MANAGEMENT OF NEPHROTIC SYNDROME

SANUSHKA NAIDOO

NETCARE ALBERTON HOSPITAL


LUNCHBOX PACK

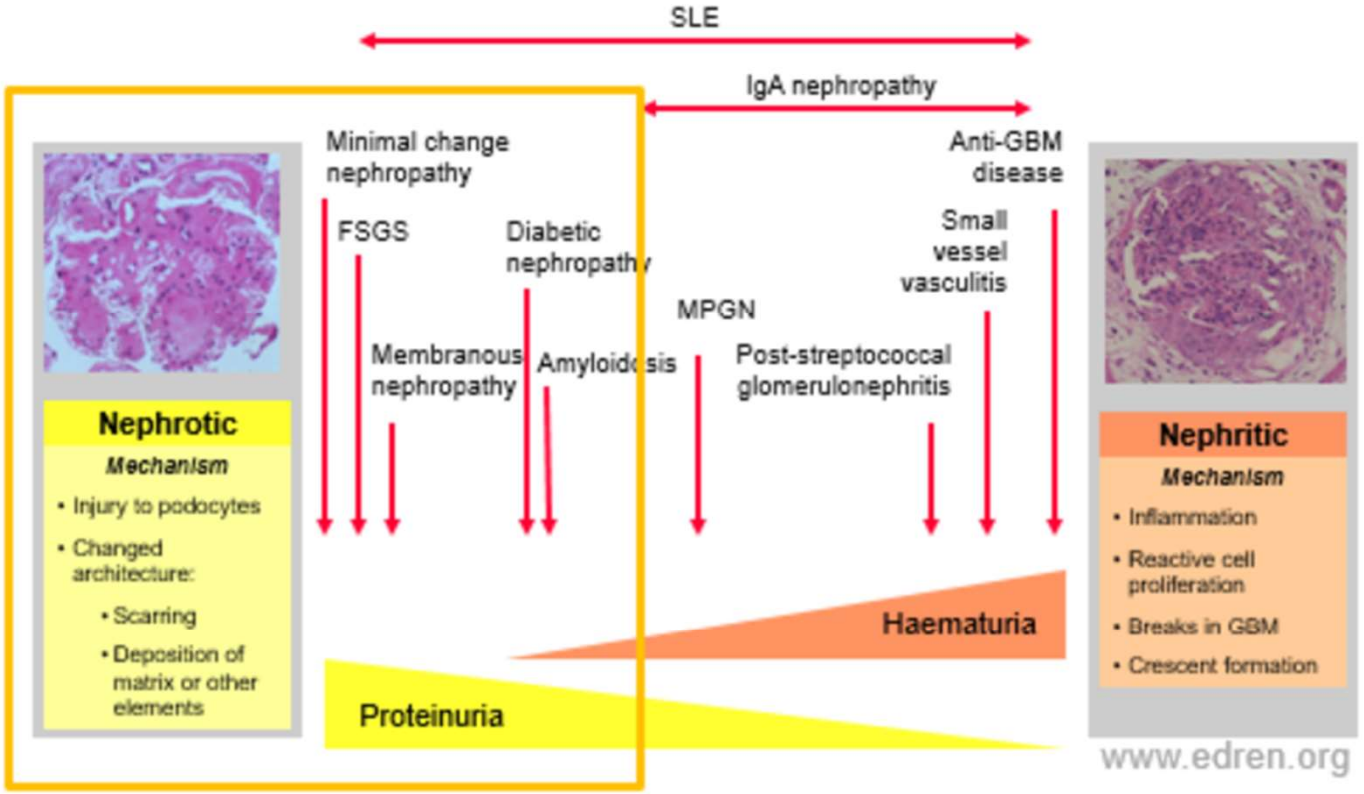
OBJECTIVES

- DEFINITION
- NEPHRITIC/NEPHROTIC SPECTRUM
- CLASSIFICATIONS/TERMINOLOGY
- SOUTH AFRICAN DATA
- MANAGEMENT
- GENETICS

DEFINITION

- OEDEMA
- HYPOALBUMINAEMIA
  - <30G/L
- PROTEINURIA
  - >200 MG/MMOL (PROT:CREAT)
  - >2MG/MG (PROT:CREAT)
  - >2+ URINE DIPSTICKS
- HYPERLIPIDAEMIA

