

# **HYPERTENSION AND THE KIDNEYS**

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# OUTLINE

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# Definition of Hypertension

- *Hypertension is defined as persistent elevation of blood pressure;*

**$\geq 140/90$ mmHg**

# Burden of Hypertension

- Hypertension is an important public health problem worldwide.
- It is a major contributing factor to the development of non-communicable diseases (NCDs) like cardiovascular disease.
- NCDs was estimated by the WHO to account for 38 million out of estimated 56 million deaths in 2012; with cardiovascular disease accounting for 46.2% of deaths.

- The number of deaths from NCDs is projected to increase to 52 million by the year 2030 with cardiovascular disease being a major contributor.
- The burden of cardiovascular disease is also on the increase especially in developing countries.
- Therefore, effective prevention and management of hypertension is key to reducing the burden of NCDs

- In Nigeria, the pooled prevalence of hypertension has increased significantly in the last four decades from 8.9% to 22.5%.
- Hypertension related diseases accounted for between 20.5-69.6 % of total admitted medical cases in various studies across Nigeria with high case fatality of up to 42.9%.
- Hypertension is a major risk factor for chronic kidney disease, coronary artery disease, stroke, arrhythmias and retinopathy.

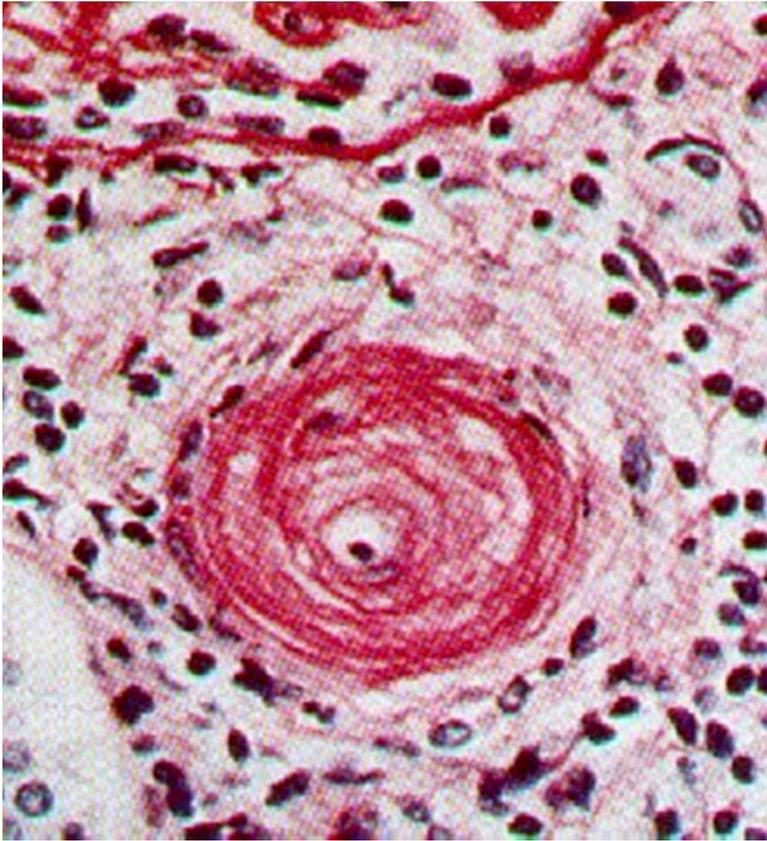
# EFFECTS OF HYPERTENSION ON KIDNEYS

- MALIGNANT NEPHROSCLEROSIS
- BENIGN NEPHROSCLEROSIS
- RAPID PROGRESSION OF CKD

# Malignant Nephrosclerosis

- Occurs in the presence of severely elevated blood pressure with evidence of ongoing target organ damage that usually involves grade 3 or 4 retinopathy
- Presents with proteinuria, microscopic hematuria which is always present and variable GFR
- May also present as acute kidney injury or Acute on Chronic kidney disease
- Characterized by presence of widespread fibrinoid necrosis of arterioles

# Malignant Nephrosclerosis



- **Hyperplastic arteriosclerosis (onion-skinning)**
- **Blood vessels have collagen deposits making the onion skinning appearance**
- **Notice how lumen gets very small**

# HYPERTENSIVE NEPHROSCLEROSIS

- Nephrosclerosis literally means "hardening of the kidney."
- Hypertensive nephrosclerosis, benign nephrosclerosis and hypertensive nephropathy describe the same clinical condition.

