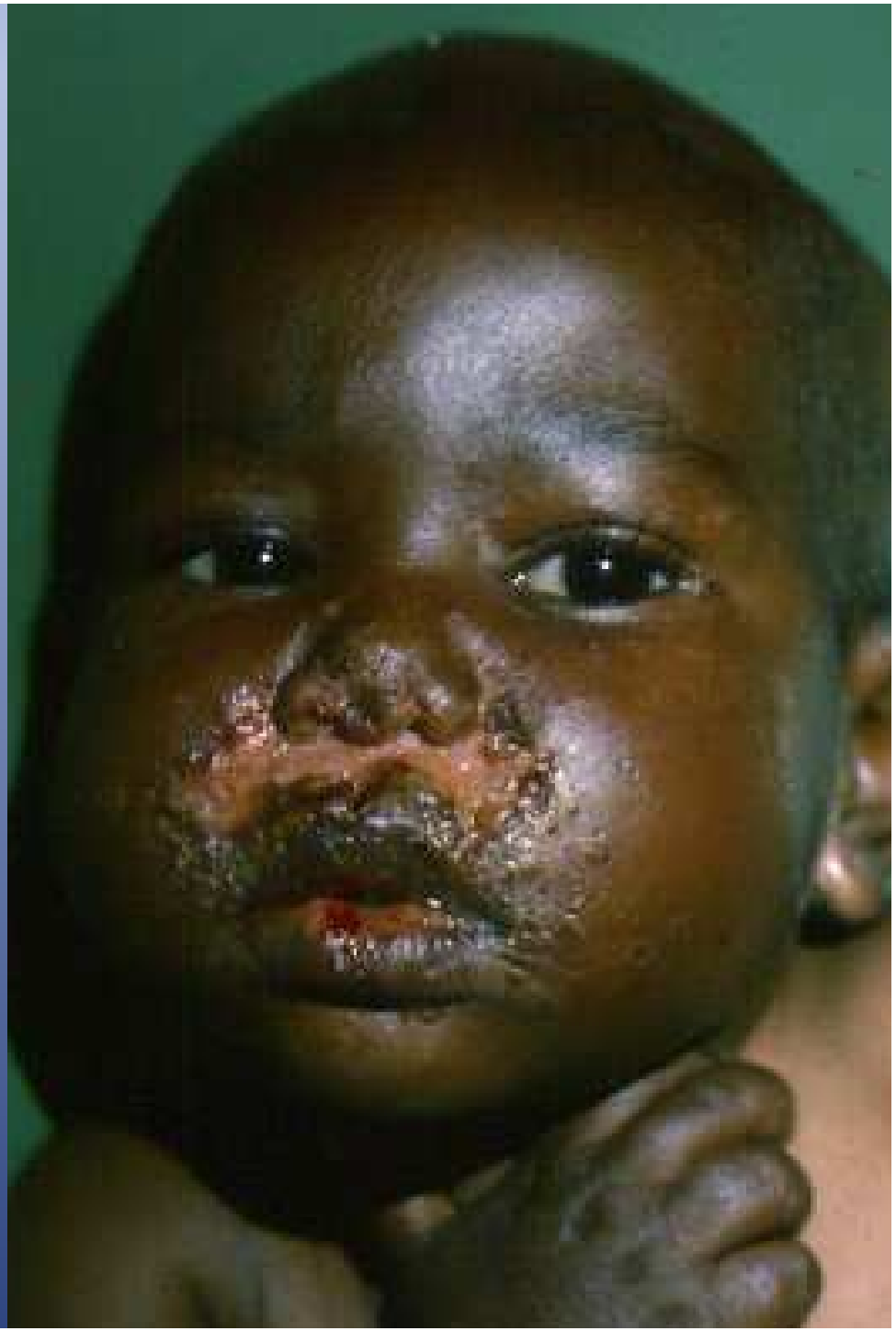


Eye signs associated with kidney disease

- Cataracts – congenital Rubella / CMV / Iatrogenic
- Leucocoria = white pupil (retinoblastoma) or aniridia
  – both associated with nephroblastoma (Wilm's tumour)
- Coloboma in UGT abnormalities (mutation of EYA gene)
- Hypertension – hypertensive retinopathy
- Retinopathy: inherited kidney diseases

Skin abnormalities commonly associated with renal disease e.g.