The spectrum of glomerular diseases



OEDEMA

- INCREASED HYDROSTATIC PRESSURE
  - CARDIAC FAILURE
  - GLOMERULONEPHRITIS
- DECREASED ONCOTIC PRESSURE
  - PROTEINS
    - WHERE ARE THEY MADE
    - WHERE ARE THEY ABSORBED
    - WHERE CAN THEY BE LOST
- LEAKY CAPILLARIES

CLASSIFICATIONS

- ACCORDING TO STEROID RESPONSIVENESS
- ACCORDING TO HISTOLOGY
- ACCORDING TO CAUSE
- ACCORDING TO AGE AT PRESENTATION

Remission
Urine albumin trace or negative on dipstick or proteinuria <4 mg/m² per h or urinary protein:creatinine ratio <200 mg/g (20 mg/mmol) for 3 consecutive days

Relapse
Urine albumin 3+ or 4+ or proteinuria >40 mg/m² per h or urinary protein:creatinine ratio >200 mg/g (20 mg/mmol) for 3 consecutive days

Frequently relapsing NS
≥2 relapses within 6 months of initial response or ≥4 in any 12 month period

Steroid-dependent NS
2 consecutive relapses occurring while weaning to alternate day steroids or within 2 weeks of steroid discontinuation

Steroid-resistant NS
Persistent proteinuria despite 60 mg/m² or 2 mg/kg for 8 weeks, after ensuring no infection or non-adherence to medication

HISTORICALLY

- ISKD 70'S
- 90% MCNS
- LIKELY TO RESPOND TO STEROIDS
- GUIDELINES FOR INITIAL MANAGEMENT AND BIOPSY
  - AGE 1 -12
  - NO SIGNIFICANT HYPERTENSION
  - NORMAL RENAL FUNCTION
  - +- MICROSCOPIC HAEMATURIA

NOW…

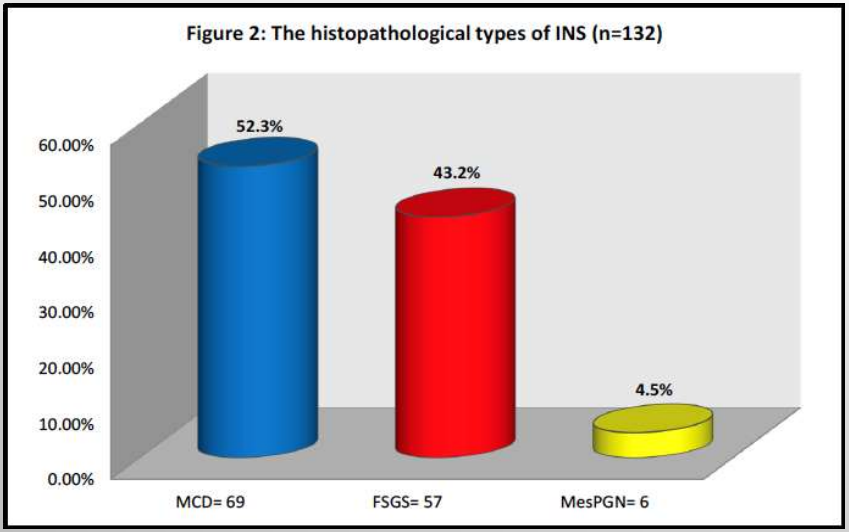
- INCREASING INCIDENCE OF FSGS GLOBALLY (UP TO 30%)
- SOUTH AFRICA DIFFERENT
- GENETIC TESTING

Table 2. Steroid response according to histopathological subtype

Steroid response	Histology: FSGS (*n*=18), *n* (%)	MesPGN (*n*=62), *n* (%)	MCD (*n*=15), *n* (%)	Total (*N*=95), *n* (%)
SRNS	15 (83)	25 (40)	3 (20)	43 (45)
SSNS	3 (17)	36 (58)	12 (80)	51 (54)
Unknown*	-	1 (2)	-	1 (1)

FSGS = focal segmental glomerulosclerosis; MesPGN = mesangioproliferative glomerulonephritis; MCD = minimal change disease; SRNS = steroid-resistant nephrotic syndrome; SSNS = steroid-sensitive nephrotic syndrome.
*One patient was lost to follow-up and therefore steroid response could not be determined.

