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Basics of PKD

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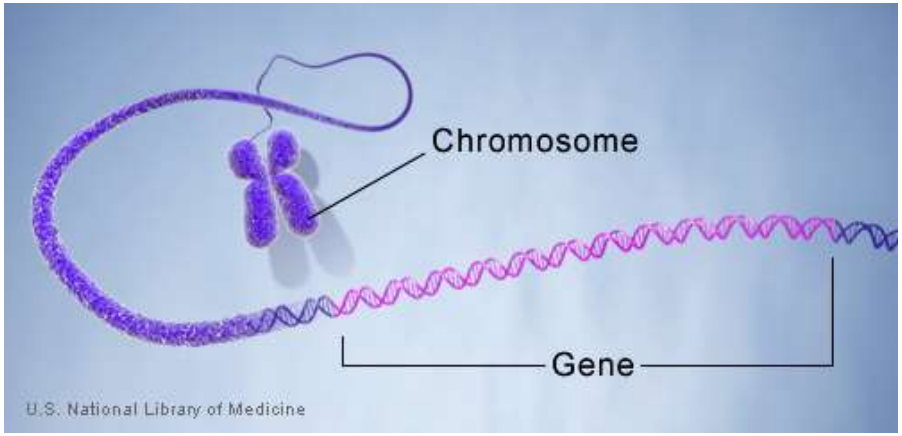
PKD is genetic

Commonest genetic cause of chronic kidney disease

Our genes make us who we are



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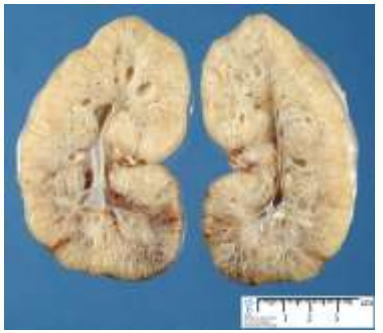
PKD is genetic

2 forms described based on *pattern* of inheritance

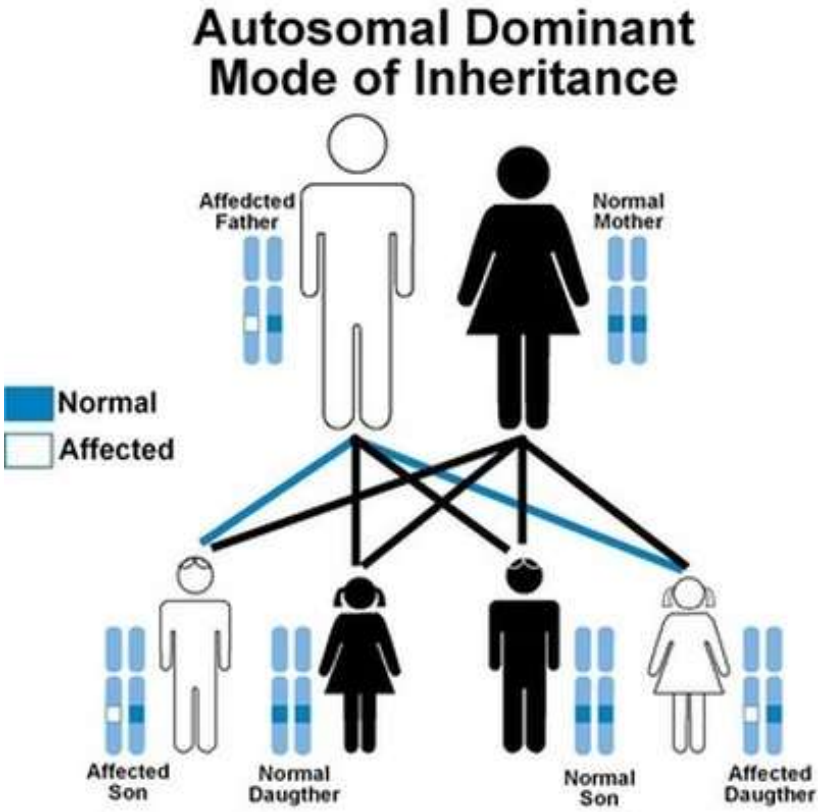
[1] ADPKD **A**utosomal **D**ominant **PKD**

[2] ARPKD **A**utosomal **R**ecessive **PKD**

Usually in children
Different pattern of kidney involvement
Liver disease



PKD is genetic



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ADPKD is genetic

Prevalence 1:400 - 1:1000

Changes in PKD genes

PKD1	85% cases	Chromosome 16
PKD2	15% cases	Chromosome 4

So what ?