# HYPERTENSIVE NEPHROSCLEROSIS

- Clinical condition characterized by long-term essential hypertension, hypertensive retinopathy, left ventricular hypertrophy, minimal proteinuria, and progressive renal insufficiency.
- Most cases are diagnosed based solely on clinical findings.
- No evidence suggesting an alternative diagnosis

# Epidemiology of hypertensive nephrosclerosis (HN)

- HN is second most common cause of ESRD after diabetes mellitus in Caucasians
- HN is the leading cause of ESRD in American Blacks
- According to the 2011 United State Renal Data System, HN accounted for 28% of patients reaching end stage renal disease.
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# HYPERTENSIVE NEPHROSCLEROSIS IN NIGERIA

- Akinsola et al in Ife 40%
  - Ojogwu et al in Benin 43-50%
  - Salako et al in Ibadan 38.9%
  - Ulasi et al in Enugu 17.4%
  - Adejumo et al in Ondo 23%
- 
- Are these differences real or do they reflect differences in accuracy of diagnosis or criteria for diagnosis ?
  - The answer is difficult.

# Sources of Controversy

- Little reduction in HN incidence with better BP control
  - unlike for stroke, CAD
- Pathologic changes seen in advancing age, small vessel disease, obesity
- Diagnosis often clinical, possibility of underlying renal disease

## Important findings from the Framingham Heart Study include

1. The combination of HT and a mild reduction in the GFR was found to be an important risk factor for the development of new-onset kidney disease.
2. Other factors noted were diabetes, obesity, smoking, and a low high-density lipoprotein cholesterol level (dyslipidemia).
3. SBP was a strong, independent predictor of a decline in kidney function among older persons with isolated systolic hypertension.

# RISK FACTORS FOR HYPERTENSIVE RENAL DISEASE

- Black race/Genetics
- Age
- Obesity
- Dyslipidemia
- Smoking
- Lower birth weight
- Pre-existing renal disease
- DM

# GENETICS

- In black people, HN occurs earlier, is more severe, and more often causes ESRD (36.8% vs 26% in white patients).
- In persons of all age groups, ESRD is more common in black people
- The rate of developing ESRD is 3.5 times higher than the rate found among whites.
- The increased susceptibility of black patients with hypertension to develop progressive renal failure cannot be explained solely by the higher prevalence of hypertension, severity of hypertension, or socioeconomic factors because the rate of new ESRD cases has remained stable in African Americans.

- The increased variant in *APOE1* gene found in blacks with increased rate of ESRD
- There is a strong association between genomic variants within MYH9 (non-muscle myosin heavy chain 9) on 22q and non-diabetic ESRD in African Americans.

# Genetic predisposition and CKD in Nigeria

- There was significant strong association between APOL1 variants and CKD in a study done in UCH, Ibadan. However, there was no significant association between CKD and MYH9 gene