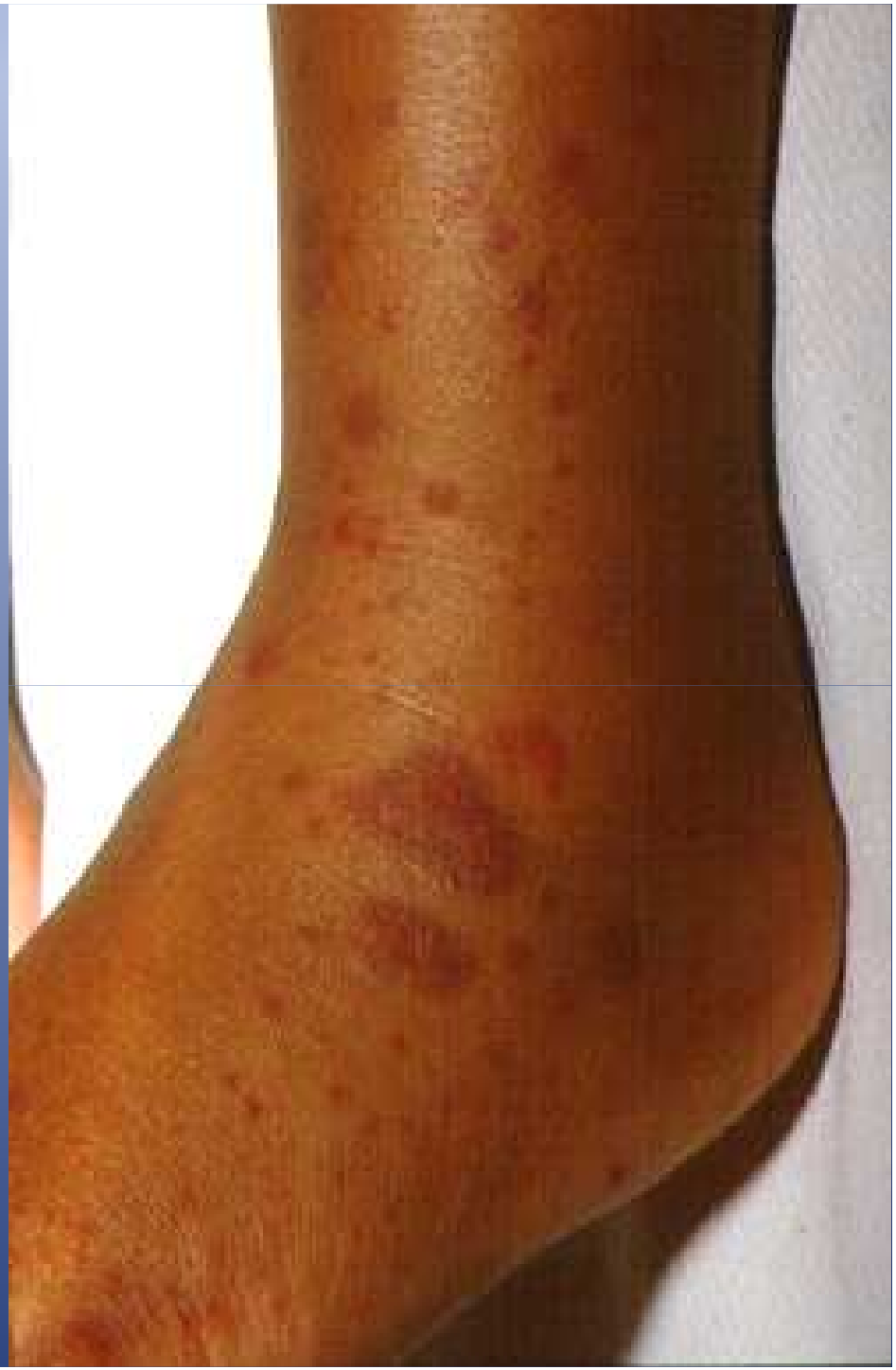
Impetigo in boy with acute post streptococcal glomerulonephritis



