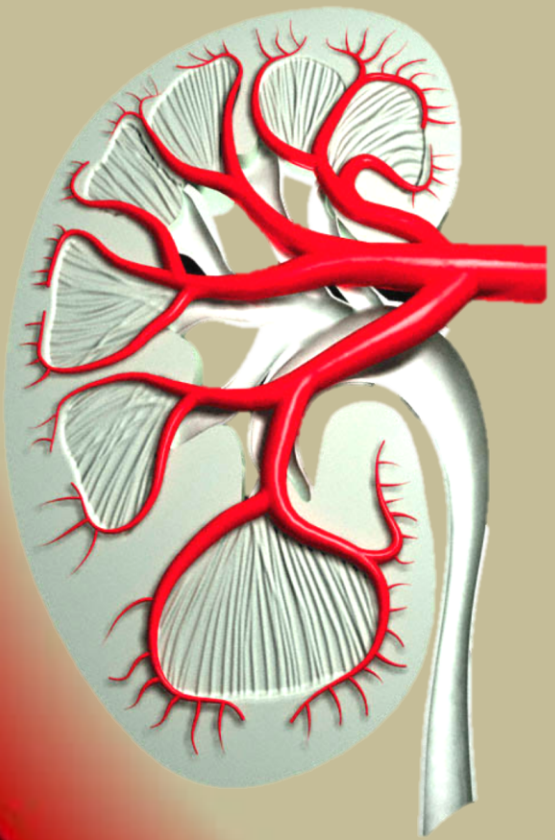
Diabetic Kidney Disease



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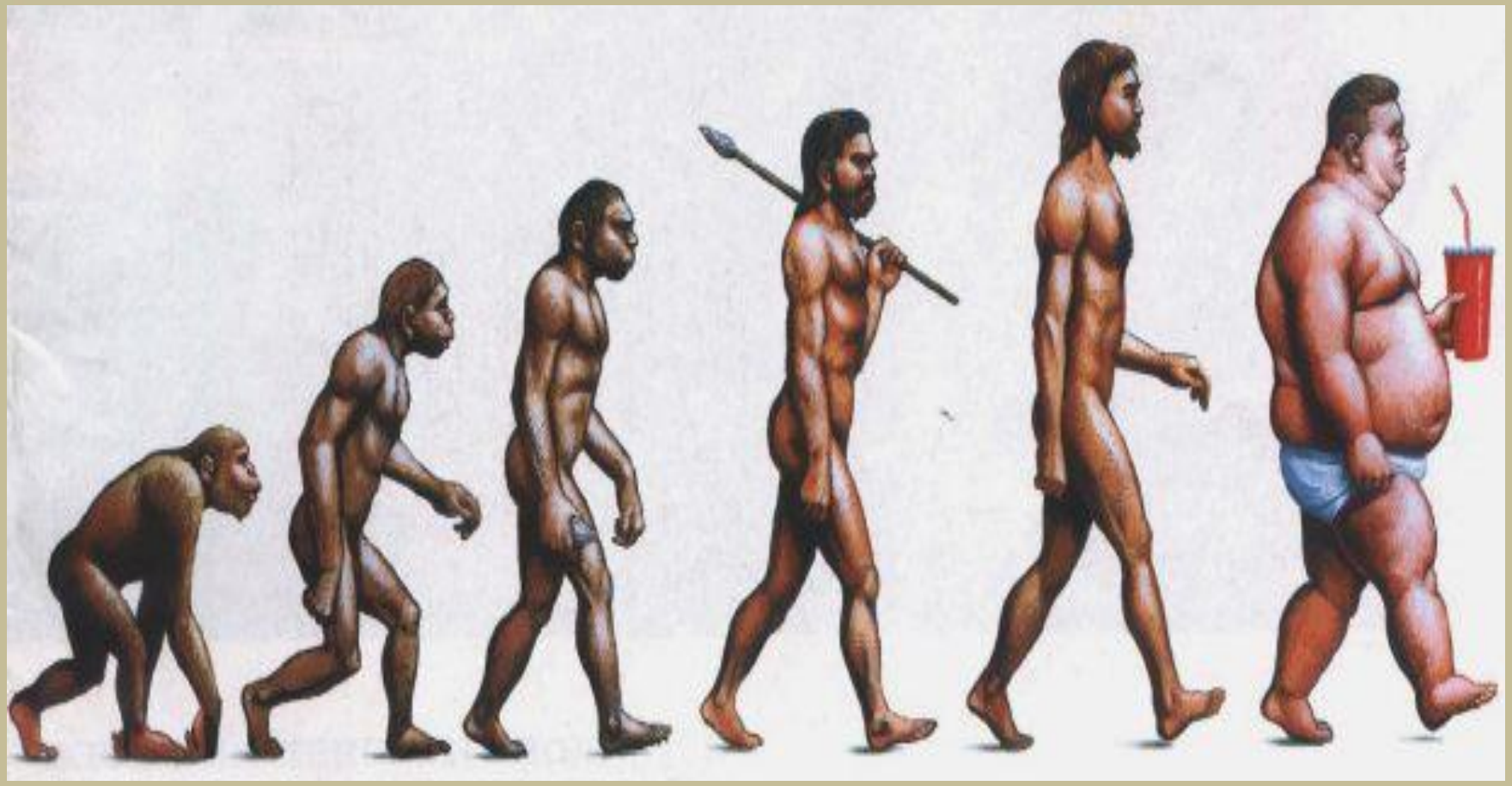
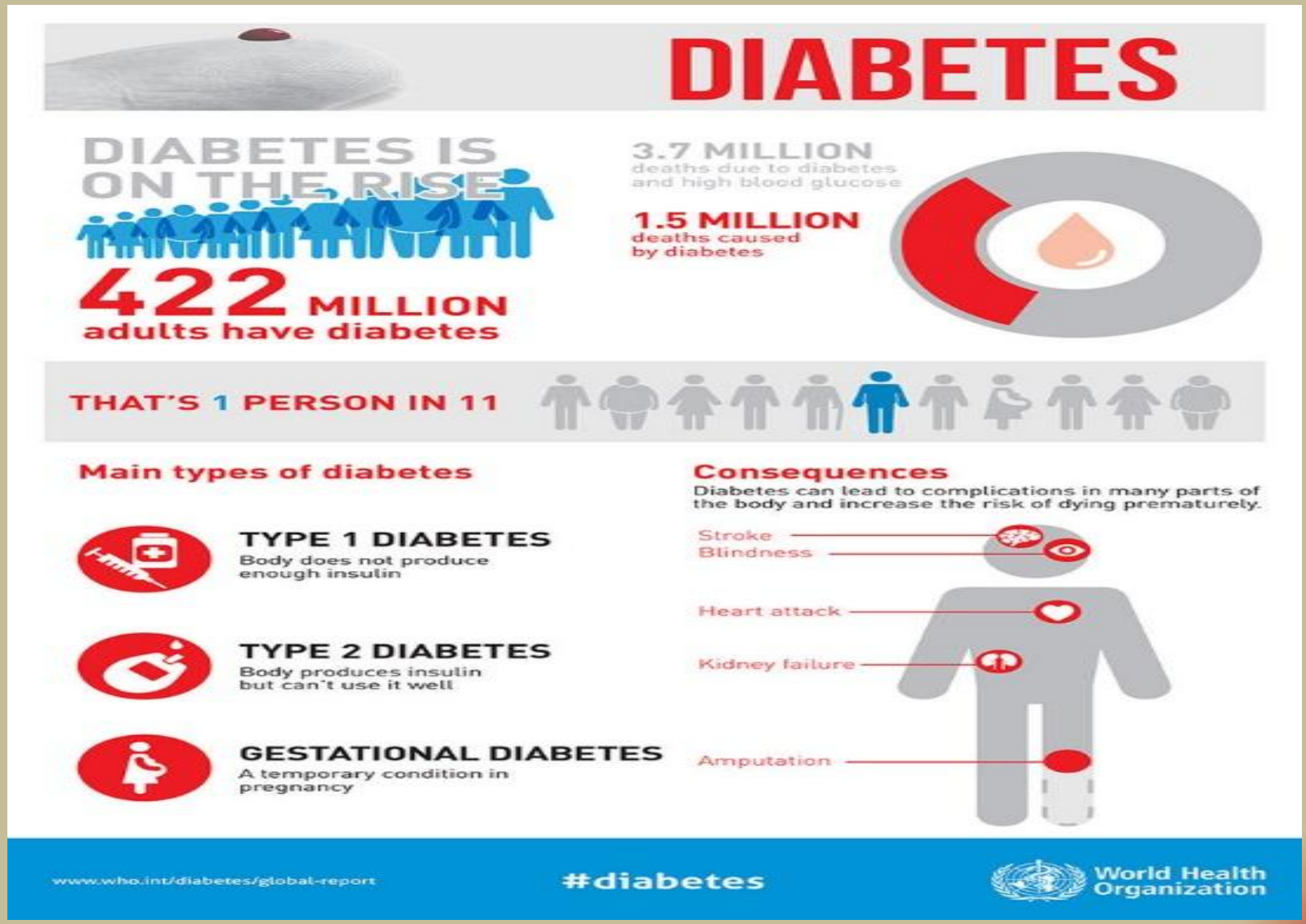
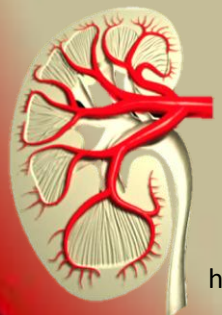