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ADPKD is genetic

PKD1 Symptoms tend to develop at earlier age
Faster progression of kidney disease

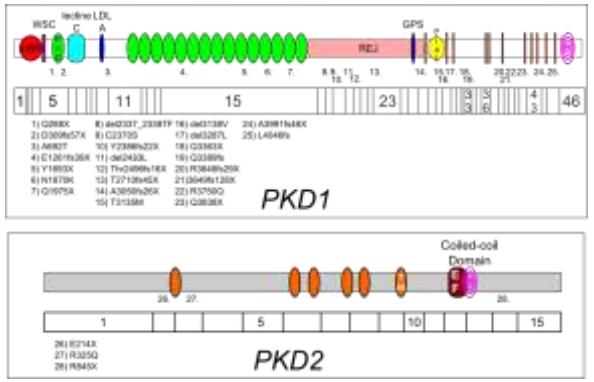
Dialysis start at 54 yrs vs 74 yrs in PKD2

ADPKD is genetic

Not the same between / within families

- *Location / type of change within gene*
- *Change in gene expression in cells*
- *Other "modifier genes" inherited differently*

So the way the condition behaves varies in family members



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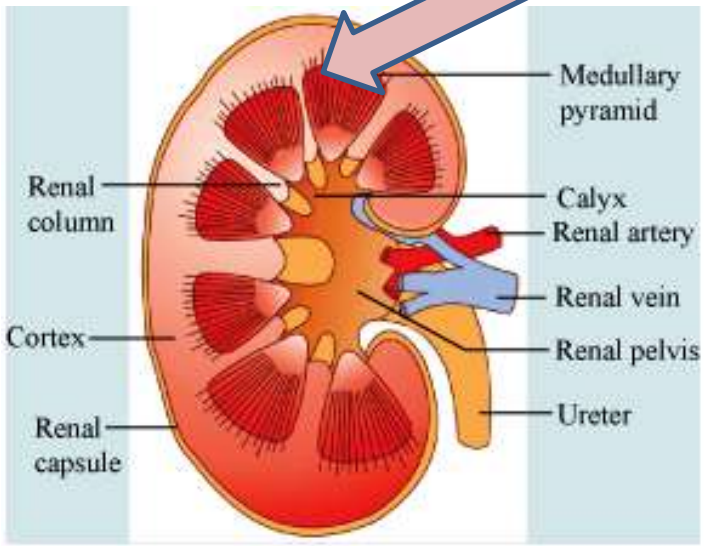
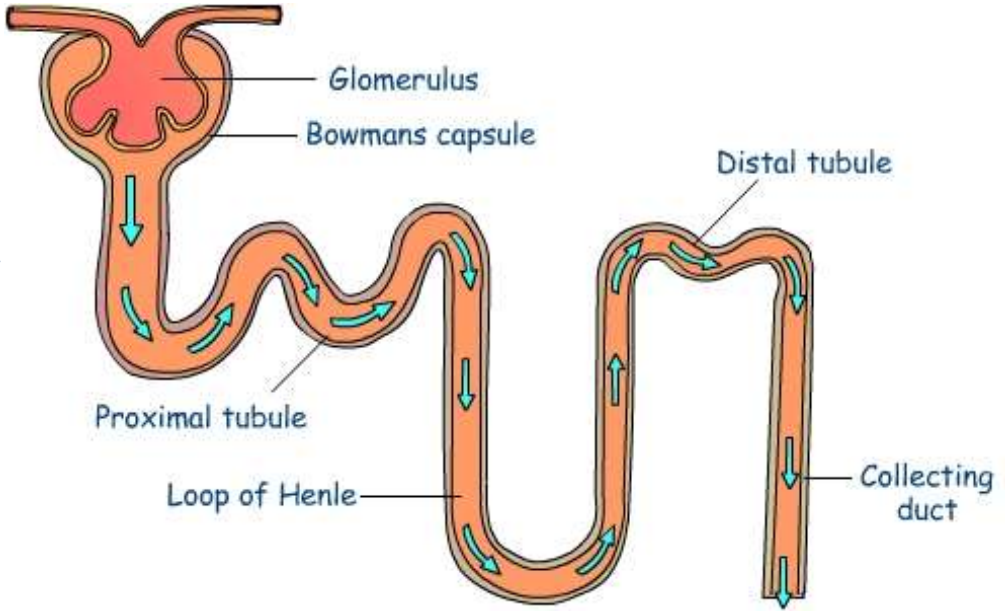
Kidneys

