Autosomal Dominant Polycystic Kidney Disease (ADPKD)

A One Page Summary Tutorial: By Dr Kristeen Barker
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Genetics

Aut Dom: M/F, 50% offspring affected
Variable phenotype within families

80% PKD1 gene (Ch16)→ polycystin 1
Severe: More cysts, big kidneys, early ESRF
Truncating PKD1 mutations most severe

15% PKD2 gene (Ch4) → polycystin 2
Milder phenotype

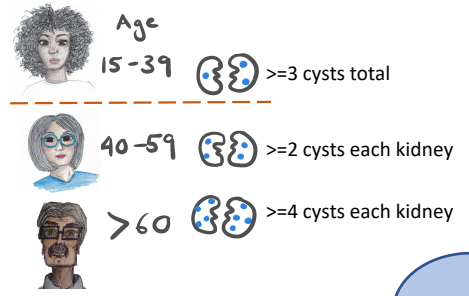
Epidemiology

Prevalence 1 in 400-1000
4th leading cause of ESRF

Extra-Renal Manifestations

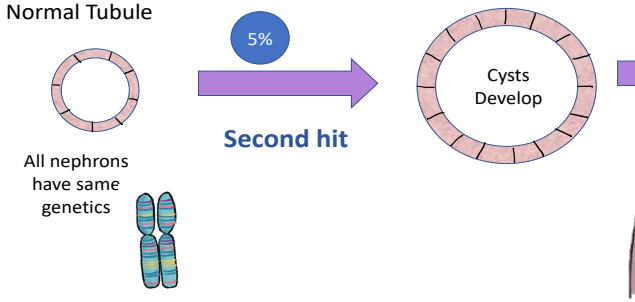
High Risk ICA:
Personal or Family Hx ICA
Neurological Sx/Headache
High Risk Profession e.g pilot
Major surgery

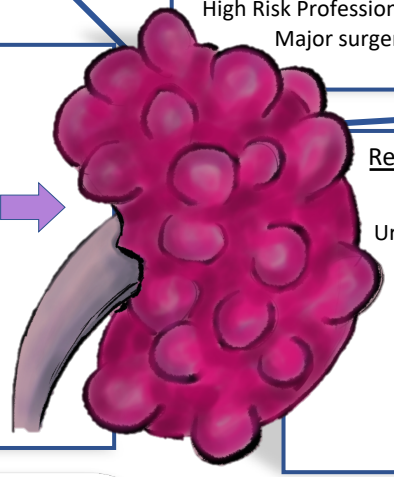
Diagnosis ADPKD with FHx & USS Kidneys



Less than 40 years not meeting these criteria cannot exclude:
→ consider MRI
(10+ cysts = ADPKD, <5 cysts excludes)

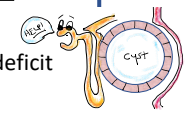
Pathophysiology





Renal Manifestations

Hypertension
Urine concentrating deficit
Albuminuria
Renal Impairment
Haematuria
Infection
Flank Pain



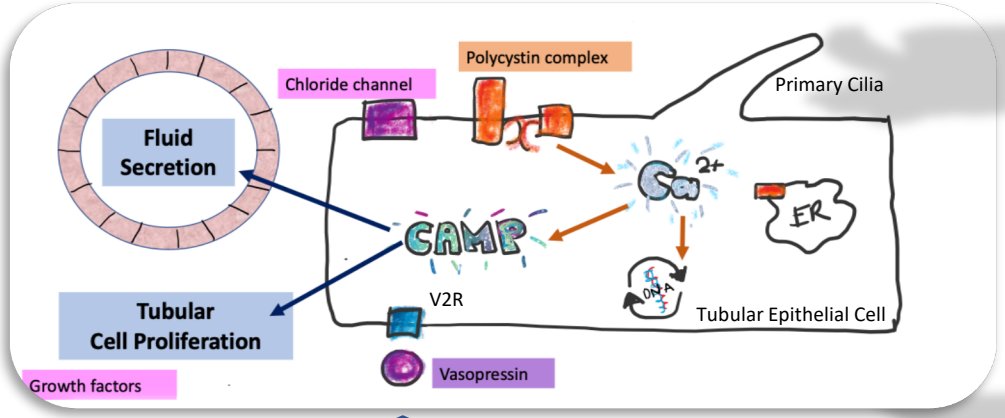
Clues for ADPKD:

Bilateral cysts (unless mosaicism)
Enlarged kidneys
Cysts in both cortex and medulla
May have liver cysts
(but not advanced liver disease)

Prognosis Assessment

Risk of progression to ESRF

Total Kidney Volume (TKV)
Mayo Classification
PROPKD



Disease Specific Treatment (consider in high risk of ESRF)

Tolvaptan: V2R (vasopressin receptor) antagonist

Potential Benefits

TEMPO: reduced rate of change in TKV by 50% compared to placebo (mostly in 1st year)
REPRISE: Decline in GFR slowed by 1.27ml/min/year compared to placebo
Assuming effect true & sustained may delay ESRF by a few years.

Medication Logistics
- ❑ Oral tab twice daily (8-9 hours apart)
- ❑ Titrated to max tolerated dose
- ❑ Optimal dose unknown
- ❑ LFTs: monthly for 18 months then 3 monthly thereafter

Drug Interactions
- ❑ Diuretics, CYP3A4 inhibitors (write to GP)

Side Effects
- ❑ GFR reduced by 20% on drug (reversible)
- ❑ Polyuria, Polydipsia (8% cannot tolerate)
- ❑ Aim for 4-5L intake/day, avoid thirst
- ❑ Liver Function Deranged in 4-5%
- ❑ Gout

General Management (all patients)

- Blood pressure:
  - ACEi/ARB first line
  - Target <=130/80 in majority
- Weight loss/avoid obesity
- Lipid lowering
- Low salt diet: 2.3-3g/day
- Hydrate well:
  - aim urine osmolarity <300mOsm/l
- Screen for ICA in high risk patients
- ECHO if cardio signs/symptoms
- Avoid exogenous female hormones (as able)
  - Promotes growth of liver cysts
- Advise on relevant care of family members
- Consider genetic counselling pre-conception.

ESRF:End Stage Renal Failure, Ch:Chromosome, ICA:Intracranial Aneurysms, Sx:symtpoms, ER:endoplasmic reticulum, FHx: Family History, USS:ultrasound, TKV:total kidney volume, GFR:glomerular filtration rate, ACEi:angiotensin converting enzyme inhibitor, ARB:angiotensin 2 receptor blocker, ECHO:echocardiogram.