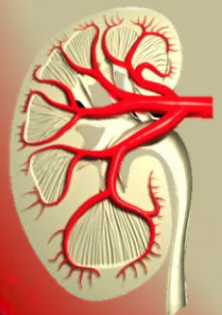
Worldwide Diabetic Prevalence





http://www.who.int/mediacentre/factsheets/fs312/en/

- 422 million people living with Diabetes.
- Which stands to 1 in every 11 adult population.
- It’s expected to rise 642 million by 2040.



WHO, Fact sheet Updated November 2017

Diabetes

- Diabetes mellitus is a clinical syndrome characterized by an increase in plasma blood glucose (hyperglycaemia).
- Fasting blood glucose ≥ 7 mmol/L; or
- 2 hour after breakfast ≥ 11.1 mmol/L; or
- Random blood sugar ≥ 11.1 mmol/L ; or
- HbA1C ≥ 7.0%

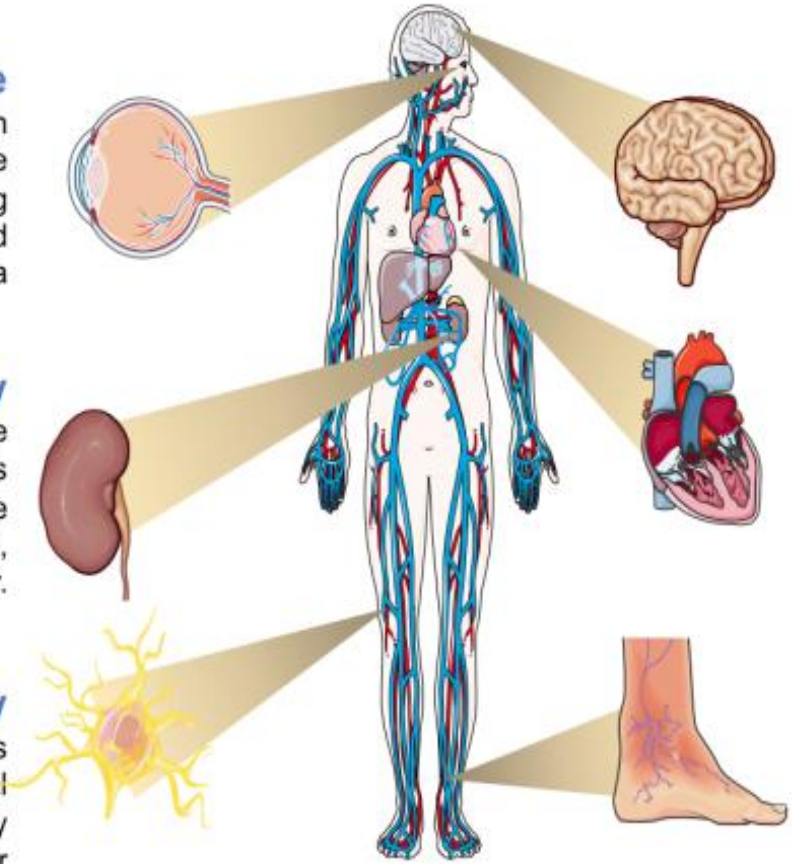
Major Complications of Diabetes

Microvascular

Eye
High blood glucose and high blood pressure can damage eye blood vessels, causing retinopathy, cataracts and glaucoma

Kidney
High blood pressure damages small blood vessels and excess blood glucose overworks the kidneys, resulting in nephropathy.