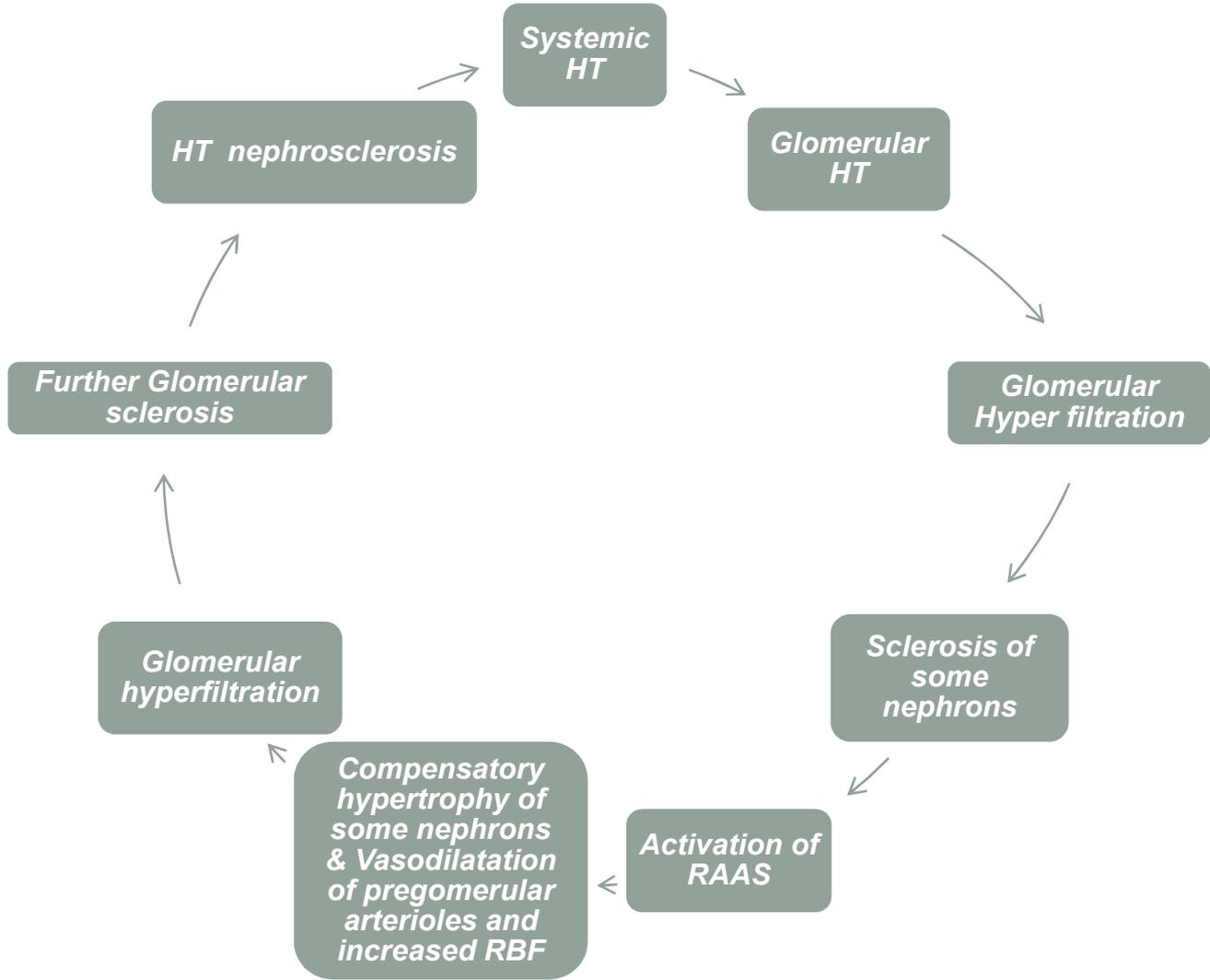
# Pathogenesis of CKD

Several renal, hormonal, physiologic, and genetic factors have been proposed as explanations for the increased rate of hypertension and progression of chronic kidney disease in black.

- These include
  - 1. Increased BP sensitivity to high-salt diet
  - 2. Increased renal vascular resistance
  - 3. Decreased renal blood flow
  - 4. Decreased nephron mass secondary to low birth weight (more common in African Americans).
  - 5. Genetics: APOL1, MYH9 genes

- **Regardless of the etiology, once HTN develops, a cycle of renal injury, nephrosclerosis, worsening of hypertension, and further renal injury is established.**

**PATHOGENESS HT NEPHROSCLEROSIS**



# Early markers of renal involvement in primary HTN

- Hyperuricemia
- N-acetyl-beta-glucosaminidase (NAG)
- Microalbuminuria
- Proteinuria- late sign

# Clinical Presentation

- Patients may present with hypertension, its complications (eg, heart failure, stroke), and/or symptoms of uremia.
- In most patients, hypertension is present for many years (usually >10 years), with evidence of periods of accelerated or poorly controlled BP.
- Features suggesting Hypertensive Nephropathy are black race, Hypertensive retinal changes, LVH, Long-standing or very severe hypertension

# Clinical Presentation

- Proteinuria usually less than 0.5 g/d
- Hypertension is diagnosed prior to the onset of proteinuria
- Hypertension precedes renal dysfunction
- No evidence of another renal disease
- Biopsy findings compatible with the diagnosis
- Upon physical examination, evidence of hypertension related target organ damage such as hypertensive changes in the retinal vessels and signs of LVH.

