Comprehensive education course for Asian diabetes educators
- Title: Seeking for the united collaboration in Asia through education

Chronic complications other than DM foot/neuropathy

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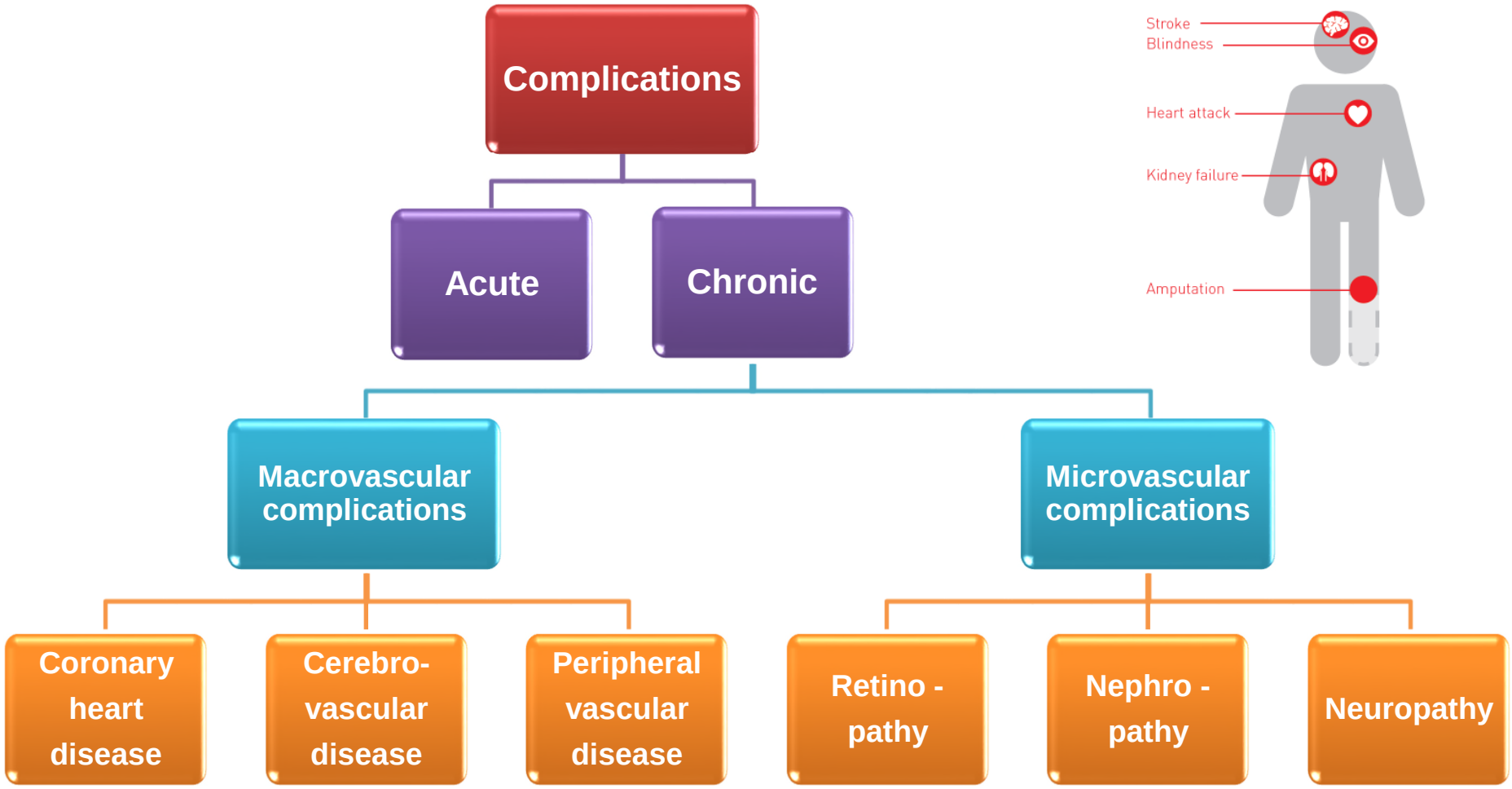
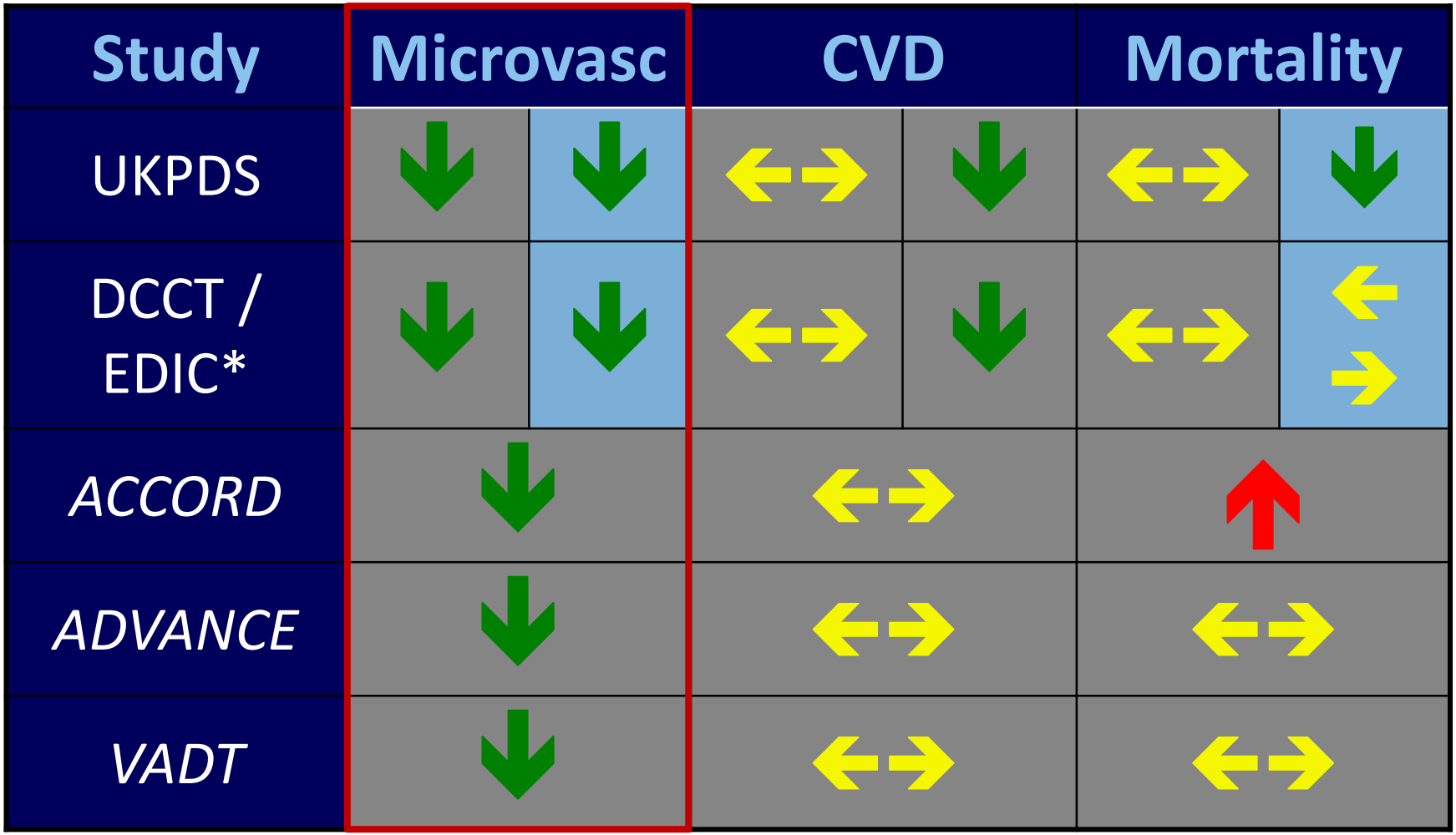
Korean Diabetes Association