Neuropathy
Hyperglycemia damages nerves in the peripheral nervous system. This may result in pain and/or numbness. Feet wounds may go undetected, get infected and lead to gangrene.



Macrovascular

Brain
Increased risk of stroke and cerebrovascular disease, including transient ischemic attack, cognitive impairment, etc.

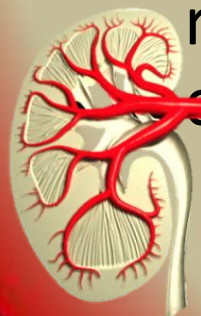
Heart
High blood pressure and insulin resistance increase risk of coronary heart disease

Extremities
Peripheral vascular disease results from narrowing of blood vessels increasing the risk for reduced or lack of blood flow in legs. Feet wounds are likely to heal slowly contributing to gangrene and other complications.

clinical.diabetesjournals.org/content/26/2/77

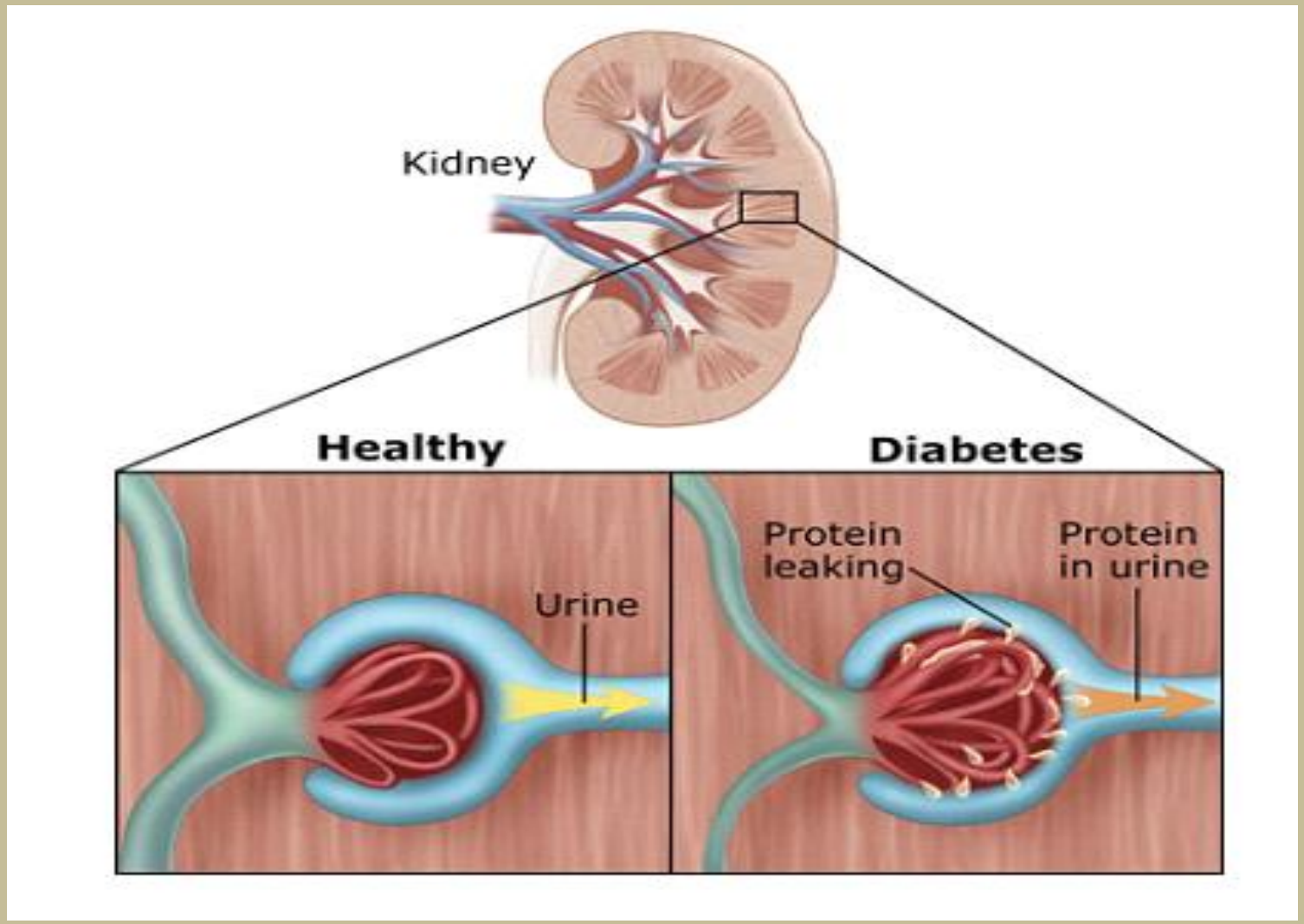
What is DKD?

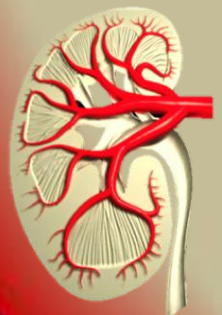
- The term Diabetic Kidney Disease (DKD) refers to kidney disease caused by diabetes.
- which is defined by elevated urine albumin excretion or reduced glomerular filtration rate GFR- (<60 ml/min/1.73 m2) or both persisting for 3 months or more – is a serious complication that occurs in 20% to 40% of all diabetics.
- Diabetic kidney disease (DKD) is a progressive condition and is an important cause of end stage renal disease (ESRD) as well as a risk factor for cardiovascular morbidity and mortality.