Primary Nephrotic Syndrome in children in Cape Town, SA
Reddy et al, SAJCH 2023
2006 – 2015



Bakhiet, Mmed, CMJAH 2004 – 2013

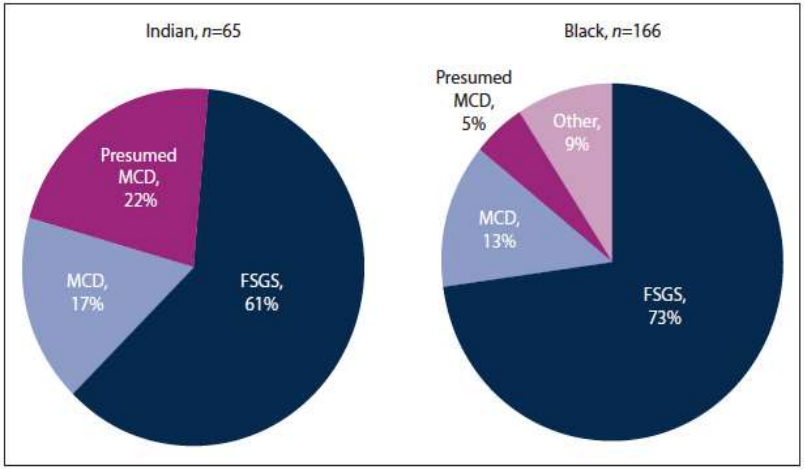
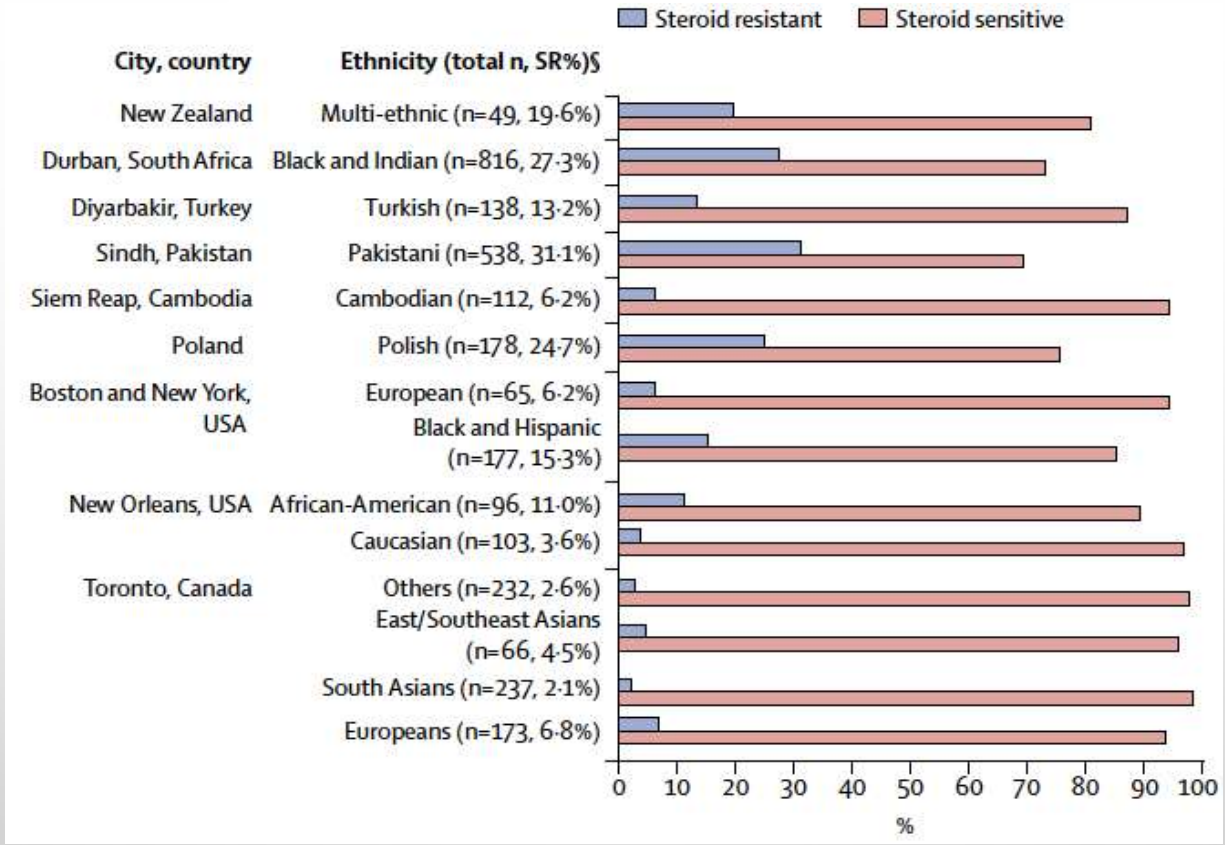