Purpura in a patient with

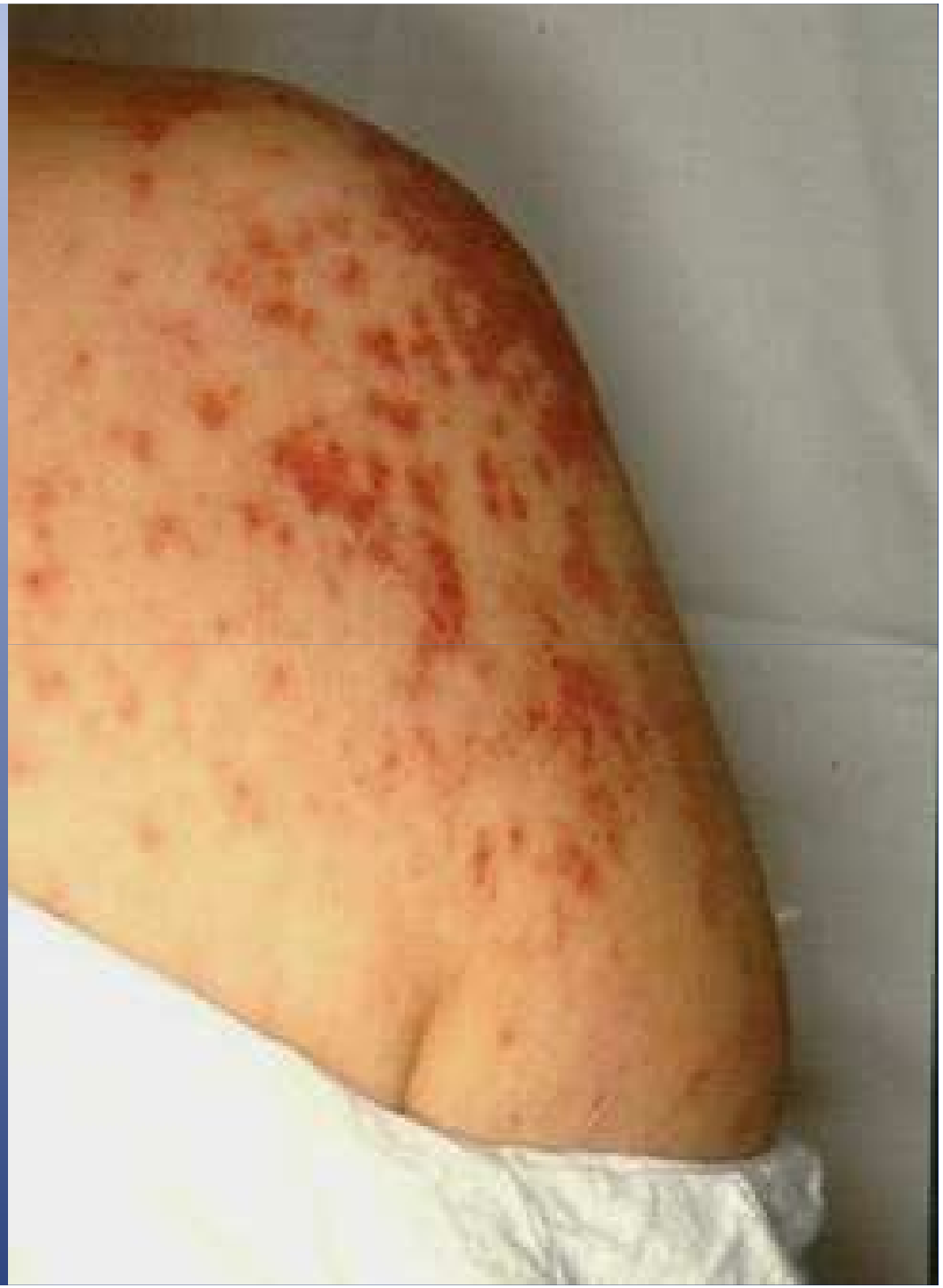
Henoch Schönlein Purpura

(HSP)