1. Clinical Journal of the American Society of Nephrology, www.cjasn.org Vol 13 January, 2017
2. Riview article, Medicine Toady- 2014 Volume 26 Number 01

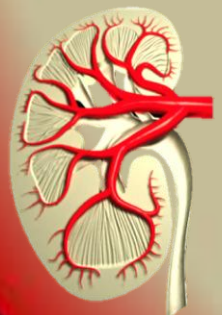
How diabetes affect the kidney





The Prevalence & Impact of Diabetic Kidney disease

- DKD is a major but under-recognized global health burden.
- Between 1990 and 2012, the number of deaths attributed to DKD raised by 94%.
- DKD develops in 40% of diabetics.
- 6 fold increase in mortality rate with DM + DKD



1. NKF Fact Sheets. http://www.kidney.org/news/newsroom/factsheets/FastFacts. Accessed Nov 5, 2014.
2. USRDS. www.usrds.org. Accessed Nov 5, 2014.
3. www.cjasn.org Vol 13 January, 2017 , American Society of Nephrology

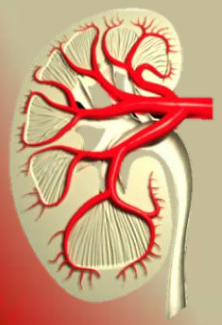
DKD Risk Factors

Modifiable

- Diabetes
- Hypertension
- History of AKI
- Frequent NSAID use

Non-Modifiable

- Family history of kidney disease, diabetes, or hypertension
- Age 60 or older (GFR declines normally with age)
- Race/Ethnicity



*Partial list
AKI, acute kidney injury

Ratio of Diabetes for ESRD

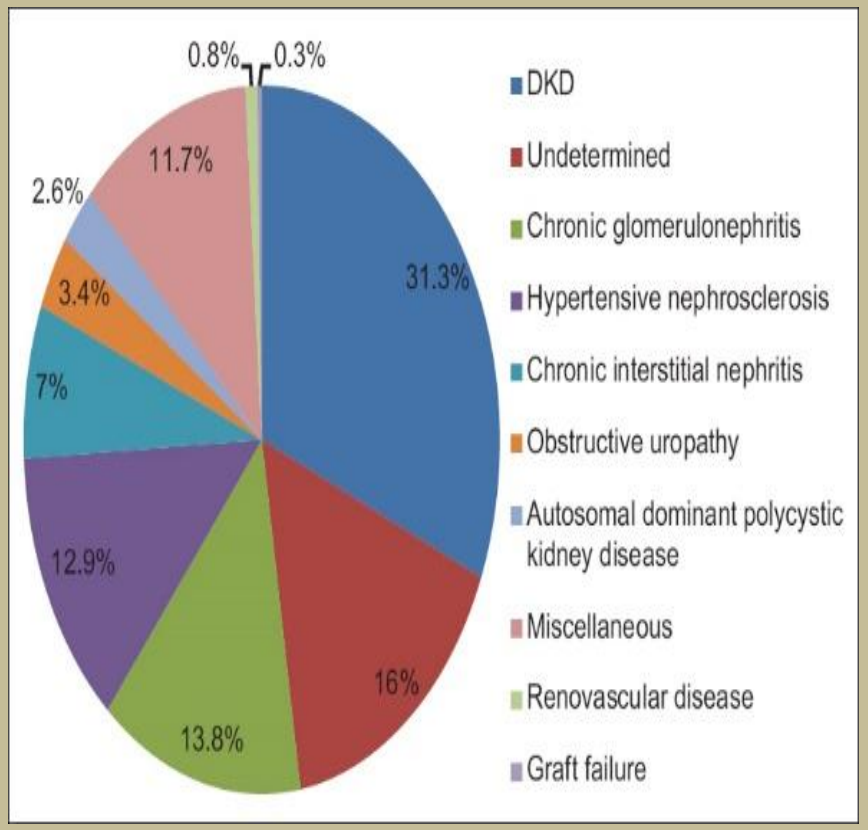


Fig: 1 - Worldwide

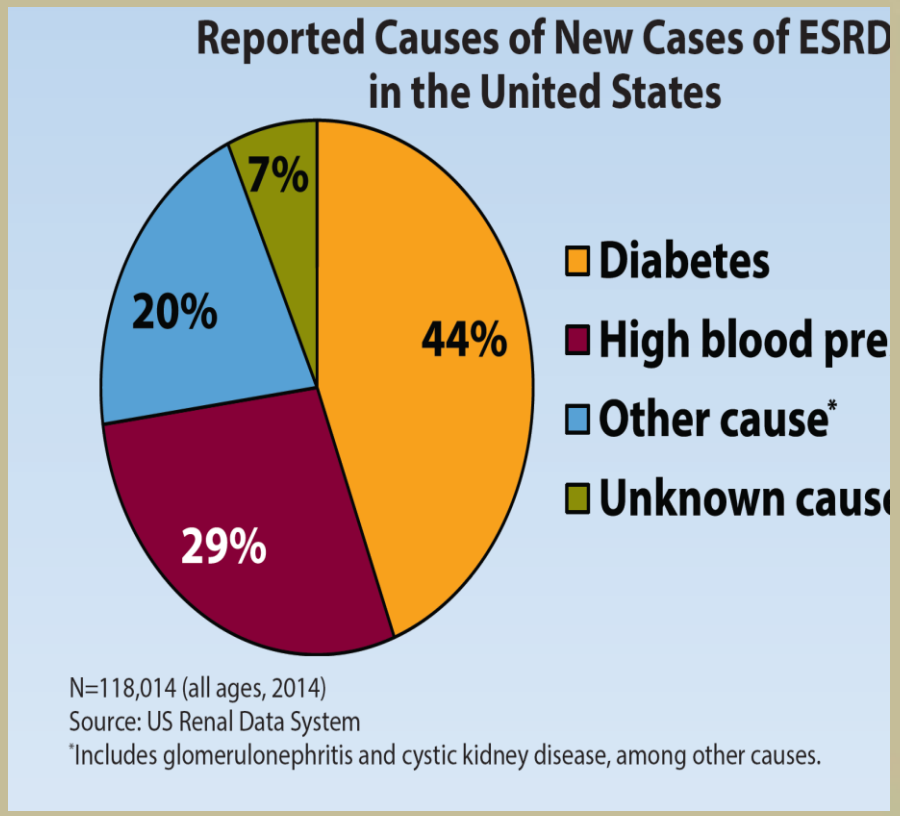


Fig: 2 – United States

Pathogenesis

The first changes coincide with the onset of microalbuminuria

↓

thickening of the glomerular basement membrane

↓

accumulation of matrix material in the mesangium.