Kidneys


Medullary pyramid
Renal column
Calyx
Renal artery
Renal vein
Cortex
Renal pelvis
Ureter
Renal capsule


Glomerulus
Bowmans capsule
Distal tubule
Proximal tubule
Loop of Henle
Collecting duct

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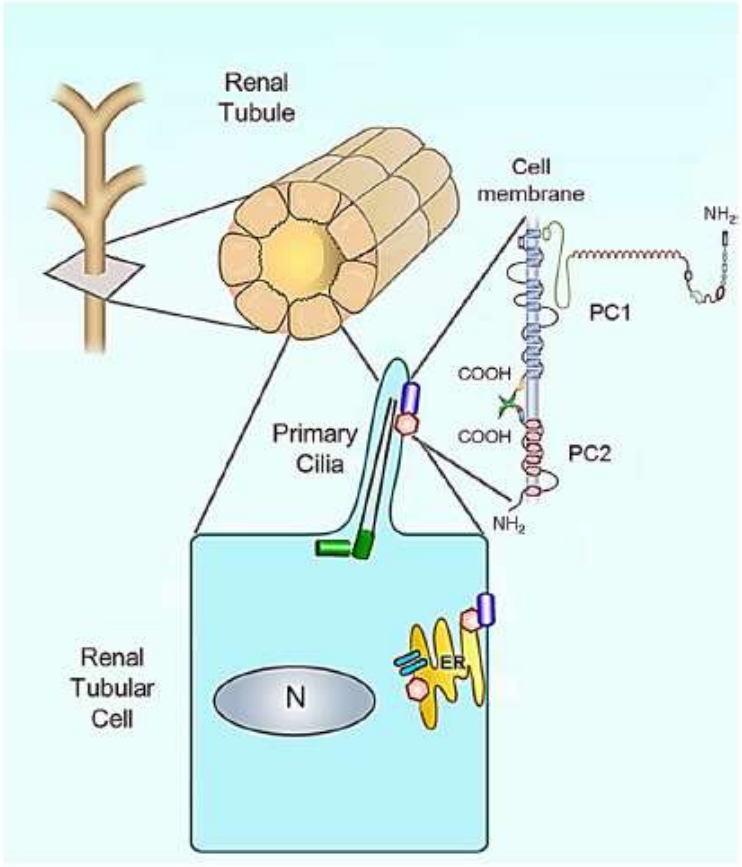
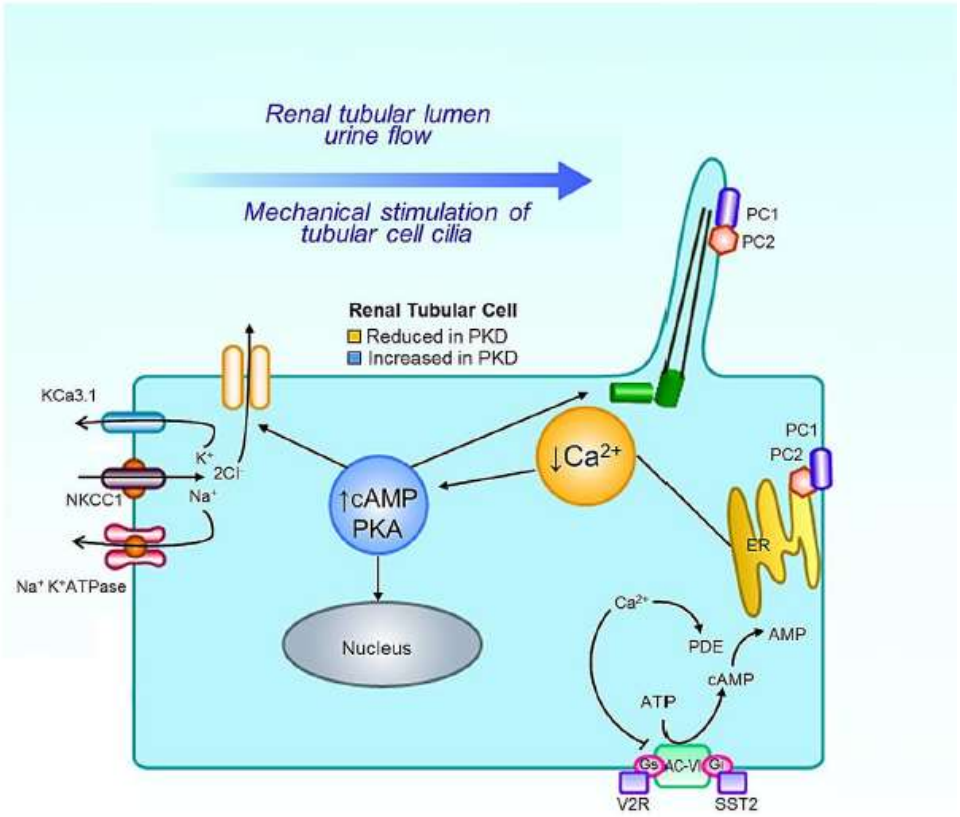
ADPKD