Complications of Diabetes



Impact of Intensive Therapy for Diabetes



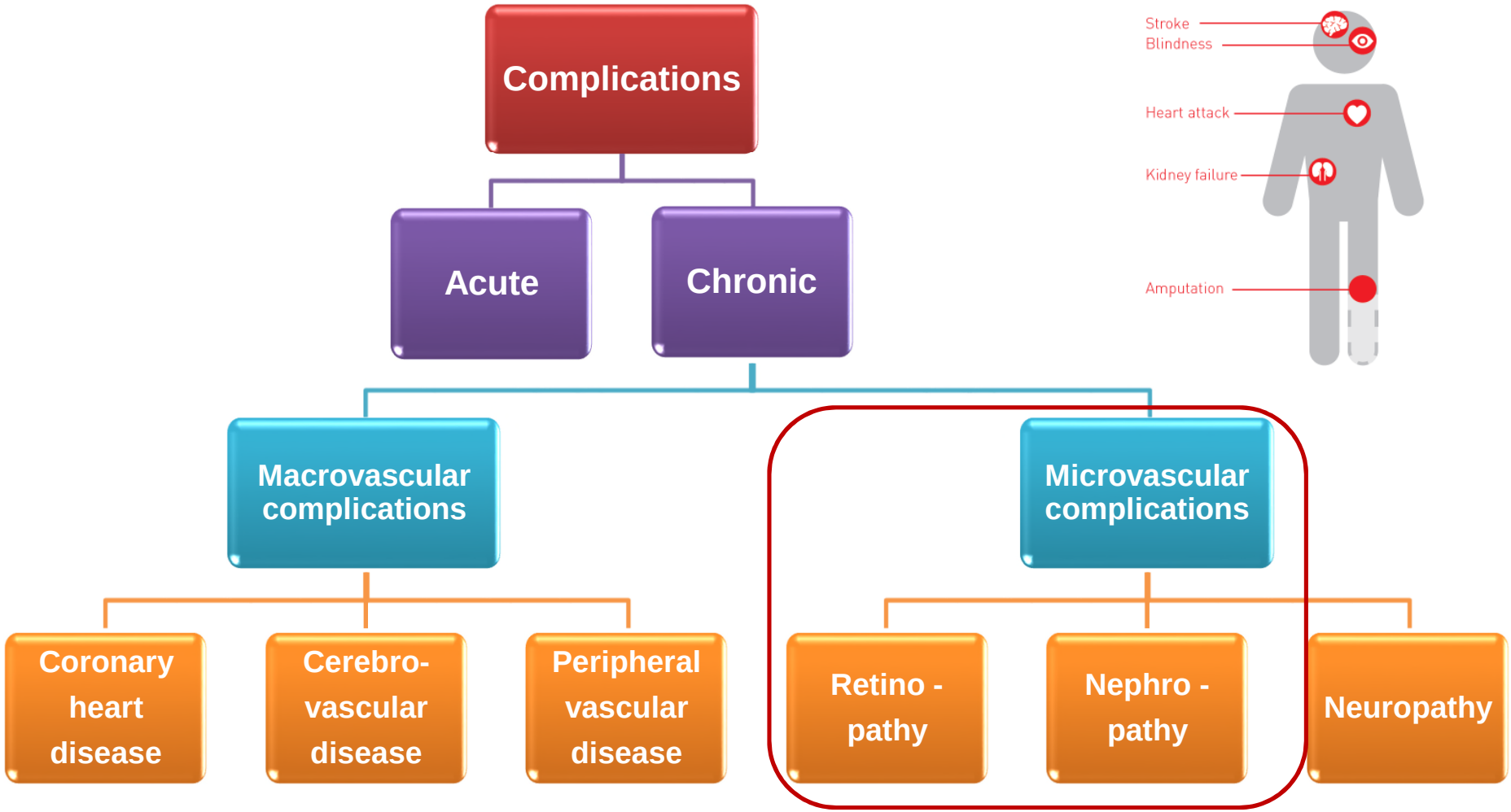
Kendall DM, Bergenstal RM. © International Diabetes Center 2009

UK Prospective Diabetes Study (UKPDS) Group. *Lancet* 1998;352:854.
Holman RR et al. *N Engl J Med*. 2008;359:1577. DCCT Research Group. N Engl J Med 1993;329;977.
Nathan DM et al. *N Engl J Med*. 2005;353:2643. Gerstein HC et al. *N Engl J Med*. 2008;358:2545.
Patel A et al. N Engl J Med 2008;358:2560. Duckworth W et al. N Engl J Med 2009;360:129. (erratum: Moritz T. *N Engl J Med* 2009;361:1024)

Initial Trial

Long Term Follow-up

Complications of Diabetes



Microvascular Complications

Microvascular complications

- **Newly diagnosed T2DM patients**
  - **Above 50% : more than one complications**
    - **Retinopathy : 21%**
    - **Nephropathy : 7%**
    - **S-Cr ≥ 1.4 mg/dL : 3%**
    - **Erectile dysfunction : 20%**

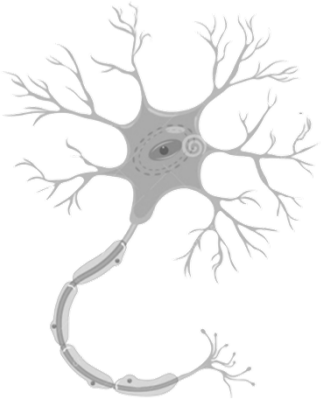
1.UKPDS Group. Diabetes Research 1990, 2.Gross JL et al. Diabetes Care, 2005,

Microvascular complications

- **Diabetic Retinopathy**

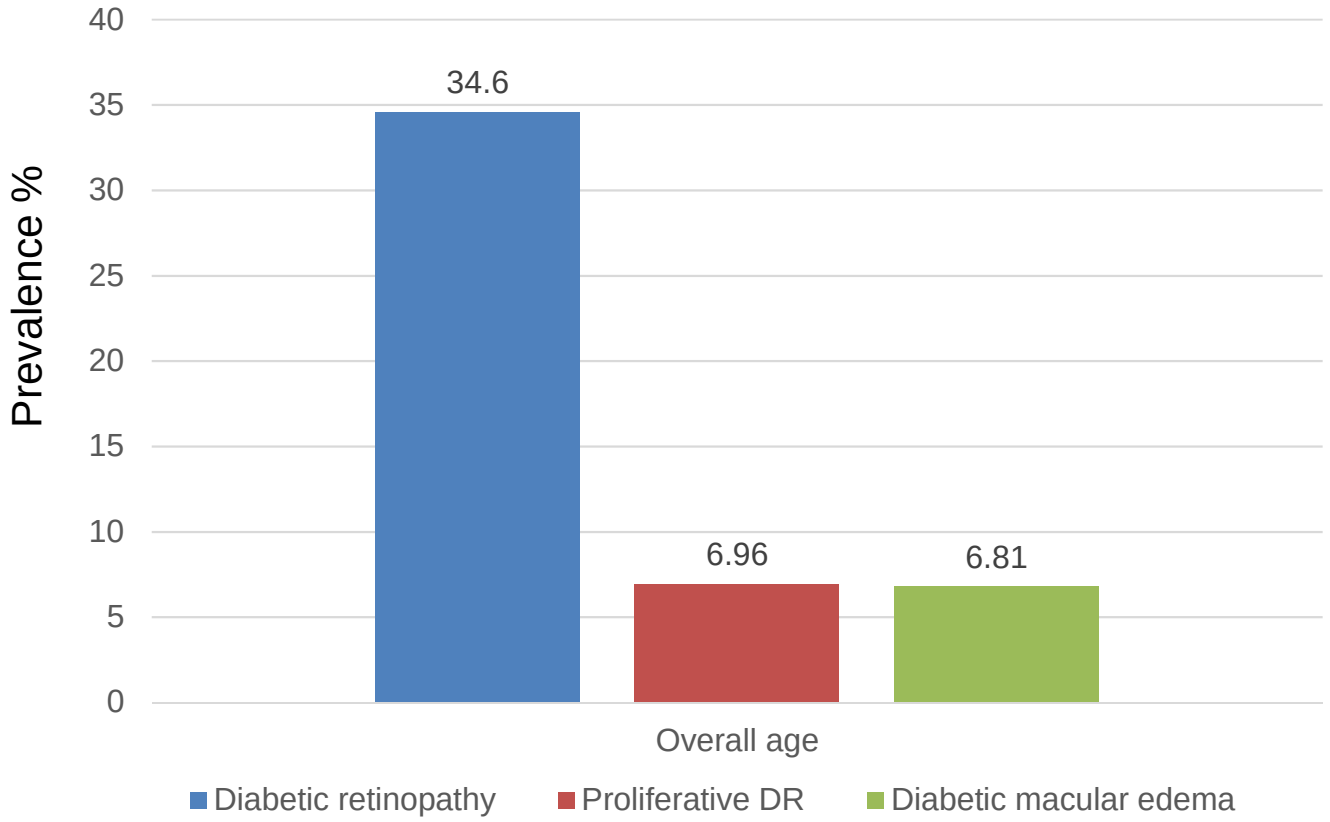
- **Diabetic Kidney Disease**

- **Diabetic Neuropathy**



Diabetic retinopathy

- **The most frequent cause of new cases of blindness among adults aged 20–74 years in developed countries.**