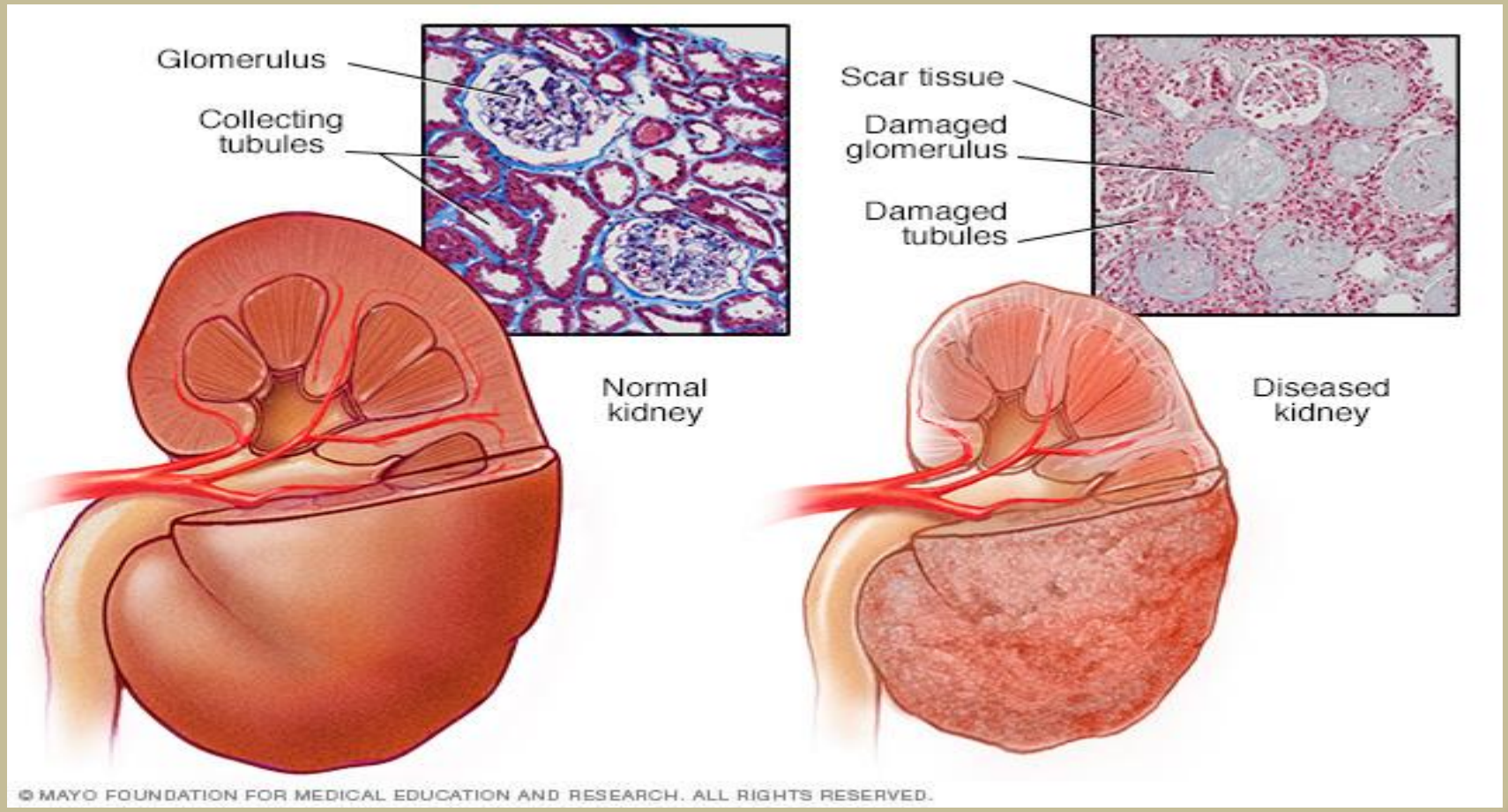
↓

Nodular deposits are characteristic,

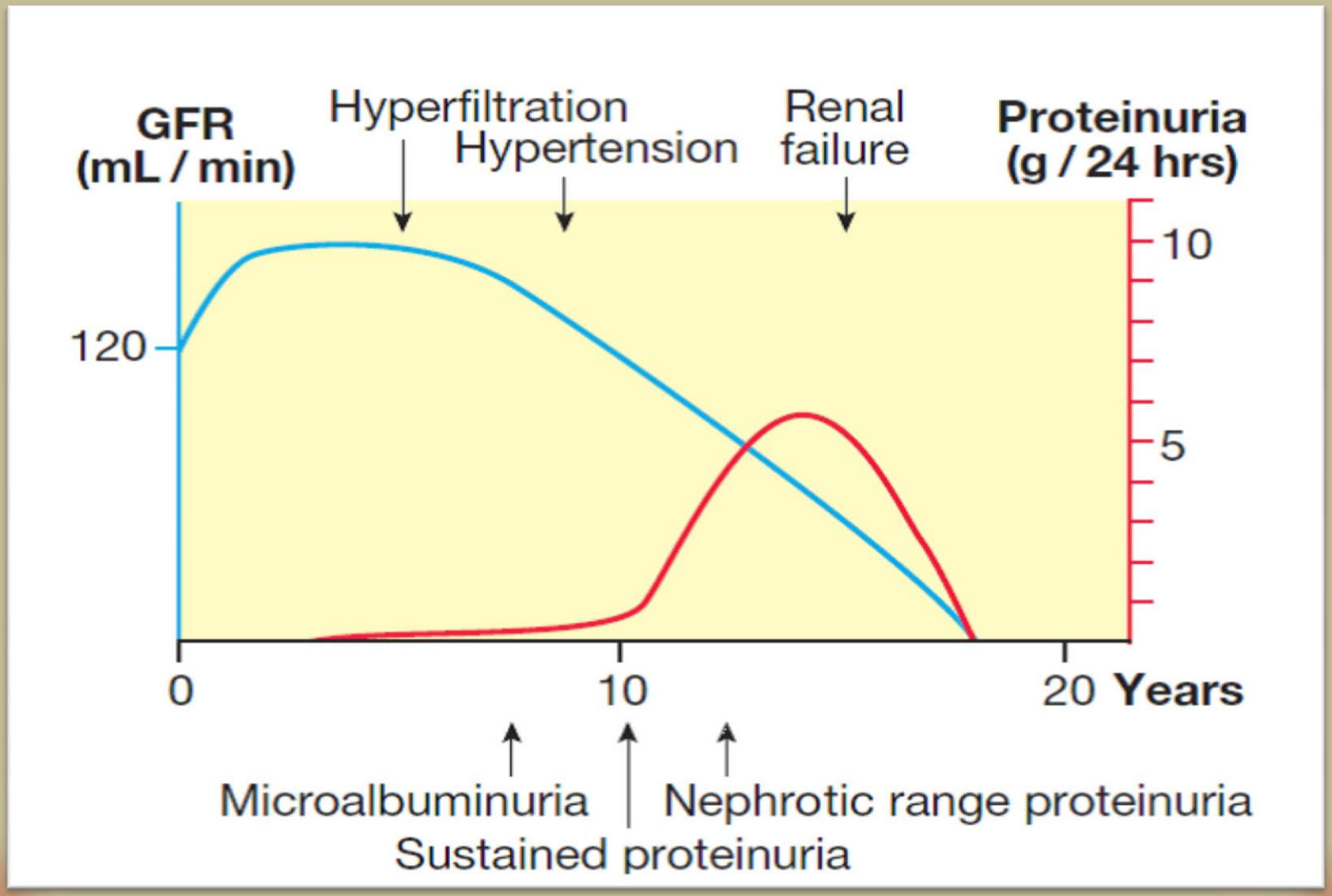
↓

glomerulosclerosis

3-D view of Normal & Diabetic affected Kidney

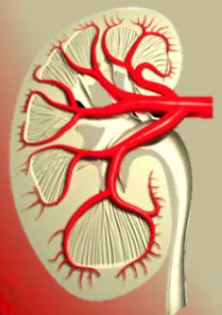


Natural history of diabetic nephropathy



SYMPTOMS OF DIABETIC KIDNEY DISEASE

- There are often no symptoms with early diabetic nephropathy. As the kidney function worsens, symptoms may include:
  - Swelling of the hands, feet, and face
  - Poor appetite
  - Nausea
  - Weakness
  - Itching (end-stage kidney disease) and extremely dry skin



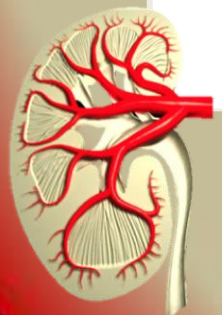
Who are to screen?

- Patients with type 1 diabetes annually from 5 yrs after diagnosis

- Patients with type 2 diabetes annually from time of diagnosis

Old Classification of DKD as Defined by Kidney Disease Outcomes Quality Initiative (KDOQI) Modified and Endorsed by KDIGO