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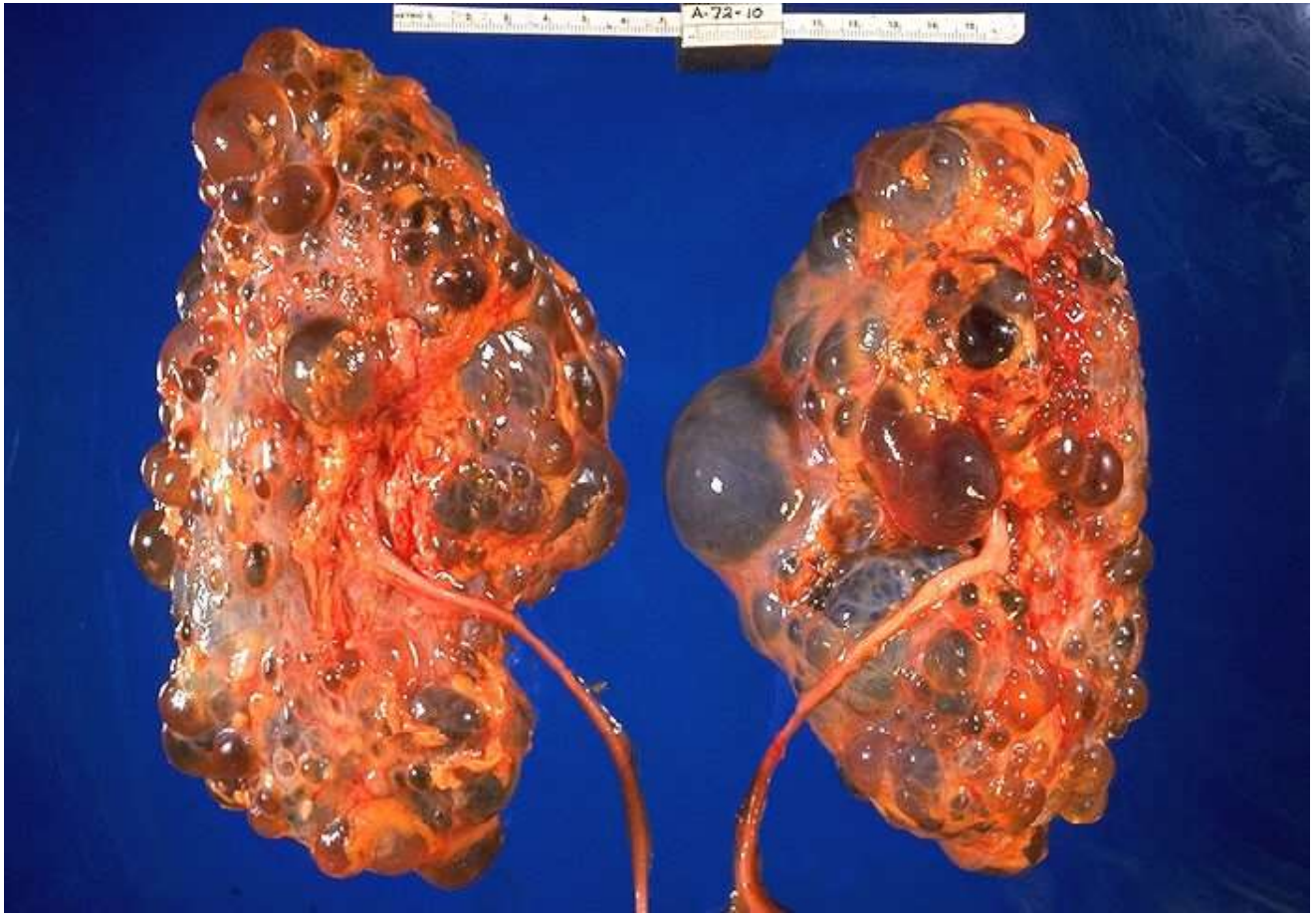
ADPKD