Diabetes Care 2018;41(Suppl. 1):S105–S118
Diabetes Care 35:556–564, 2012

Eye disease in people with diabetes

- Diabetic retinopathy
- Diabetic cataract
- Cranial nerve palsies leading to diplopia
- Diabetic papillopathy

Transient changes in vision

Cause - changes in blood glucose levels cause osmotic changes in the lens of the eye

As a result, visual acuity can increase or decrease

This change is not permanent and will resolve when blood glucose levels stabilize

Risk factors

- Duration of diabetes
- Chronic hyperglycemia
- Diabetic kidney disease
- Hypertension
- Dyslipidemia
- Pregnancy

Diabetes Care 2018;41(Suppl. 1):S105–S118

Retinopathy in people with diabetes

A silent complication with no initial symptoms

- When symptoms occur, treatment is more complicated
- Screening for retinopathy is of the utmost importance

(Kempen, O'Colmain, Leske, et al., 2004)

Screening

Initial dilated and comprehensive eye examination

Type 1	• Within 5 years after the onset of diabetes
Type 2	• At the time of the diagnosis

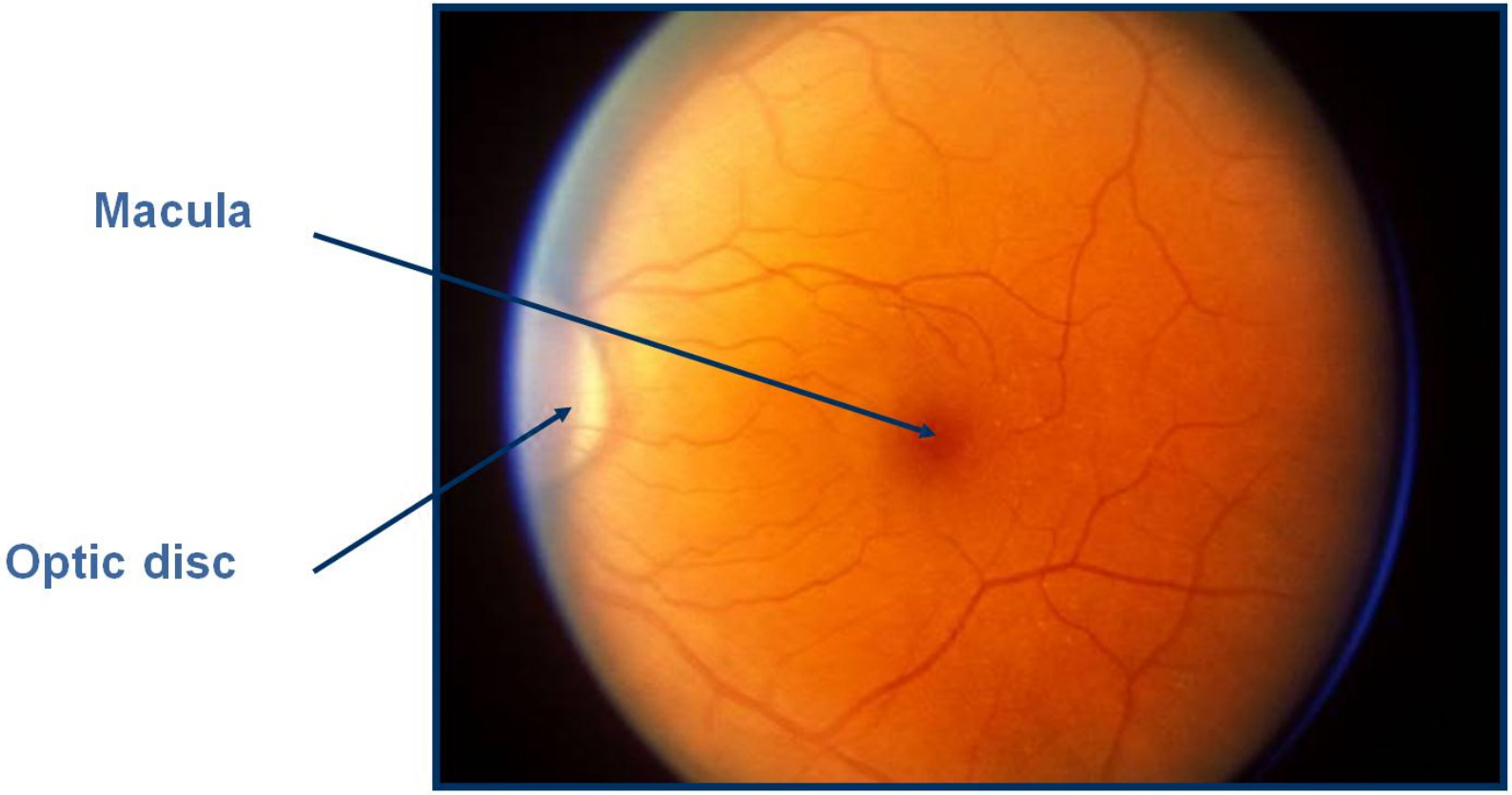
Diabetes Care 2018;41(Suppl. 1):S105–S118

Screening of pregnant women

- Pregnancy is associated with a rapid progression of diabetic retinopathy.
- Women with preexisting type 1 or type 2 diabetes who are planning pregnancy or pregnant should be counseled on the risk of development and/or progression of diabetic retinopathy
- Eye examinations should occur
  - before pregnancy or
  - in the first trimester in patients
- Monitoring
  - Every trimester and for 1 year postpartum as indicated by the degree of retinopathy

Diabetes Care 2018;41(Suppl. 1):S105–S118
2019 Treatment Guidelines for Diabetes

Normal retina (LEFT)



Diabetic retinopathy

1. **Non-proliferative diabetic retinopathy:**

   minimal, mild, moderate, severe

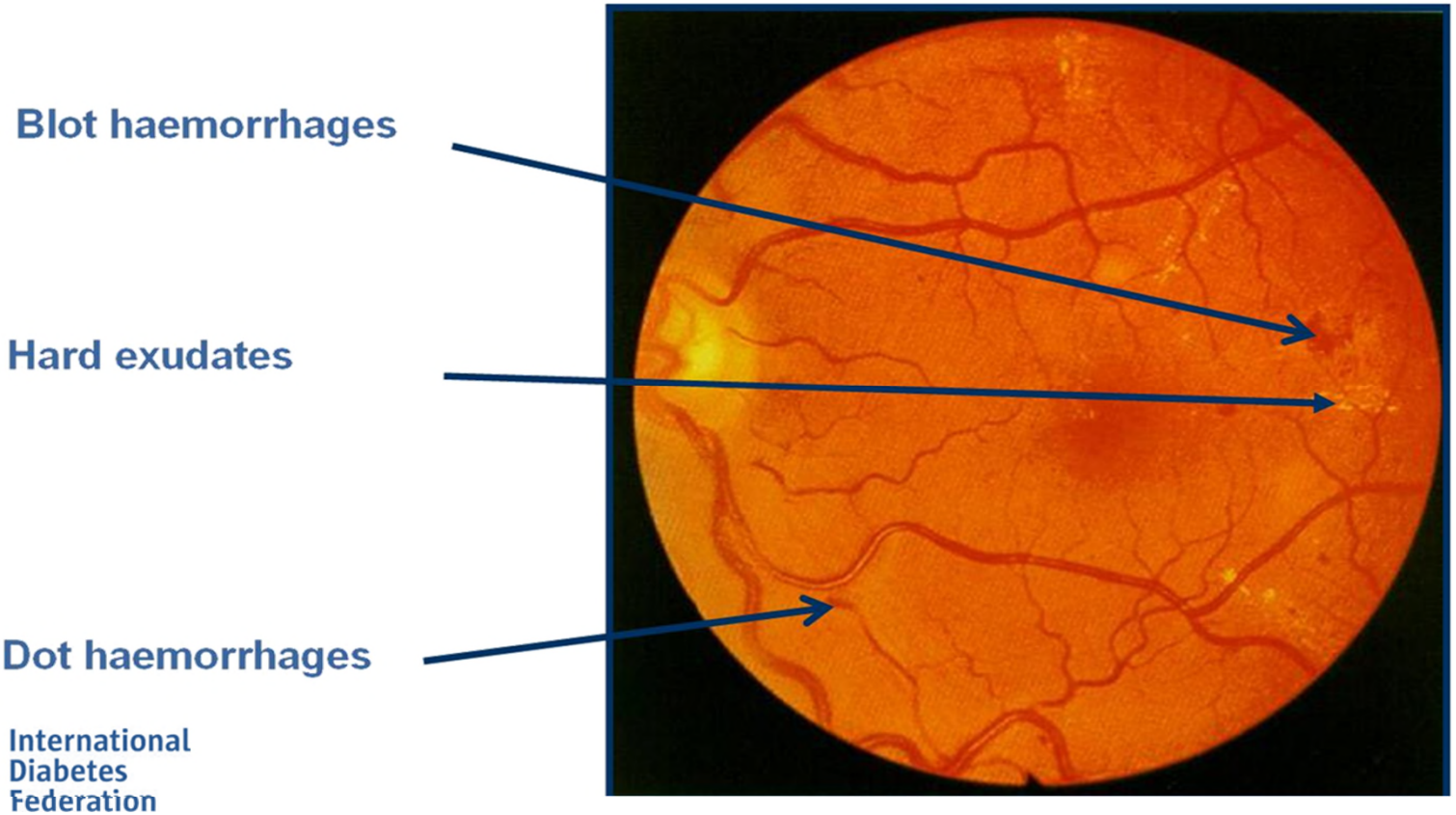
2. **Proliferative Diabetic Retinopathy (PDR):**