Stage	Description	Classification by Severity	Classification by Treatment
1	Kidney damage with normal or increased GFR	GFR ≥ 90	
2	Kidney damage with mild decrease in GFR	GFR of 60-89	T if kidney transplant
3	Moderate decrease in GFR	GFR of 30-59	recipient
4	Severe decrease in GFR	GFR of 15-29	D if dialysis
5	Kidney failure	GFR < 15	D if dialysis

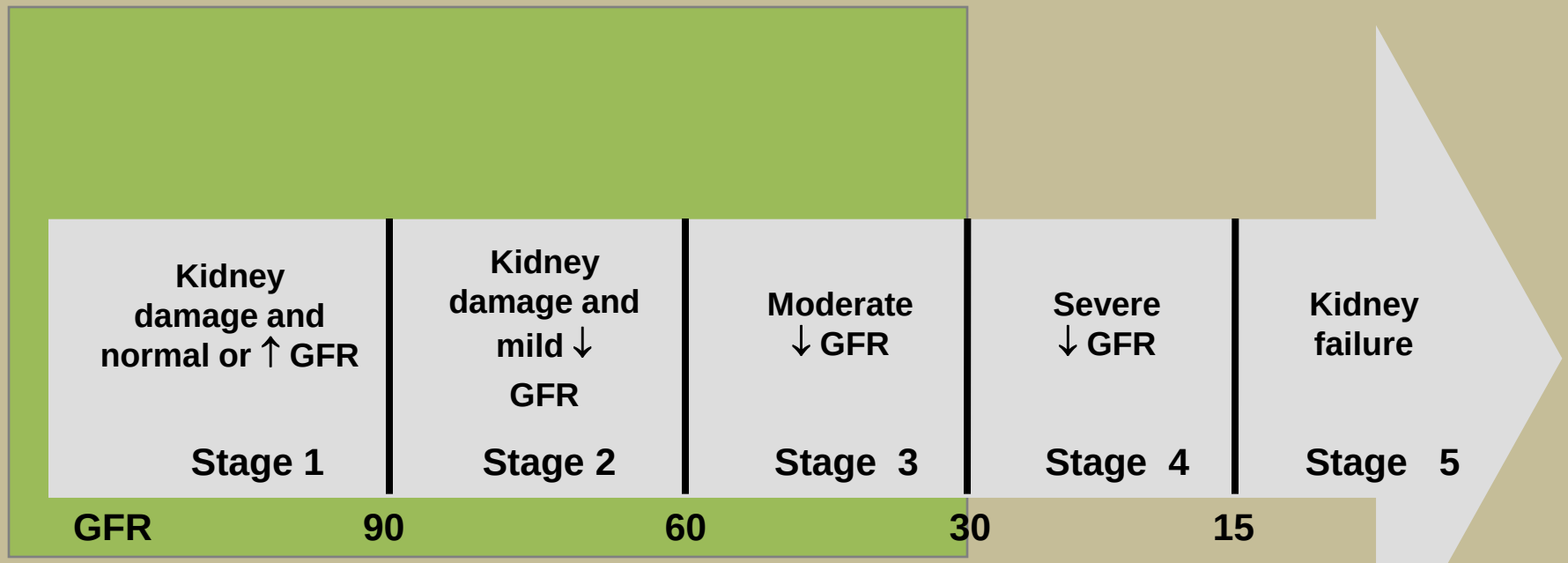


Note: GFR is given in mL/min/1.73^2 m^2

National Kidney Foundation. KDOQI Clinical Practice Guidelines for Chronic Kidney Disease: Evaluation, Classification, and Stratification. Am J Kidney Dis 2002;39(suppl 1):S1-S266

KDIGO, Kidney Disease: Increasing Global Outcomes

Who Should be Involved in the Patient Safety Approach to CKD?



Primary Care Practitioner **Nephrologist**

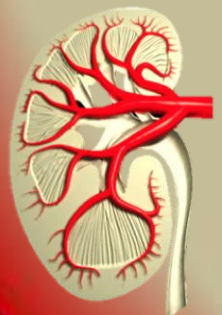
Consult?