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ADPKD diagnosis

Routine screening where there is a family history

Work-up for new-onset high blood pressure

Incidental finding

- Pregnancy / trauma
- Blood in urine / recurrent infections

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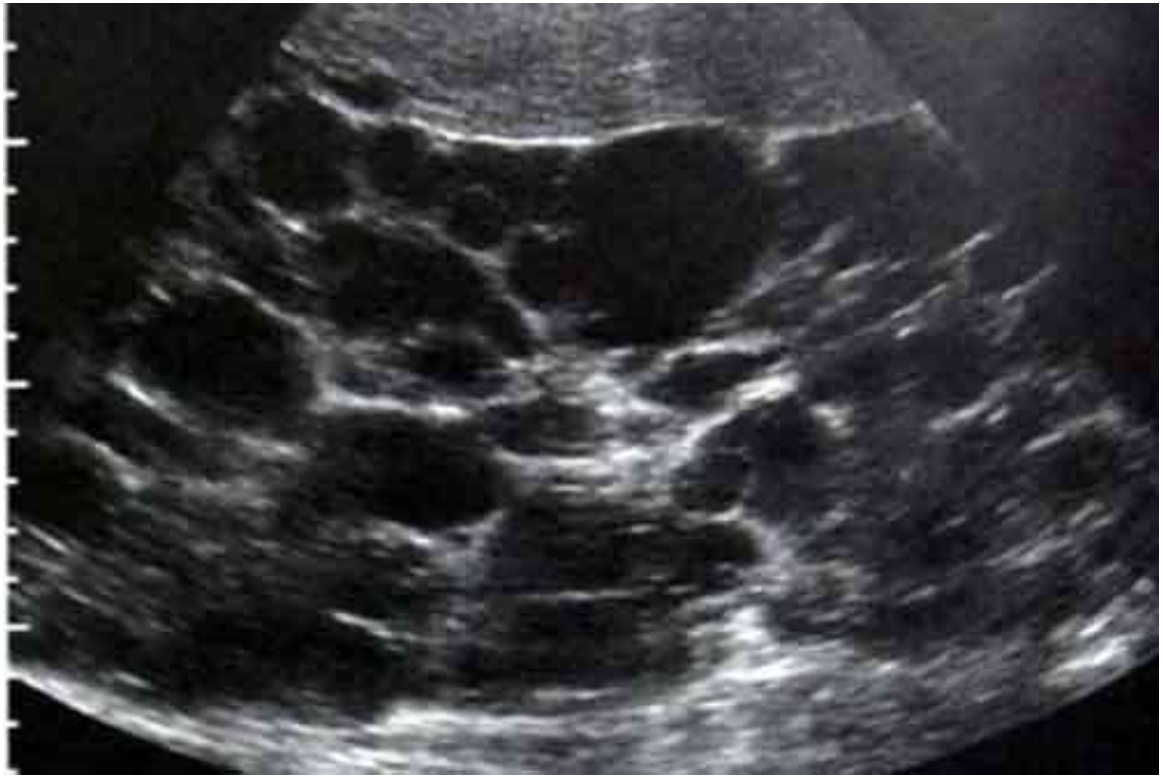
ADPKD diagnosis



ADPKD diagnosis

In about 25% people with ADPKD there is no clear family history ..