   early PDR, high-risk PDR, advanced PDR

* Maculopathy, macular edema seen most often

Mild-moderate non-proliferative diabetic retinopathy (NPDR)

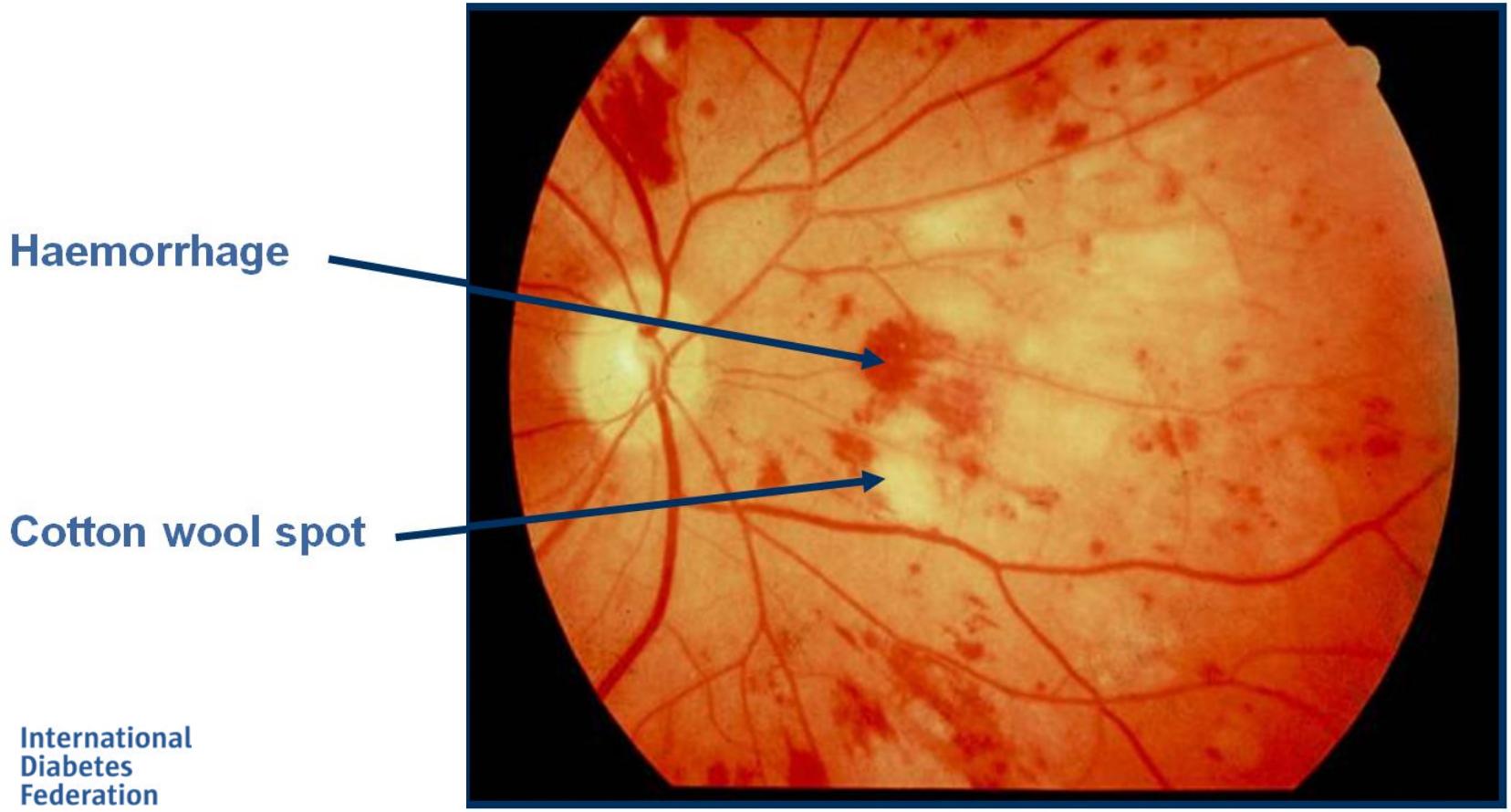
1. Minimal retinopathy : only one or two microaneurysms
2. Mild NPDR : microaneuryms as well as dot or blot haemorrhages
3. Moderate NPDR : hard exudates – deposits of lipids