Patient safety

The Patient (always)
and other subspecialists (as needed)

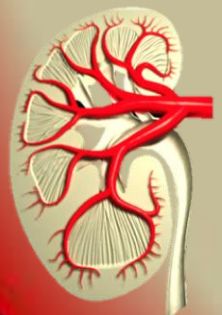
Management of DKD & its Complication

- Standard Therapy
    1. Life style modification Strategies
    2. Blood glucose control
    3. Blood pressure control
    4. Cardiovascular Disease and Risk Management



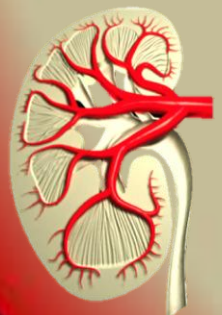
Life style Modification Strategies

1. Smoking cessation
2. Healthy diet
3. Exercise
4. Weight reduction



Blood glucose control-

- We recommend a target HbA1c-
  - HbA1c ~7.0% to prevent or delay progression of the microvascular complications of diabetes, including DKD.
  - Target HbA1c be extended above 7.0% in individuals with co-morbidities or limited life expectancy and risk of hypoglycemia.



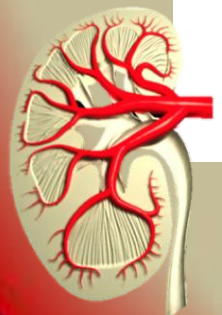
Ref- Target HbA1c National Kidney Foundation. KDOQI clinical practice guideline for diabetes and CKD: 2012 update. Am. J. Kidney Dis. 2012;60:850–886.

OAD for Diabetic kidney disease patient - Metformin

Recommendations for use of Metformin based on eGFR

eGFR level (mL/min per 1.73 m	Action
≥ 60	No renal contraindication to metformin Monitor renal function annually
<60 and ≥45	Continue use
	Increase monitoring of renal function (every 3–6 months)
< 45 and ≥ 30	Prescribe metformin with caution
	Use lower dose (e.g., 50%, or half-maximal dose)
	Closely monitor renal function (every 3 months)
	Do not start new patients on metformin
< 30	Stop metformin

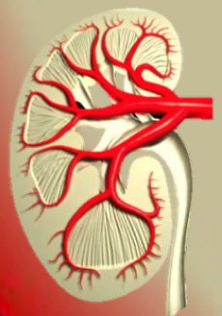
Lipska KJ, et al. Diabetes Care. 2011;34(6):1431-1437.



OAD for Diabetic kidney disease patient – SU & others

Dose Adjustment for Insulin Compounds and Oral Medicines for Diabetes in CKD

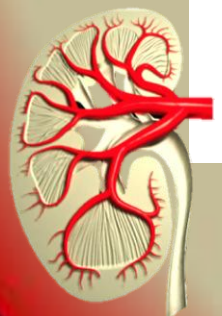
Medication Class and Agents		CKD stages 3, 4, and 5 ND
First-generation sulfonylureas		Avoid use
Second-generation sulfonylureas	Glipizide	No dose adjustment
	Glimepiride	Start conservatively at 1 mg daily
	Glyburide	Avoid use
	Gliclazide	No dose adjustment
Thiazolidinediones	Pioglitazone	No dose adjustment
Alpha-glucosidase inhibitors	Acarbose	Avoid if GFR <30 mL/min/1.73 m



OAD for Diabetic kidney disease patient – DPP4

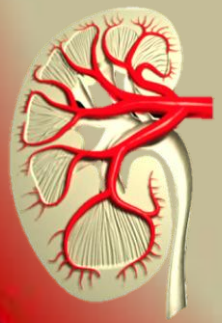
Dose Adjustment for Insulin Compounds and Oral Medicines for Diabetes in CKD

Medication Class and Agents	CKD stages 3, 4, and 5 ND
DPP-4 inhibitor	
Sitagliptin	GFR >50 mL/min/1.73 m2: 100 mg daily GFR 30-50 mL/min/1.73 m2: 50 mg daily
Saxagliptin	GFR > 50 mL/min/1.73 m GFR < 50 mL/min/1.73 m
Linagliptin	No dose adjustment
Vildagliptin	GFR > 50 mL/min/1.73 m GFR < 50 mL/min/1.73 m
Incretin mimetic	
Exenatide	Not recommended in GFR <30 mL/min/1.73 m
Liraglutide	Not recommended in GFR <60 mL/min/1.73 m



2. Blood Pressure Control

- Slow decline in kidney function
- Blood pressure control[1]
  - ACR <30 mg/g: ≤140/90 mm Hg
  - ACR 30-300 mg/g: ≤130/80 mm Hg*
  - ACR >300 mg/g: ≤130/80 mm Hg
  - Individualize targets and agents according to age, coexistent CVD, and other comorbidities
  - ACEi or ARB (ACEi is the first line treatment for diabetic hypertensive)



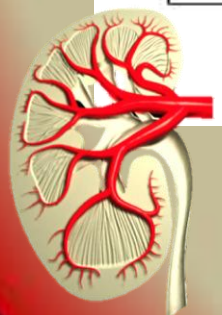
*Reasonable to select a goal of 140/90 mm Hg, especially for moderate albuminuria (ACR 30-300 mg/g.)[2]

1) Kidney Disease: Improving Global Outcomes (KDIGO) Blood Pressure Work Group. *Kidney Int Suppl*. (2012);2:341-342.
2) KDOQI Commentary on KDIGO Blood Pressure Guidelines. *Am J Kidney Dis*. 2013;62:201-213.

Guideline recommendation for BP target in DKD

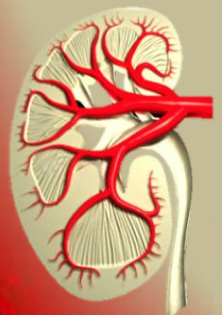
	KDIGO	JNC 8
Aluminuria < 30 mg/d	≤140 / 90 (1B)	≤ 140 / 90
Aluminuria 30-300 mg/d	≤130 / 80 (2D) ACEI or ARB (2D)	E for SBP A for DBP if over 30 E for DBP if under 30
Aluminuria > 300 mg/d	≤130 / 80 (2C) ACEI or ARB (1B)	ACEI or ARB for all CKD regardless of diabetic or proteinuric status

JNC8. JAMA. 2014;5;311(5):507-20.
National Kidney Foundation. KDOQI clinical practice guideline for diabetes and CKD: 2012 update. Am. J. Kidney Dis. 2012;60:850–886.