Is there a family history ?

Kidney cysts – how many & where in kidneys ?

Age

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ADPKD diagnosis

More cysts “allowed” the older you get

Usually do an ultrasound scan

Can do CT / MRI – higher detail

Chapman et al. Kidney Int (2015); 88:17

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ADPKD screening

Not recommended in children [<18yrs old]

Age	USS findings	Age	USS findings
	Genetics unknown		**PKD1** heritage
15-39	3+ on one side or both	15-30	2+ on one side or both
40-59	2+ in each kidney	30-59	2+ in each kidney
60+	4+ in each	60+	4+ in each kidney

Chapman et al. Kidney Int (2015); 88:17

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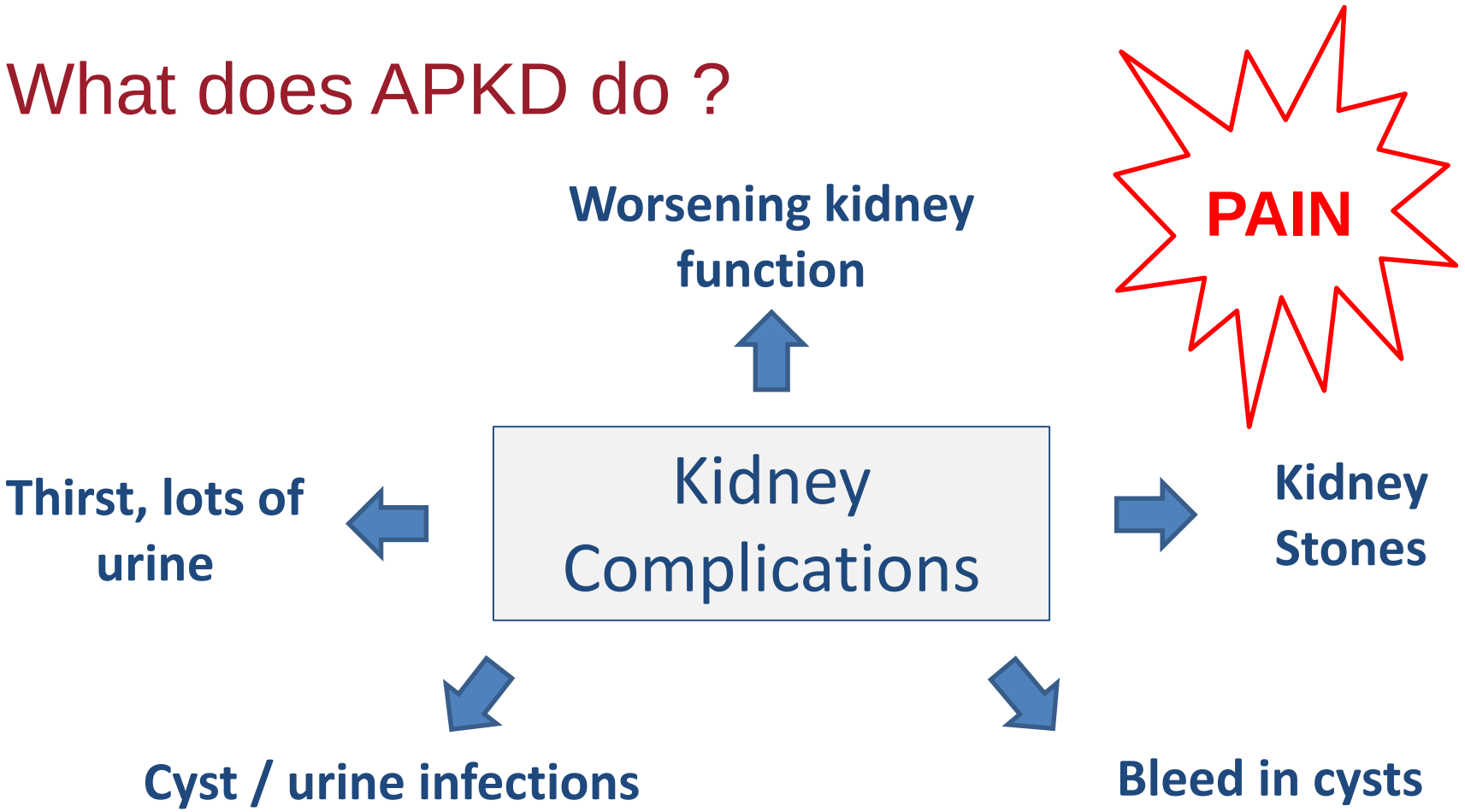
What does APKD do ?