Fig. 2. Histopathology in Indian and black African children with primary nephrotic syndrome. (MCD = minimal change disease; FSGS = focal segmental glomerulosclerosis; other = membranoproliferative glomerulonephritis, membranous glomerulonephritis and mesangioproliferative glomerulonephritis.)

Primary Nephrotic Syndrome in the new Millennium in Kwa-Zulu Natal, South Africa
Abumregha et al, SAMJ 2020
2003 – 2018



Ethnic differences in Childhood Nephrotic syndrome
Canchlani et al
Frontiers in Pediatrics 2016

MANAGEMENT

- COMPLICATIONS OF THE DISEASE
- THE DISEASE ITSELF

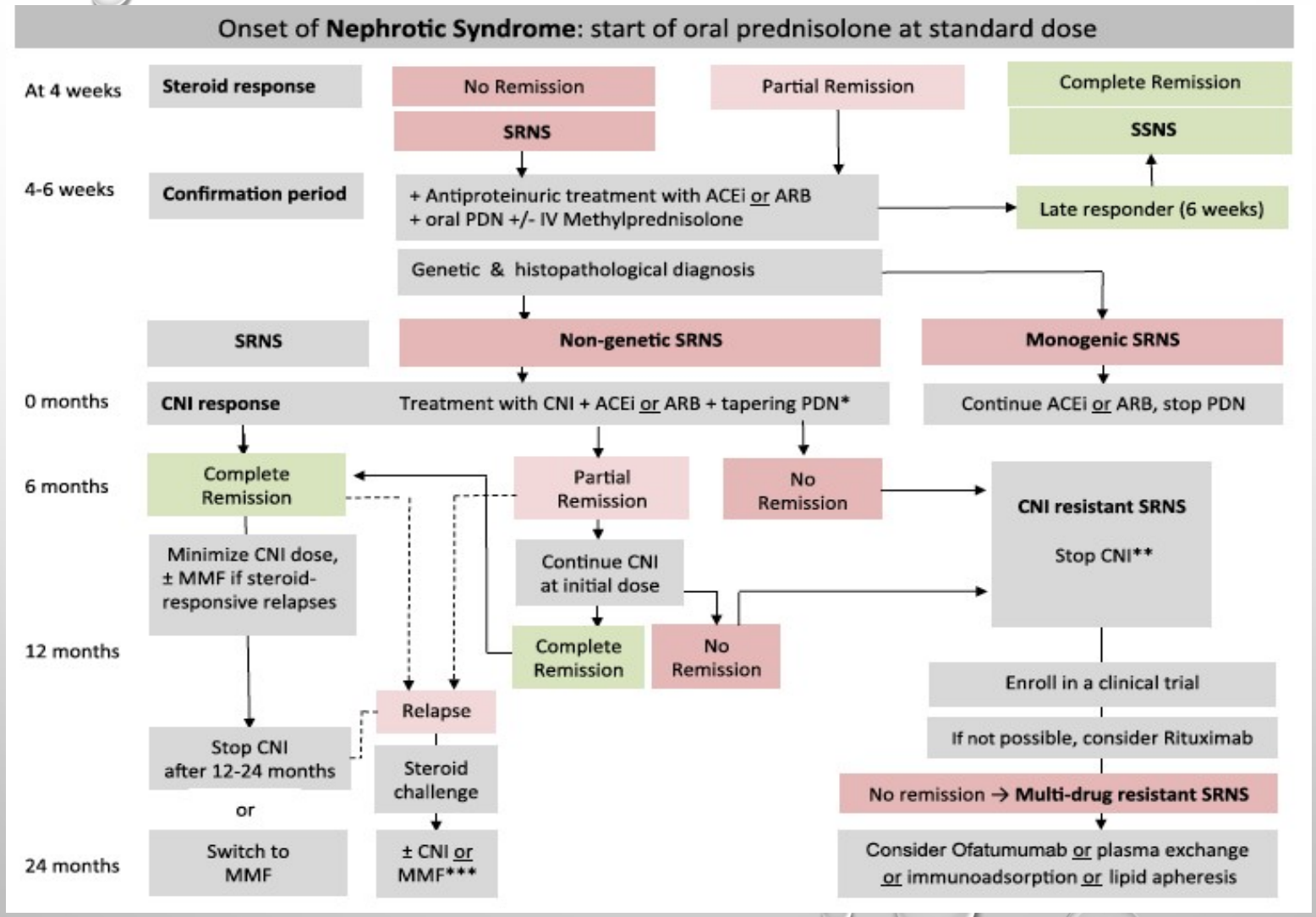
COMPLICATIONS

- URINE LOSS OF PROTEINS
  - ALBUMIN
  - IMMUNOGLOBULINS AND COMPLEMENT
  - THYROID BINDING GLOBULIN
  - VITAMIN D BINDING GLOBULIN
  - TRANSFERRIN
  - LIPOPROTEIN LIPASE
  - PROTEIN C AND PROTEIN S

ACTUAL DISEASE

- STEROID SENSITIVE
- STEROID RESISTANT

Steroid Resistant Nephrotic Syndrome: IPNA



GENETICS