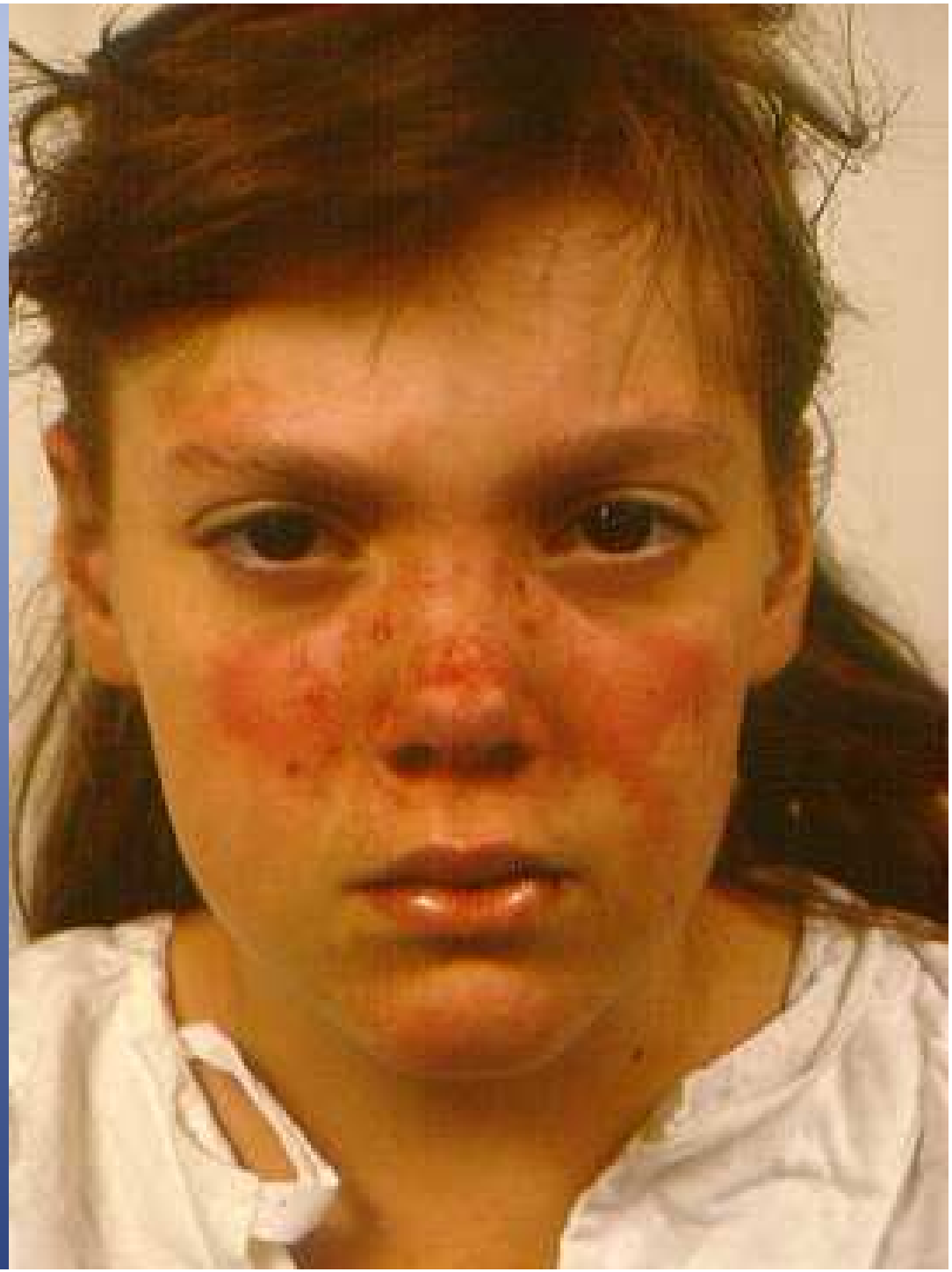
Skin manifestations associated with collagen vascular disease e.g. in SLE / PAN