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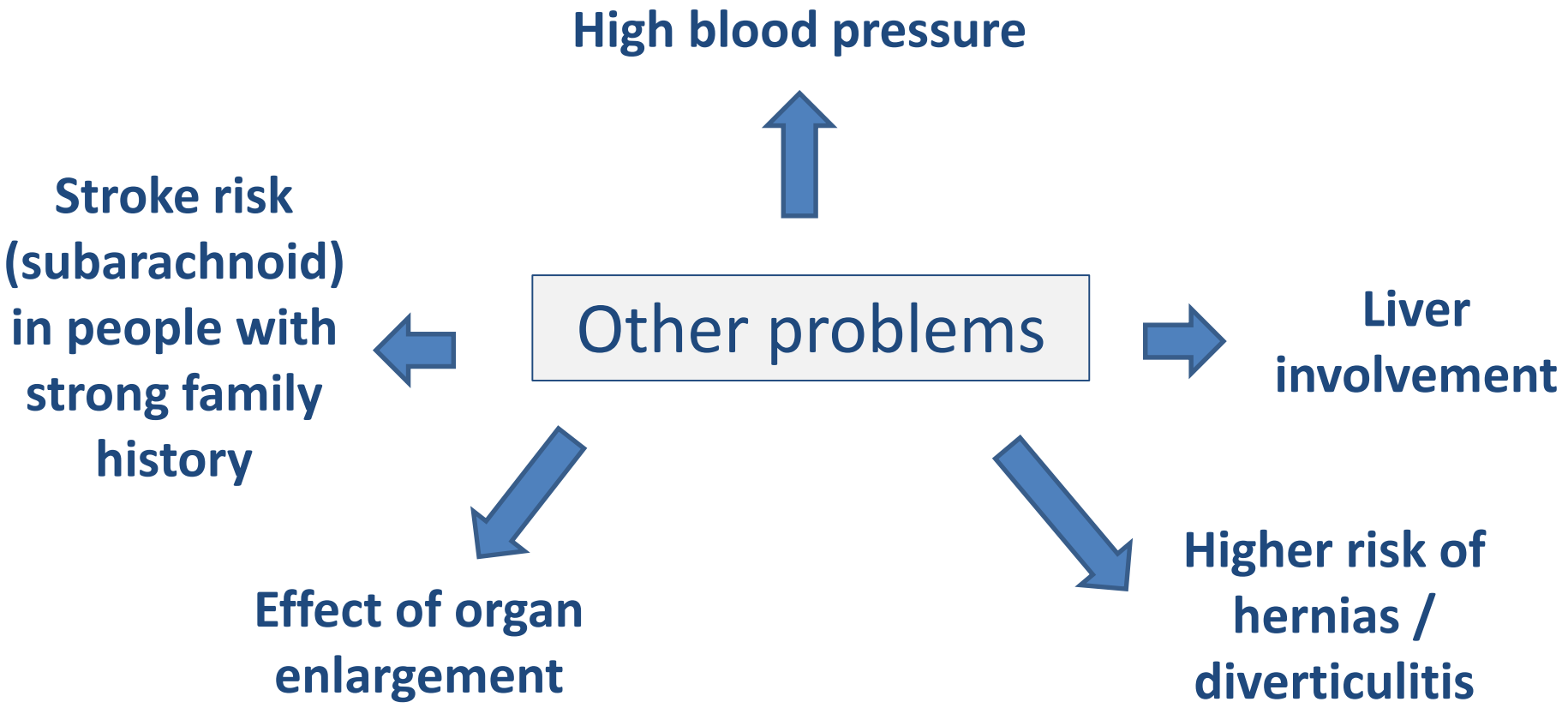
What does APKD do ?