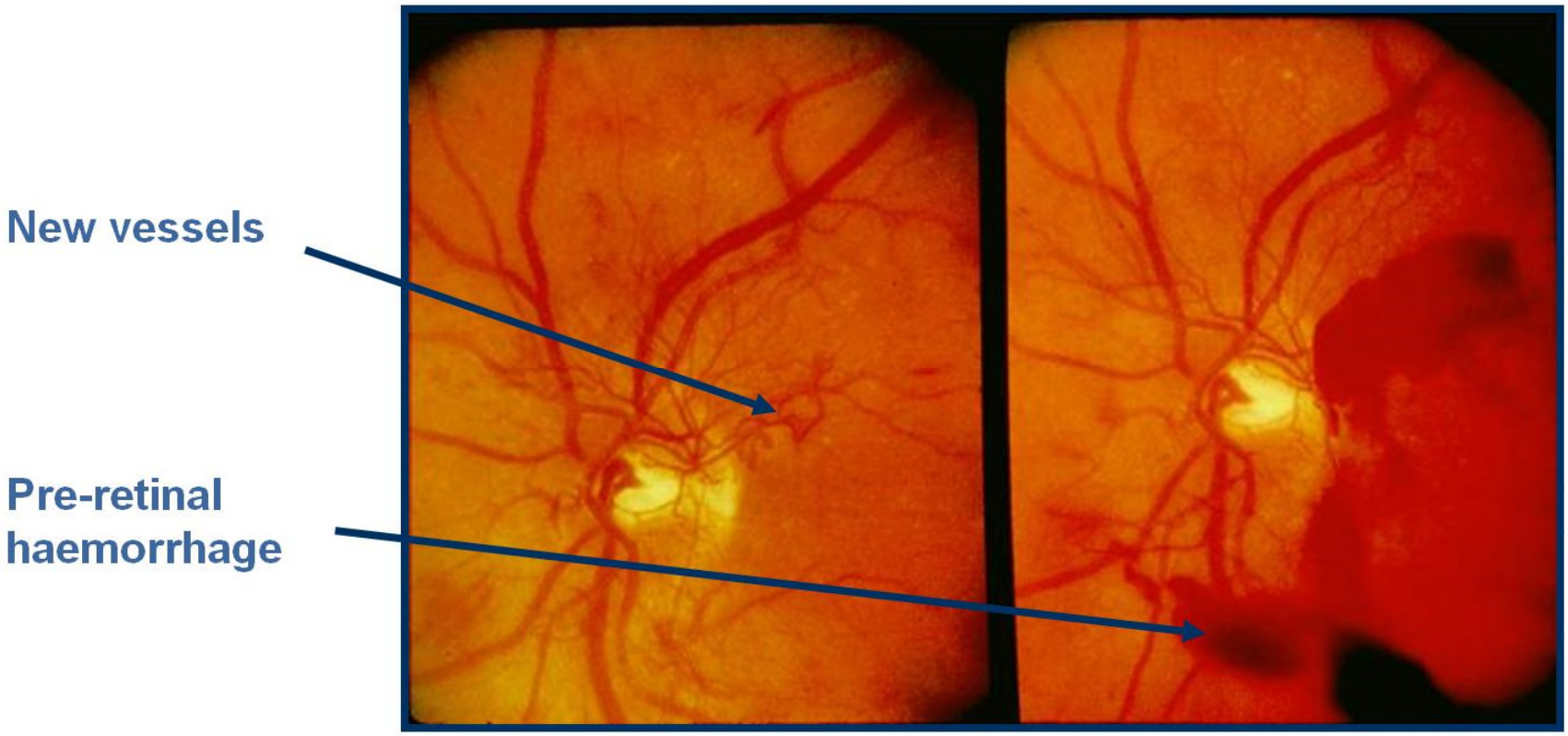
International Diabetes Federation

Severe non-proliferative retinopathy

1. Venous beading or looping
2. Multiple haemorrhages
3. Multiple soft exudates or cotton wool spots which indicate areas of ischaemia
4. A condition called intra-retinal microvascular abnormalities (IRMA)

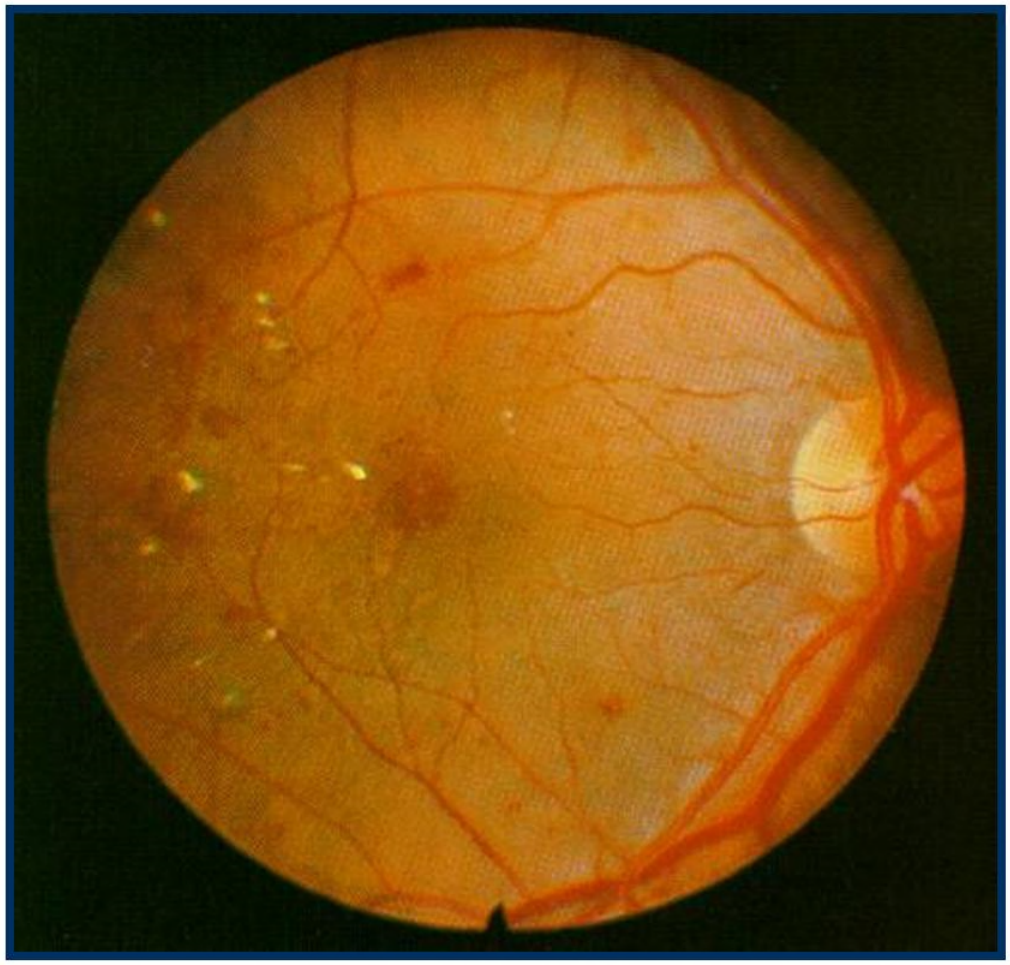


Proliferative retinopathy



Macular oedema

the swelling of the macula
Eyesight is reduced
Laser therapy is required.



Recommendation

- **Optimize glycemic control**
- **Optimize blood pressure**
- **Optimize serum lipid control**

Reduce the risk
or
slow the progression

Diabetes Care 2019;42(Suppl. 1):S124–S138
2019 Treatment Guidelines for Diabetes

Recommendation

With no retinopathy

- **Repeat the examination every 1- 2 years**

With retinopathy

- **Refer to ophthalmologist**
  - subsequent dilated retinal examinations should be repeated at least annually by an ophthalmologist or optometrist.

- **Retinopathy is progressing or sight-threatening**
  - then examinations will be required more frequently

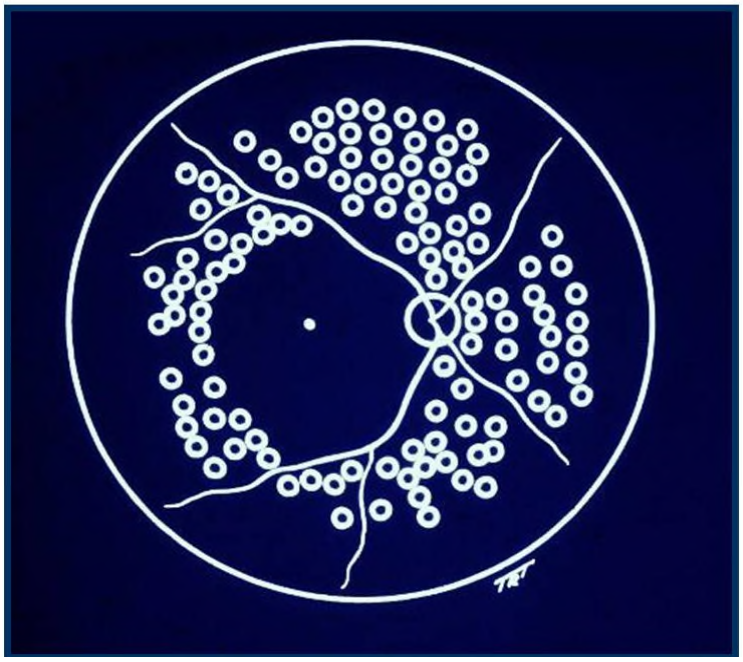
Diabetes Care 2019;42(Suppl. 1):S124–S138
2019 Treatment Guidelines for Diabetes