# Laboratory Evaluation

- There are 3 objectives when evaluating a hypertensive patient:
  - (1) Revealing identifiable causes of high BP
  - (2) Identifying other cardiovascular risk factors: such as dyslipidemia, obesity, DM
  - (3) Evaluating for evidence of end organ damage such as kidneys, eyes, heart.

# INVESTIGATIONS

- Urinalysis
- Urine microscopy
- Albumin creatinine ratio
- FBS, 2 Hour post prandial
- EUCr
- Calculate GFR using online calculators or apps
- ECG
- Chest Xray
- Serum Uric acid
- Fasting Serum Lipid profile
- Ophthalmoscopy

# Additional Investigations in those with Renal complications

- Abdomino-pelvic Scan
- Renal Artery Doppler
- Renal biopsy if indicated
- Serum calcium, phosphate, PTH
- Iron studies

# Diagnosis

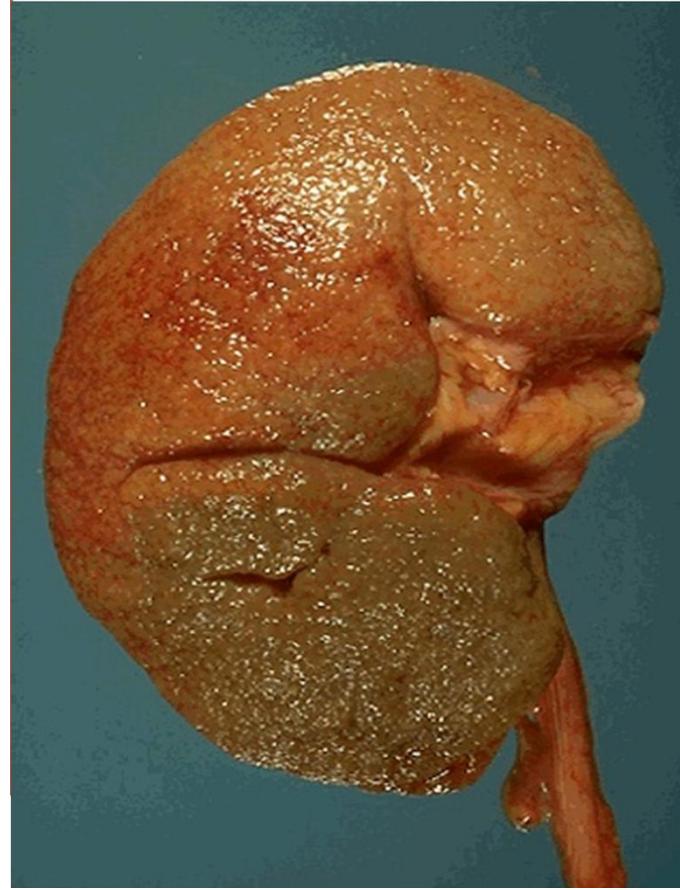
- Diagnosis of hypertensive nephrosclerosis is one of exclusion without biopsy.
- Gross pathologic examination shows the kidneys are shrunken and scarred.
- Renal biopsy specimens often show glomeruli obsolescence, interstitial fibrosis, arterial intimal fibroplasia, arteriolar hyalinization in arterioles most notably afferent, and small arteries (arcuate and interlobular artery).