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ADPKD Management

[1] BP Control <130/80 mmHg

Advocate tight control <120/75 mmHg ideally
Preferential use of ACEi / ARB = “prils” / “sartans”
No evidence for both at same time

[2] Lipid Control

CKD - greater rates of vascular disease
No data that statins impact directly on PKD progression in practice

[3] High fluid intake > 3 litres / day

[4] Tolvaptan [?]

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Thank you

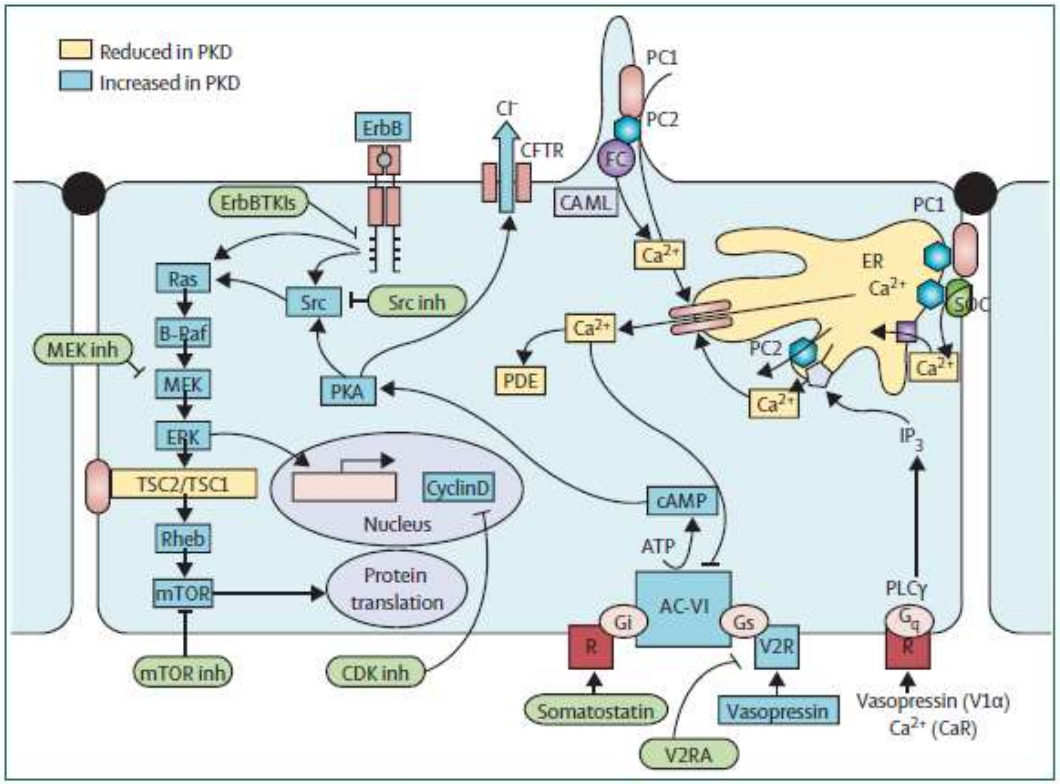

***Figure 4:* Hypothetical pathways up-regulated or down-regulated in polycystic kidney disease**
Potential therapeutic agents for polycystic kidney disease are shown in green boxes. AC-VI=adenylyl cyclase 6. CDK=cyclin-dependent kinase. ER=endoplasmic reticulum. MAPK=mitogen-activated protein kinase. mTOR=mammalian target of sirolimus. PC1=polycystin-1. PC2=polycystin-2. PDE=phosphodiesterase. PKA=protein kinase A. R=receptor. TSC=tuberous sclerosis proteins tuberin (TSC2) and hamartin (TSC1). V2R=vasopressin V2 receptor. V2RA=vasopressin V2 receptor antagonists.

Torres et al. Lancet (2007); 369:1287-1301