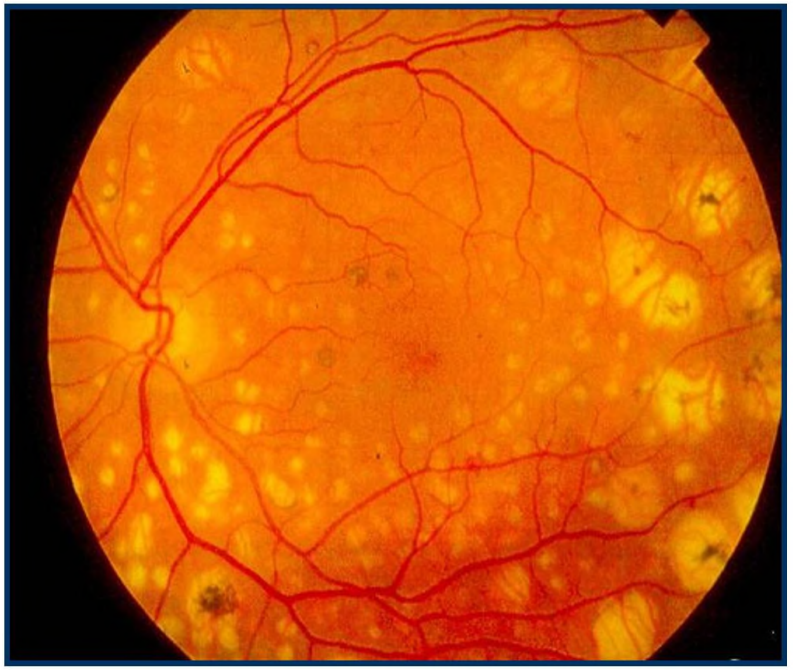
Treatment

- Promptly refer **to ophthalmologist**
  - Any level of macular edema
  - Severe nonproliferative diabetic retinopathy
  - Proliferative diabetic retinopathy

Treatment

- Laser photocoagulation therapy
  - in patients with high-risk proliferative diabetic retinopathy
  - in some cases, severe nonproliferative diabetic retinopathy





(Photo courtesy of Dr. Jeffry Gerson O.D., F.A.A.O. WestGlen Eyecare & Omni Eye Center of Kansas City)

Diabetes Care 2019;42(Suppl. 1):S124–S138
2019 Treatment Guidelines for Diabetes

Treatment

- Intravitreal injections of anti–vascular endothelial growth factor
  - for central-involved diabetic macular edema
  - to reduce the risk of vision loss in patients with proliferative diabetic retinopathy

- The presence of retinopathy is not a contraindication to aspirin therapy for cardioprotection, as aspirin does not increase the risk of retinal hemorrhage.

Diabetes Care 2019;42(Suppl. 1):S124–S138
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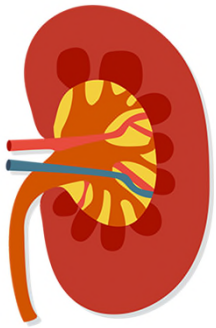
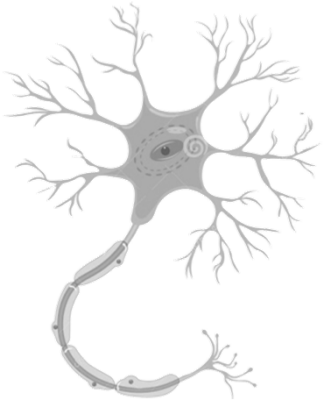
Microvascular complications

- Diabetic Retinopathy

- **Diabetic Kidney Disease**



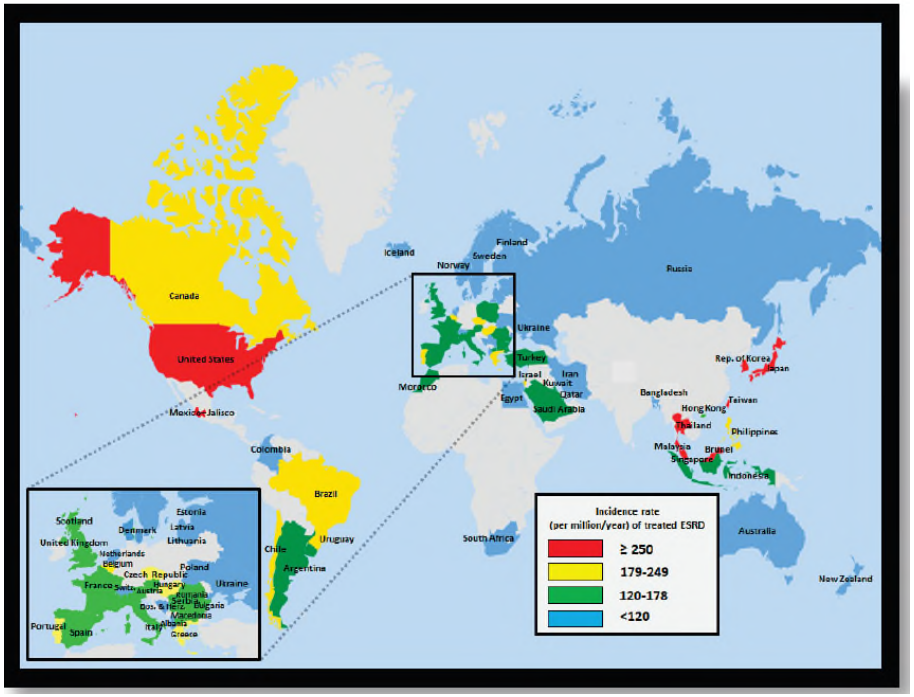
- Diabetic Neuropathy



Diabetic Kidney Disease

- The **single most common cause** of End stage Renal Disease in the world

Geographic variations in the incidence rate of treated ESRD (per million population/year),by country, 2015

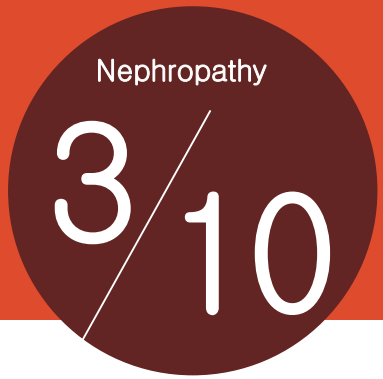


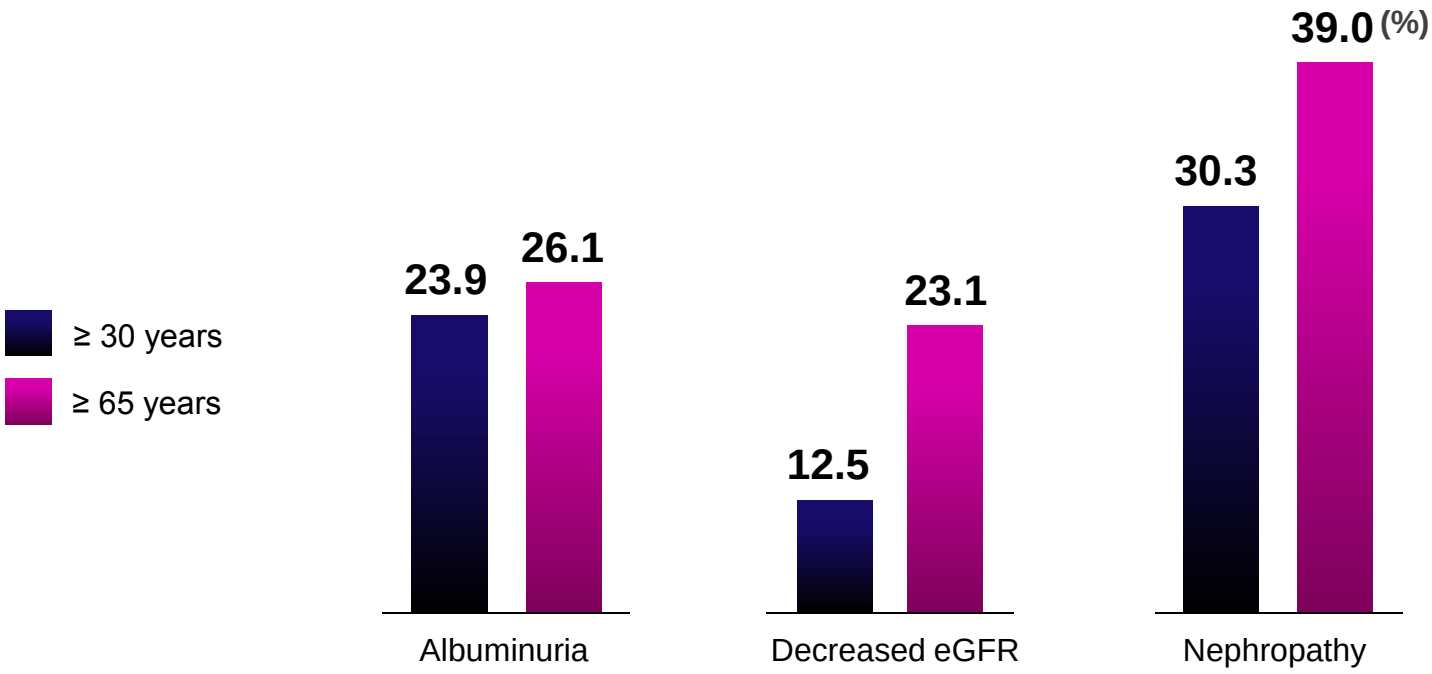
USRDS 2017 Annual Data Report, Vol 2, ESRD

Nephropathy in Diabetes

The prevalence of diabetic nephropathy (albuminuria or decreased eGFR) is 30.3%.