Slowing DKD Progression: ACEi *or* ARB

- Risk/benefit should be carefully assessed in the elderly and medically fragile
- Check labs after initiation
  - If less than 25% SCr increase, continue and monitor
  - If more than 25% SCr increase, stop ACEi and evaluate for RAS
- Continue until contraindication arises, no absolute eGFR cutoff
- Better proteinuria suppression with low Na diet and diuretics
- Avoid volume depletion
- Avoid ACEi and ARB in combination[1,2]
  - Risk of adverse events (impaired kidney function, hyperkalemia)



1) Kunz R, et al. *Ann Intern Med*. 2008;148:30-48.
2) Mann J, et al. ONTARGET study. *Lancet*. 2008;372:547-553.

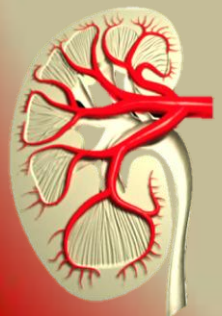
3.Cardiovascular Disease and Risk Management

- Lipid lowering therapy
  - In adults >50 yrs, statin when eGFR ≥ 60 ml/min/1.73m^2; statin or statin/ezetimibe combination when eGFR < 60 ml/min/1.73m^2
  - In adults < 50 yrs, statin if history of known CAD, MI, DM, stroke
- Aspirin is indicated for secondary but not primary prevention

Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. *Kidney Int Suppls*. 2013;3:1-150.

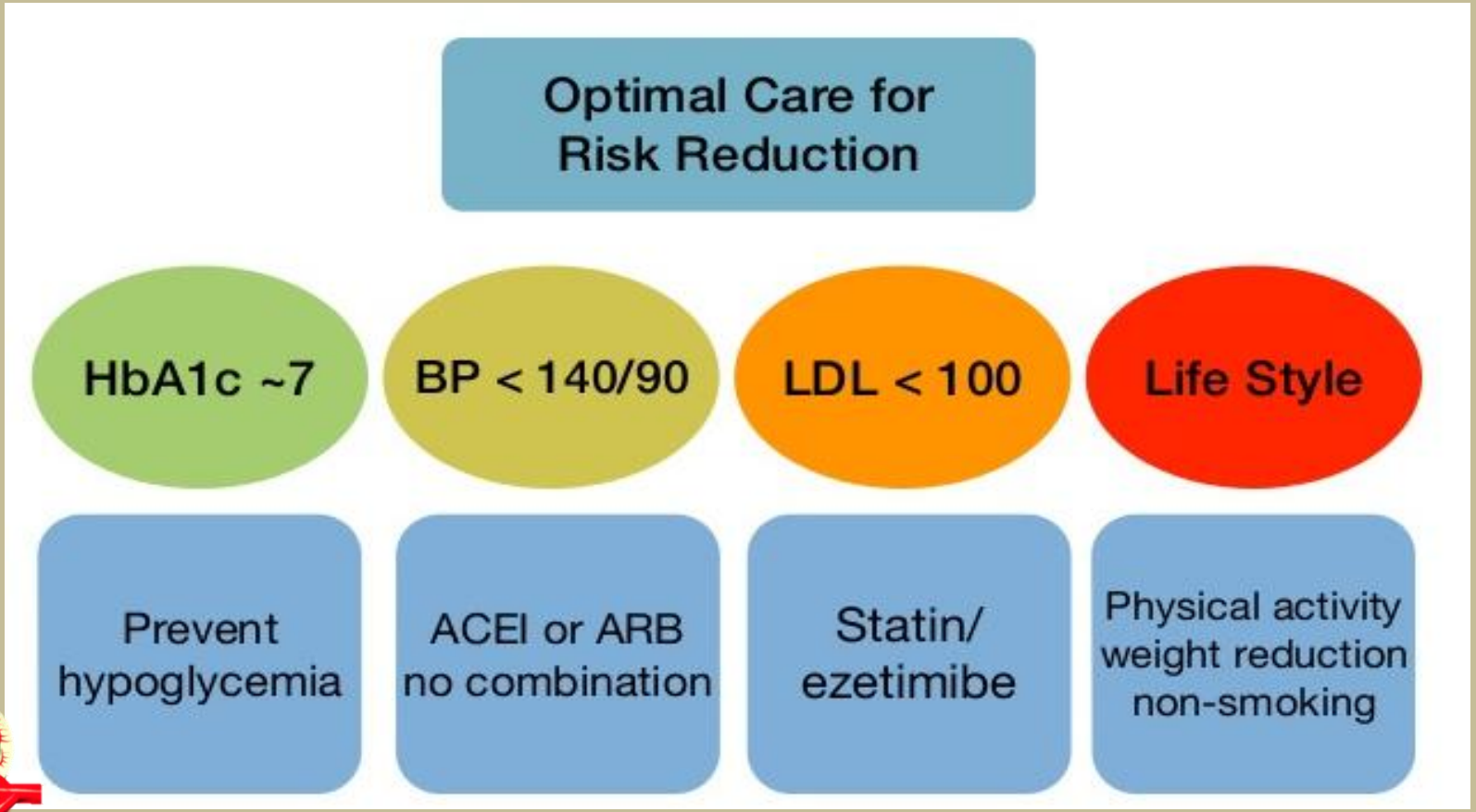
Detect and Manage CKD Complications

- Metabolic acidosis
  - Usually occurs later in CKD
  - Serum bicarb >22mEq/L
  - Correction of metabolic acidosis may slow CKD progression and improve patients functional status[1,2]
- Hyperkalemia
  - Reduce dietary potassium
  - Stop NSAIDs, COX-2 inhibitors, potassium sparing diuretics (Spironolactone)
  - Stop or reduce beta blockers, ACEi/ARBs
  - Avoid salt substitutes that contain potassium

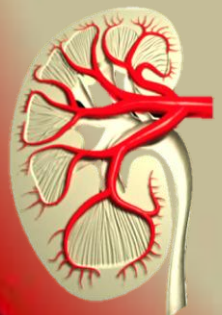


1) Mahajan, et al. *Kidney Int*. 2010;78:303-309.
2) de Brito-Ashurst I, et al. *J Am Soc Nephrol*. 2009;20:2075-2084.

Key point to remember for management of DKD



- Early diagnosis of DN remains critical in preventing long term devastating outcomes of renal loss.
- Internist should play an important role.



for Your Attention