- BEFORE 2000 ONLY TWO MONOGENIC FORMS OF NS REPORTED IN THE LITERATURE
- NOW >80
- "PODOCYTOPATHY"
- WHY IMPORTANT?
  - >95% OF CHILDREN WITH A GENETIC CAUSE OF SRNS WILL NOT RESPOND TO IMMUNOTHERAPY
  - MAY HELP GUIDE GENE TARGETED THERAPY
- SOUTH AFRICA SMALL STUDIES - *NPHS2* V260E (GOVENDER ET AL, ASHARAM ET AL)

- THE CHILDHOOD NEPHROTIC SYNDROME PROJECT UNDERTAKEN BY THE HUMAN HEREDITY AND HEALTH IN AFRICA KIDNEY DISEASE NETWORK (H3AKDRN)
- OVER 500 CHILDREN ENROLLED
- JOHANNESBURG
  - PROF KRAUSE NHLS
  - TEST FOR WT1 AND NPHS2 - BATCH SAMPLES

SUMMARY

- NEED DATA FOR OUR POPULATION!
- HIGHER INCIDENCE OF SRNS AND FSGS WITH PROGRESSION TO ESKF
- HIGHER BURDEN OF INFECTIOUS DISEASES AND MALNUTRITION
- LIMITED BY ACCESS TO DRUGS OR DRUG MONITORING
- FOR GENERAL PAEDIATRICIAN
  - RECOGNISE THE SIGNS
  - REFER EARLY IF POSSIBLE OR SPEAK TO A FRIENDLY NEPHROLOGIST
  - BE ABLE TO RECOGNISE AND TREAT THE ACUTE COMPLICATIONS


peace ♥ love ♥ kidneys