"Three among 10 persons with diabetes have albuminuria or decreased renal function"





The definition of nephropathy is increased albuminuria determined by albumin-creatinine ratio > 30 ug/mg of creatinine and/or estimated glomerular filtration rate (estimated GFR, eGFR) < 60 mL/min/1.73 m². GFR (mL/min/1.73 m²) by MDRD equation = $175 \times (S_{Cr})^{-1.154} \times (Age)^{-0.203} \times (0.742 \text{ if female})$.

Diabetes Fact Sheet 2016

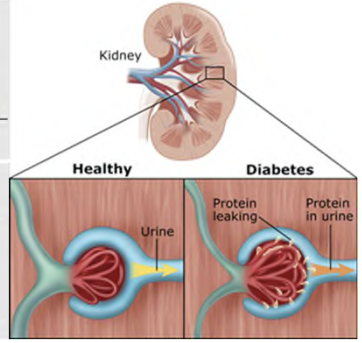
Diagnosis

- **Urinary albumin**
  - **e.g., spot urinary albumin–to–creatinine ratio(UACR)**

Table 11—Definitions of abnormalities in albumin excretion

Category	Spot collection (μg/mg creatinine)
Normal	<30
Increased urinary albumin excretion*	≥30

*Historically, ratios between 30 and 299 have been called microalbuminuria and those 300 or greater have been called macroalbuminuria (or clinical albuminuria).



- Two of three specimens of UACR collected within a 3- to 6-month period should be abnormal before considering a patient to have albuminuria.

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Diagnosis

- **estimated Glomerular Filtration Rate(eGFR)**

Stage	Description	GFR (ml/min per 1.73 m^2 body surface area)
1	Kidney damage* with normal or increased GFR	≥90
2	Kidney damage* with mildly decreased GFR	60–89
3	Moderately decreased GFR	30–59
4	Severely decreased GFR	15–29
5	Kidney failure	<15 or dialysis

GFR = glomerular filtration rate

*Kidney damage defined as abnormalities on pathologic, urine, blood, or imaging tests.

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Diagnosis

- **estimated Glomerular Filtration Rate(eGFR)**

Variable	Results	Previous Results	Reference
BUN	9	*8*	6~20 mg/dL
Creatinine	0.71	*0.69*	0.7~1.2 mg/dL
eGFR (MDRD)	117.4	*121.4*	~ mL/min/1.73 m^2
eGFR (CKD-EPI)	109.4	*110.7*	~ mL/min/1.73 m^2

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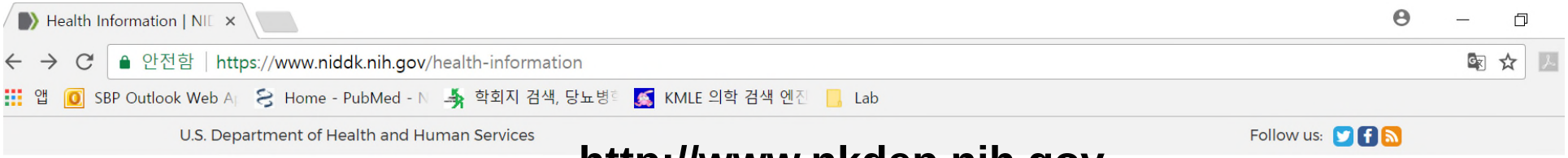

http://www.nkdep.nih.gov.

for Children (Conventional Units)

for Children (SI Units)

NKDEP

Contact Us

Health Information Center

- Phone: 1-800-860-8747
- TTY: 1-866-569-1162
- Email: healthinfo@niddk.nih.gov
- Hours: 8:30 a.m. to 5 p.m. eastern time, M-F

For Patients and Families

For Health Care Professionals

$$GFR = 141 \times \min(S_{cr}/\kappa, 1)^{\alpha} \times \max(S_{cr}/\kappa, 1)^{-1.209} \times 0.993^{Age} \times 1.018\ [\text{if female}] \times 1.159\ [\text{if black}]$$

where:
S_{cr} is serum creatinine in mg/dL,
κ is 0.7 for females and 0.9 for males,
α is -0.329 for females and -0.411 for males,
min indicates the minimum of S_{cr}/κ or 1, and
max indicates the maximum of S_{cr}/κ or 1.

The equation does not require weight because the results are reported normalized to 1.73 m^2 body surface area, which is an accepted average adult surface area.

Serum creatinine	1.2	**(mg/dL)**
Age*	65	
African American	○ Yes ◉ No	
Gender	◉ Male ○ Female	
	Calculate Clear	
GFR value:	**Above 60**	**mL/min/1.73 m^{2}****

*This equation should only be used for patients 18 and older.

The NKDEP presently recommends reporting estimated GFR values ***greater than or equal to 60 mL/min/1.73 m^2* simply as "≥60 mL/min/1.73 m^2", not an exact number.

Screening

At least once a year

Type 1	• ≥ 5 years after the onset of diabetes
Type 2	• in all patients regardless of treatment and in all patients with comorbid hypertension

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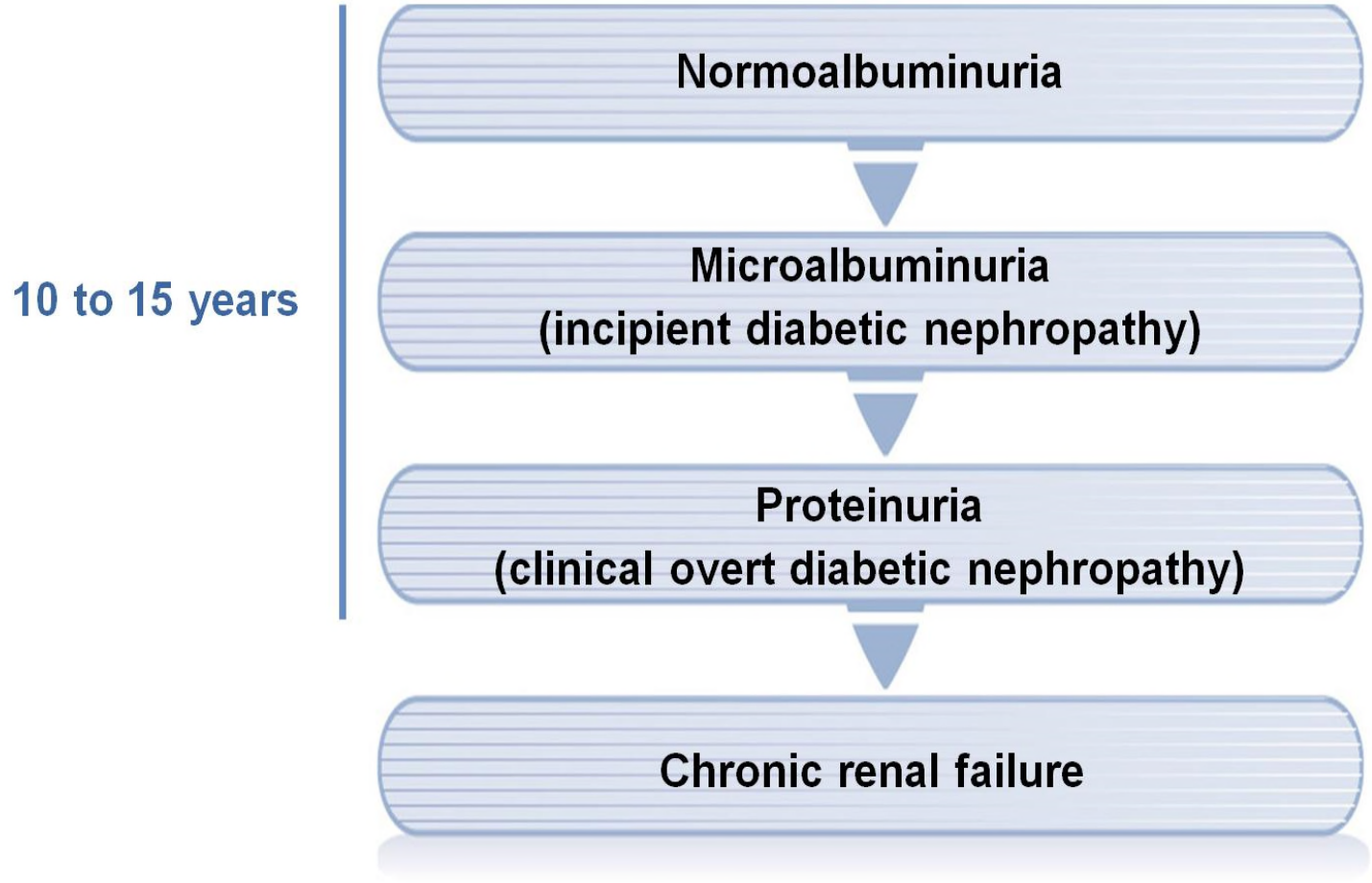
2019 Treatment Guidelines for Diabetes