- Vasculitis
- Purpura
- Erythema nodosum



Skin Manifestations of SLE

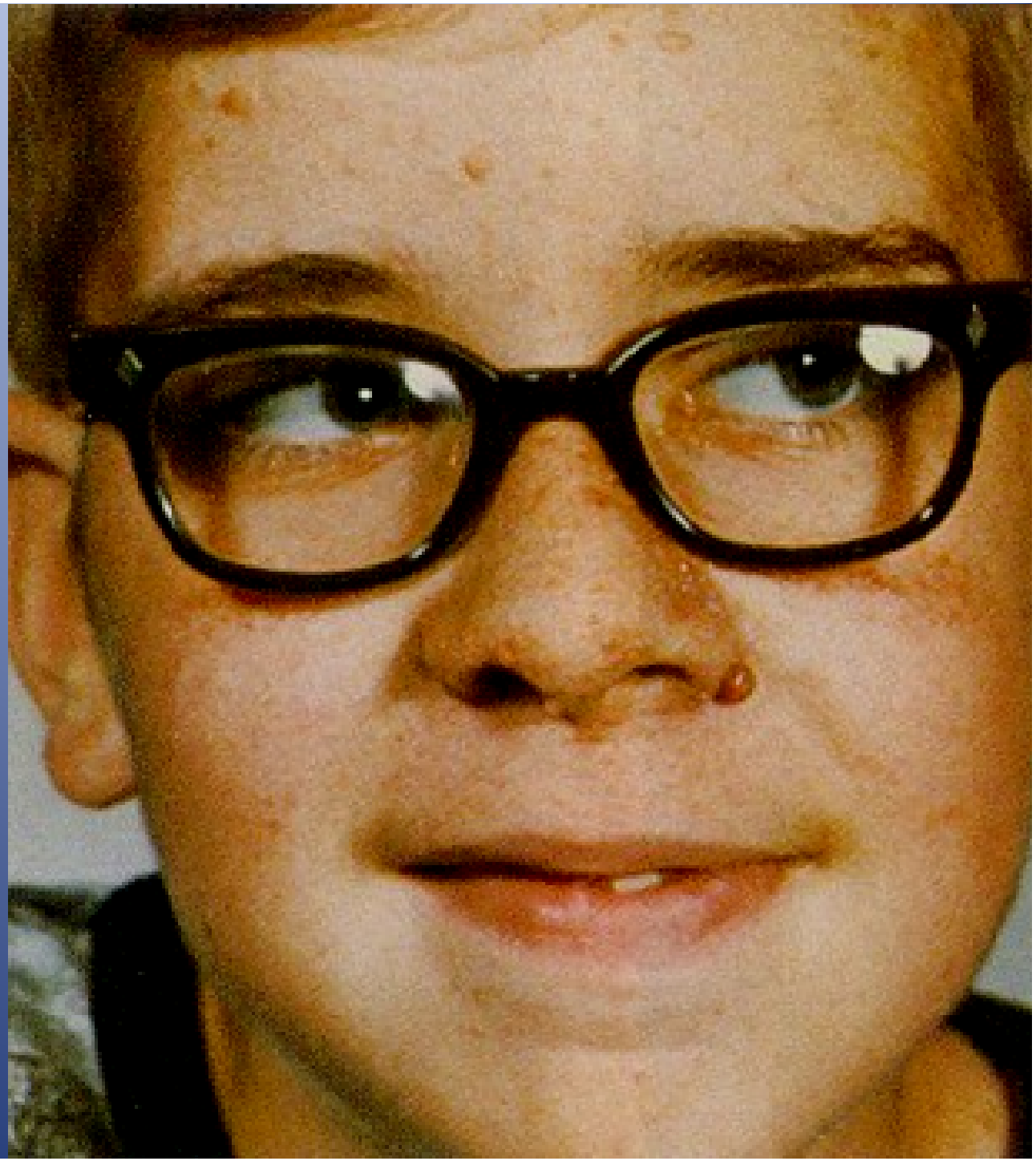
Butterfly rash



Skin Manifestations of SLE

Increased nailbed capillaries

- Tuberous sclerosis
- Adenoma sebaceum
- Angiomyolipoma in kidneys