# Gross Appearance of Kidney

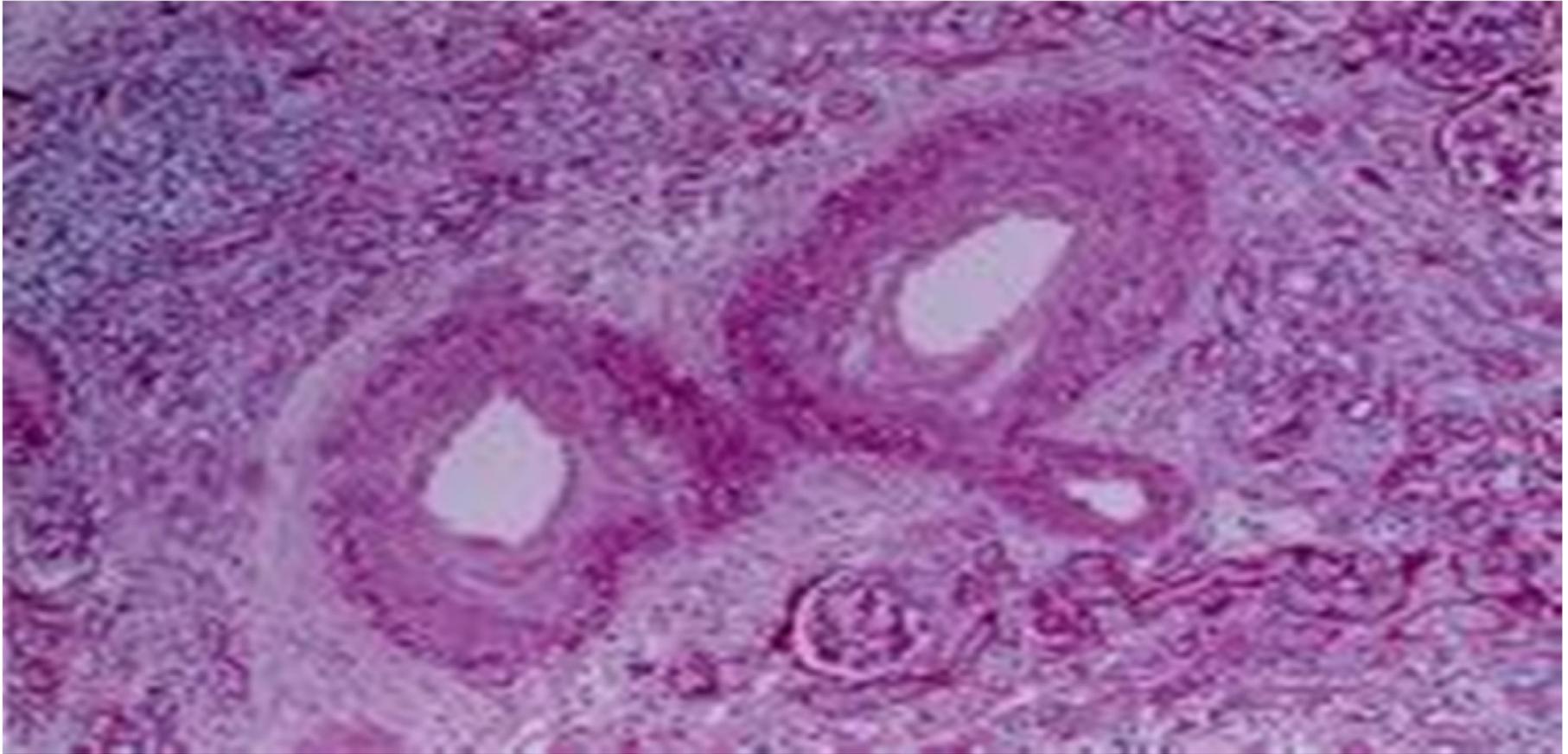
NORMAL KIDNEY



HTN  
NEPHROSCLEROSIS

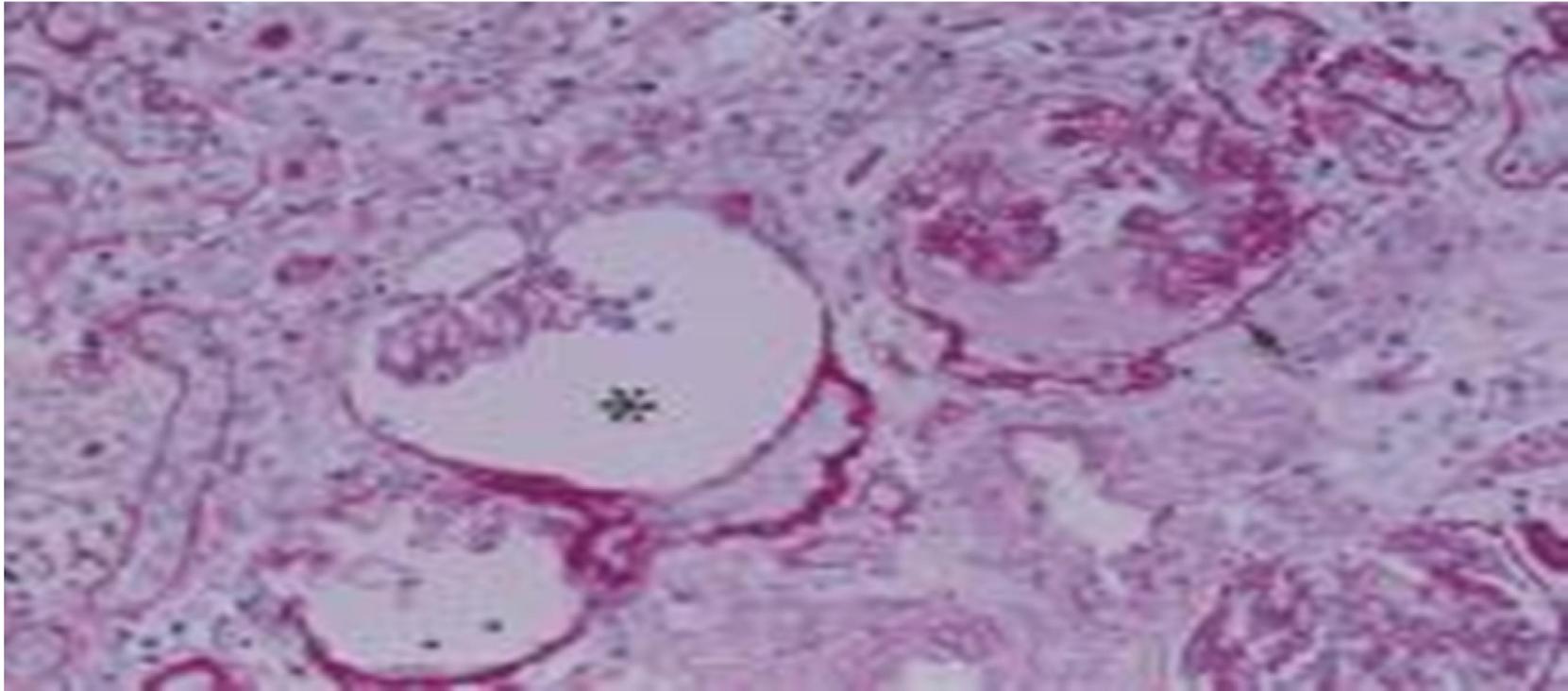


# Diagnosis



Nephrosclerosis. Fibrointimal proliferation of the arcuate artery (periodic acid-Schiff stain at 150X magnification).

# Nephrosclerosis.



The glomerular tuft is shrunken, with wrinkling of the capillary walls (asterisk), global glomerular sclerosis (arrow), and complete obliteration of the capillary loops and glomerular ischemia (periodic acid-Schiff stain at 250X magnification).

# Prevention and treatment of hypertensive renal disease

- Improve Obstetric care to avoid LBW babies
- Adopt healthy lifestyle: Regular exercise, avoid smoking, low salt diet
- Adequate Blood pressure control
- Holistic cardiovascular care
- Early referral for co-management with Nephrologists when indicated

# BLOOD PRESSURE CONTROL

- BP control is paramount
- ACEI, ARB, RI are reno-protective
- Caution with ACEI, ARB, RI in renal artery stenosis
- ACEI, ARB, RI are very useful in diabetics
- Dihydropyridine Ca-antagonists such as amlodipine and nifedipine may worsen proteinuria

# TARGET BP

- Gen population <140/90
- Chronic renal disease
  - proteinuria < 1g/24 hrs <130/80
  - proteinuria >1g/24 hrs <125/75
- GFR < 15mL/min <140/90
  
- No benefit in further reduction - AASK  
102-107 vs <92mmHg

- ACEI + ARB ?

reduce proteinuria well but poorer renal outcome

- Statins if there is dyslipidemia

- Adequate Glycaemic control in Diabetics

# Take Home Message

- Uncontrolled hypertension can accelerate the decline of renal function in patients with primary renal disease
- The available data do not support the hypothesis that high BP is the **ONLY** factor determining ESRD in these patients. Therefore, there must be multiple risk factor evaluation and treatment

# Take Home Message

- ACEIs are of benefit in slowing progression of kidney disease
- Ensure early diagnosis and referral of hypertensive patients with renal complications to Nephrologists.
- ***86% of CKD patients present very late to nephrologist (when they are already in CKD Stage 5)***

*Adejumo OA, Akinbodewa AA, Okaka EI, Alli OA, Ibukun IA. Chronic Kidney Disease in Nigeria; Late presentation is still the norm. Nigerian Medical Journal 2016;57(3):185-189*

THANKS FOR  
YOUR  
ATTENTION