Natural history of chronic kidney disease



Diabetic Kidney Disease

CKD stage†			Focus of kidney-related care			
Stage	eGFR (mL/min/1.73 m^2)	Evidence of kidney damage*	Diagnose cause of kidney injury	Evaluate and treat risk factors for CKD progression**	Evaluate and treat CKD complications***	Prepare for renal replacement therapy
No clinical evidence of CKD	≥60	−				
1	≥90	+	✓	✓		
2	60–89	+	✓	✓		
3	30–59	+/−	✓	✓	✓	
4	15–29	+/−		✓	✓	✓
5	<15	+/−			✓	✓

CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate. †CKD stages 1 and 2 are defined by evidence of kidney damage (+), while CKD stages 3–5 are defined by reduced eGFR with or without evidence of kidney damage (+/−). At any stage of CKD, the degree of albuminuria, observed history of eGFR loss, and cause of kidney damage (including possible causes other than diabetes) may also be used to characterize CKD, gauge prognosis, and guide treatment decisions. *Kidney damage is most often manifest as albuminuria (UACR ≥30 mg/g Cr) but can also include glomerular hematuria, other abnormalities of the urinary sediment, radiographic abnormalities, and other presentations. **Risk factors for CKD progression include elevated blood pressure, hyperglycemia, and albuminuria. ***See **Table 11.2**.

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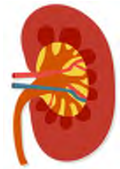
Diabetic Kidney Disease



Complication	Medical and laboratory evaluation
Elevated blood pressure	Blood pressure, weight
Volume overload	History, physical examination, weight
Electrolyte abnormalities	Serum electrolytes
Metabolic acidosis	Serum electrolytes
Anemia	Hemoglobin; iron testing if indicated
Metabolic bone disease	Serum calcium, phosphate, PTH, vitamin 25(OH)D

Complications of chronic kidney disease (CKD) generally become prevalent when estimated glomerular filtration rate falls below 60 mL/min/1.73 m^2 (stage 3 CKD or greater) and become more common and severe as CKD progresses. Evaluation of elevated blood pressure and volume overload should occur at every clinical contact possible; laboratory evaluations are generally indicated every 6–12 months for stage 3 CKD, every 3–5 months for stage 4 CKD, and every 1–3 months for stage 5 CKD, or as indicated to evaluate symptoms or changes in therapy. PTH, parathyroid hormone; 25(OH)D, 25-hydroxyvitamin D.

Diabetes Care 2019;42(Suppl. 1):S124–S138

Recommendation

- **Optimize glucose control (A)**

- **Optimize blood pressure control (A)**

Antihyperglycemic agents

- For patients with type 2 diabetes and diabetic kidney disease, consider use of a sodium-glucose cotransporter 2 inhibitor in patients with an eGFR ≥30 and particularly in those with >300 mg/g albuminuria to reduce risk of CKD progression, cardiovascular events, or both. A

- In patients with CKD who are at increased risk for CV events, use of a glucagon-like peptide 1 receptor agonist may reduce risk of progression of albuminuria, cardiovascular events, or both.C

Diabetes Care 2019;42(Suppl. 1):S124–S138

Antihyperglycemic agents by eGFR

e-GFR	CKD1-2	CKD3a	CKD3b	CKD4	ESRD
	≥ 60	45-59	30-44	15-29	< 15
Metformin		Maximum ≤1000mg/day	Contraindication	Contraindication	Contraindication

The revised FDA guidance states that metformin is contraindicated in patients with an eGFR < 30 mL/min/ 1.73m^2.

eGFR should be monitored while taking metformin, the benefits and risks of continuing treatment should be reassessed when eGFR falls<45 mL/min/1.73 m^2, metformin should not be initiated for patients with an eGFR<45 mL/min/1.73 m^2.

Metformin should be temporarily discontinued at the time of or before iodinated contrast imaging procedures in patients with eGFR 30– 60 mL/min/1.73 m^2.

2019 Treatment Guidelines for Diabetes

Antihyperglycemic agents by eGFR

e-GFR	CKD1-2	CKD3a	CKD3b	CKD4	ESRD
	≥ 60	45-59	30-44	15-29	< 15
SGLT2 inhibitors					
Dapagliflozin	10 mg	Contraindication	Contraindication	Contraindication	Contraindication
Empagliflozin	10 mg/25 mg	Cautious	Contraindication	Contraindication	Contraindication
Ertugliflozin	5 mg	Cautious	Contraindication	Contraindication	Contraindication
Ipragliflozin	50 mg	Contraindication	Contraindication	Contraindication	Contraindication
Sulfonylurea					
Gliclazide			Cautious	Cautious	Cautious
Glimepiride			Cautious	Cautious	Cautious
Glipizide			Cautious	Cautious	Cautious
Alpha-glucosidase inhibitors					
Acarbose				Contraindication	Contraindication
Voglibose				No Reference	No Reference
Thiazolidinedione					
Pioglitazone	15/30 mg	15/30 mg	15/30 mg	15/30 mg	15/30 mg
Lobeglitazone	0.5 mg	0.5 mg	0.5 mg	0.5 mg	0.5 mg
GLP-1 receptor agonists					
Lixisenatide				No Reference	No Reference
Liraglutide					No Reference
Dulaglutide					

*e-GFR ≥ 50 용량 조절 불필요, ¶ e-GFR < 60 시작 금지, **e-GFR < 25 금지
용량 조절 불필요. CKD, chronic kidney disease
2019년 4월 기준, 식품의약품안전처의 허가사항에 준하여 작성되었음.

2019 Treatment Guidelines for Diabetes

Treatment

- ACE inhibitor or angiotensin receptor blocker

Periodically monitor serum creatinine and potassium levels for the development of increased creatinine or changes in potassium when ACE inhibitors, angiotensin receptor blockers, or diuretics are used.

Treatment

- **Nutrition**
  - For people with nondialysis-dependent chronic kidney disease, dietary protein intake should be approximately 0.8 g/kg body weight per day(the recommended daily allowance).
  - For patients on dialysis, higher levels of dietary protein intake should be considered.

Recommendation

- Patients should be referred **for evaluation for renal replacement treatment if they have an eGFR<30 mL/min/1.73 m^2.**

- Promptly refer to a physician experienced in the care of kidney disease for **uncertainty about the etiology of kidney disease, difficult management issues, and rapidly progressing kidney disease.**

Recommendation

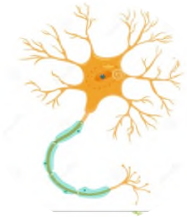
- **Alternative or additional causes of kidney disease**
  - An active urinary sediment (containing red or white blood cells or cellular casts)
  - rapidly increasing albuminuria or nephrotic syndrome,
  - rapidly decreasing eGFR,
  - the absence of retinopathy (in type 1 diabetes)

Take Home Message

- General Recommendation : Optimize glucose control
- Screening
  - Type 1 :5 years after the onset of diabetes
  - Type 2 :At the time of the diagnosis

Diabetic Retinopahy → Initial dilated & comprehensive eye examination → Laser photocoagulation Anti-VEGF

Diabetic Kidney Disease → Urine albumin eGFR → ACE inhibitor ARB



Diabetic Neuropathy

Thank you for your attention