Musculoskeletal System

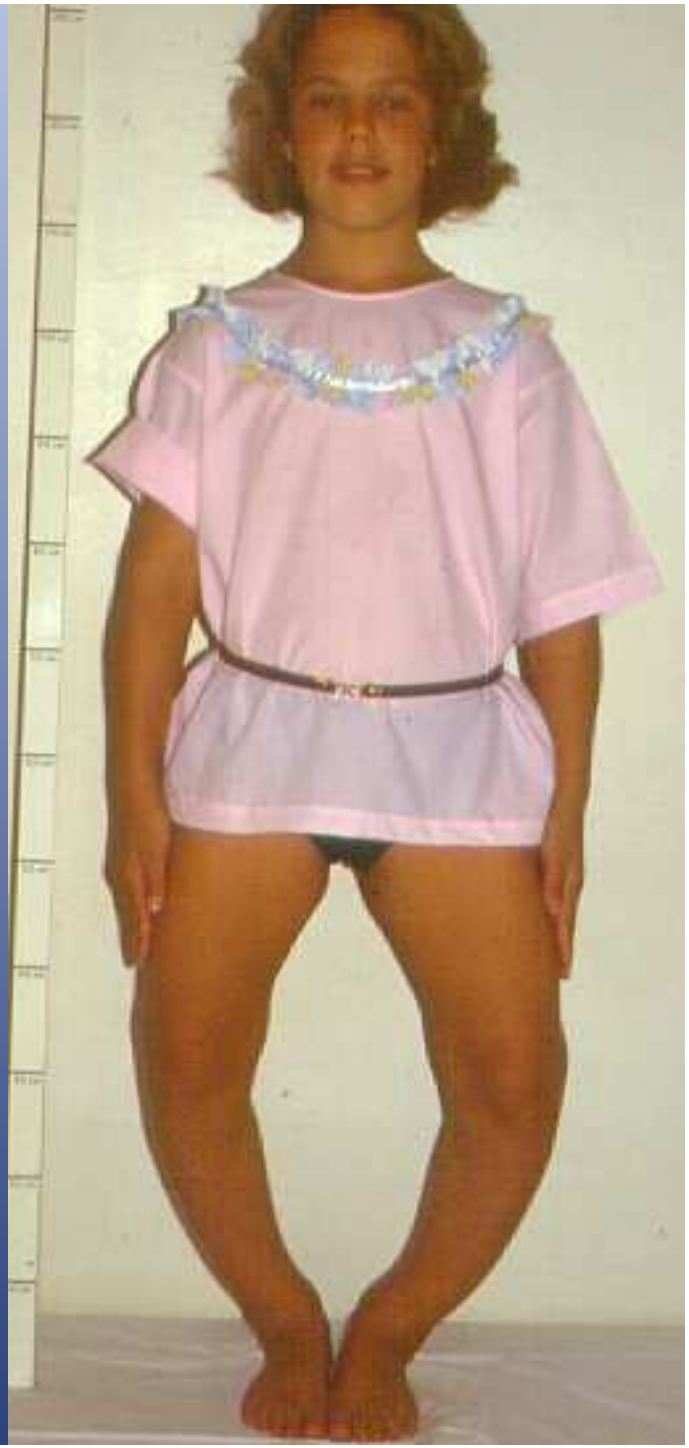
Rickets in children >2 years

≠ nutritional problem

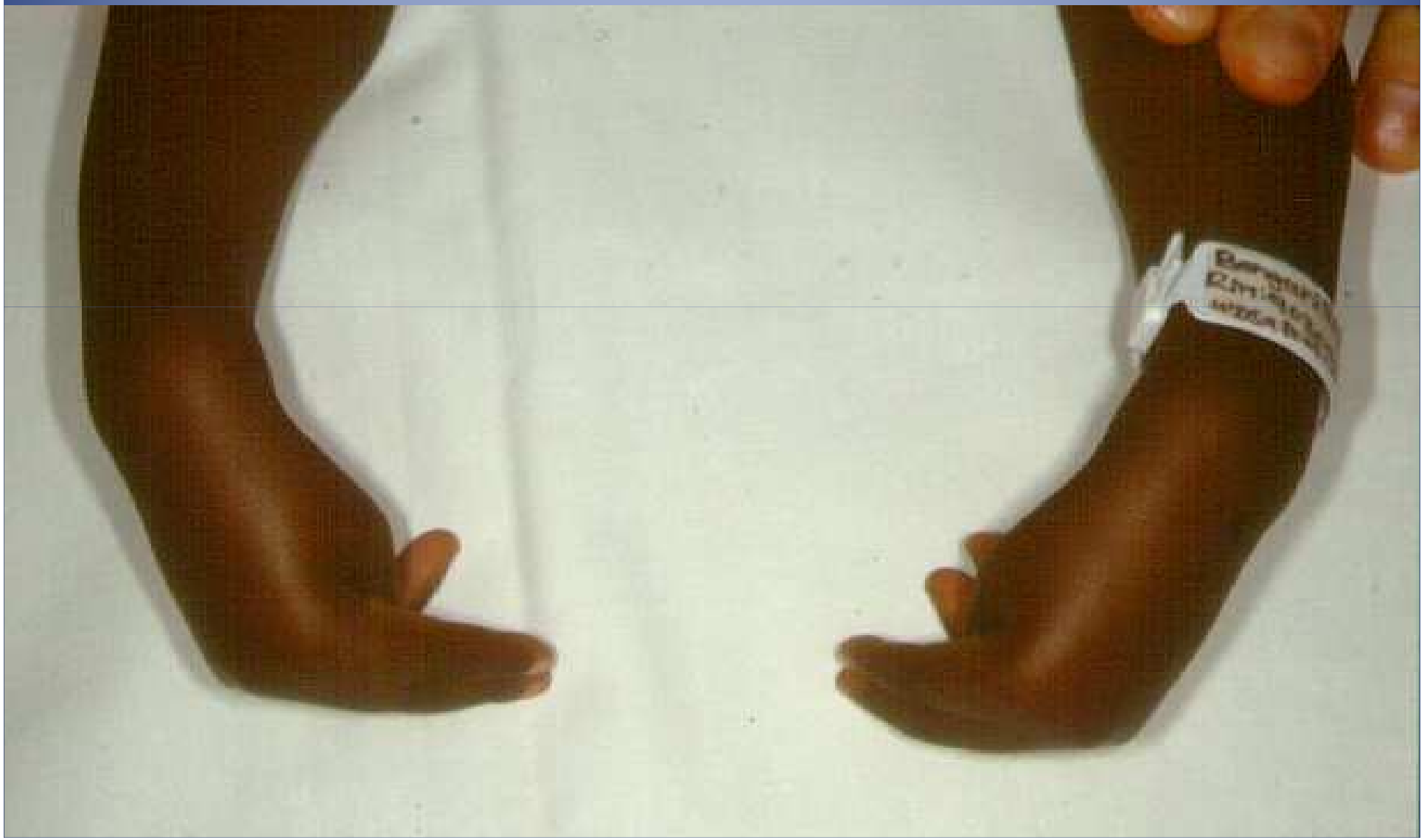
= usually due to renal tubulopathy

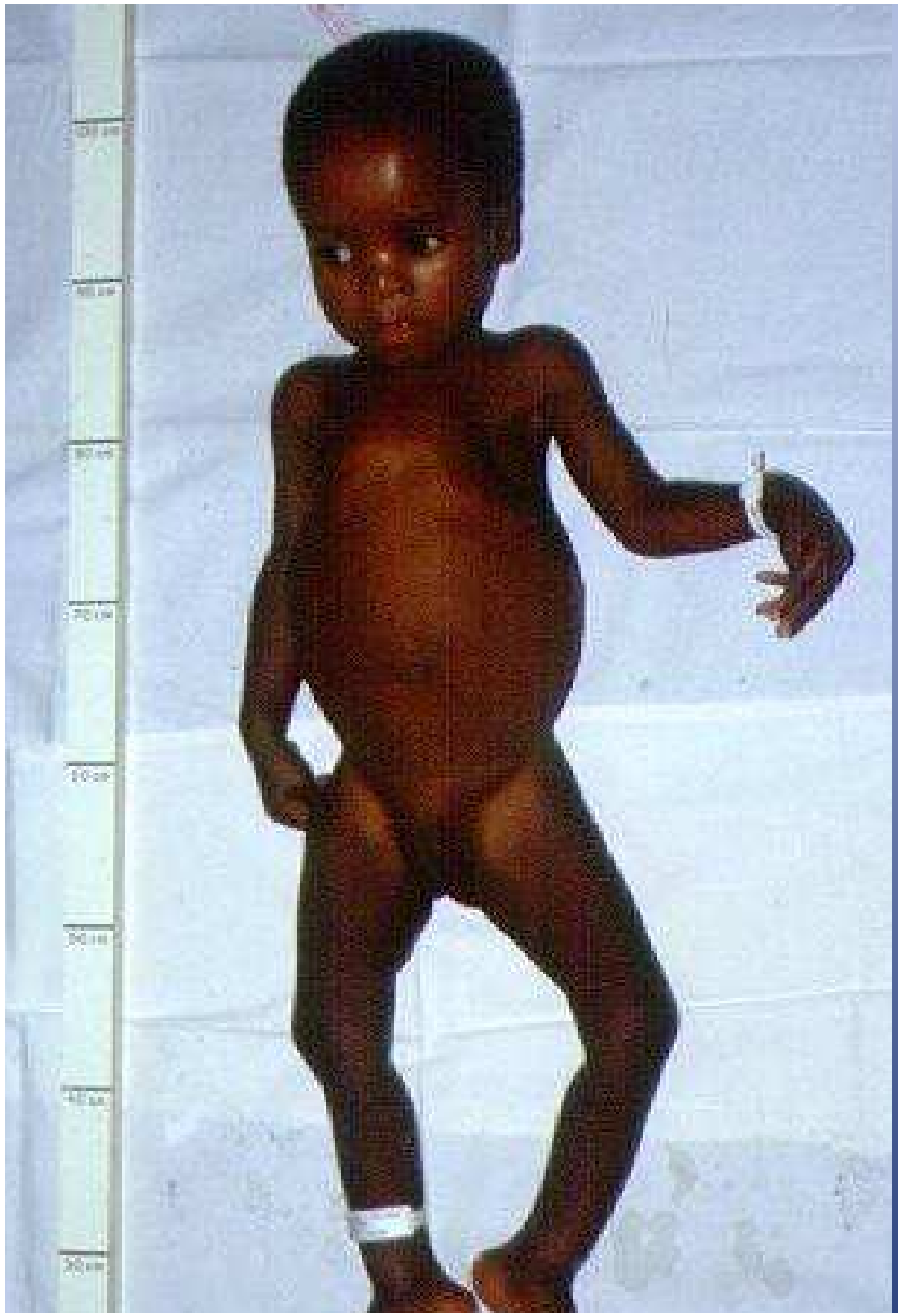
Features

- Skeletal deformities
- Bone pain
- Spontaneous fractures
- Weakness/delayed motor milestones
- Assess hearing
- Check eyes



Tetany in a child with renal rickets





Renal rickets

Bossing

Chest deformities

Hypotonia

Tetany

References

1. Johnson RJ, Feehally J. Comprehensive Clinical Nephrology. 2nd ed. London: Mosby; 2003
2. KDOQI clinical practice guidelines for chronic kidney disease: evaluation, classification and stratification. Kidney Disease Outcome Quality Initiative. Am J Kidney Dis 2002;39: S1-S246
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