Diagnosing ARPKD/CHF* FACT SHEET

Overview: ARPKD/CHF is a chronic, progression disorder, affecting primarily two organs, the liver and kidneys.

Principle Clinical Diagnostic Criteria: ARPKD/CHF can be diagnosed by a definitive, previous family history of a sibling with ARPKD, CHF, or Caroli's Disease/Syndrome, clinical findings and diagnostic radiological findings. If clinical findings and diagnostic testing are negative, genetic testing can confirm no disease. Genetic testing also confirms a diagnosis. Biopsies are no longer needed to confirm a diagnosis. If a patient has ARPKD, they always have some degree of CHF. Suspect ARPKD with Congenital Hepatic Fibrosis, or Caroli's.

CLINICAL FINDINGS/MANIFESTATIONS

Prenatal Findings	**a)** Oligohydramnios (low or absent amniotic fluid). **b)** May have absence of fetal bladder filling (does not necessarily correlate with postnatal severity). **c)** Grossly enlarged, "bright" echogenic kidneys, in some cases can be seen as early as 13 weeks gestation, yet may not be visualized until the 3rd trimester or after birth.
Postnatal and Childhood Findings	**a)** Possible Potter's facies or syndrome (severe cases), and inguinal/umbilical hernias (not indicative of severity). **b)** May have respiratory distress that requires ventilation due to spontaneous pneumothroaxes, huge cystic kidneys and underdeveloped lungs (lung maturation dependent on sufficient amniotic fluid during fetal lung development). Respiratory failure/complications are responsible for 30-50% infant mortality . **c)** Huge flank areas, large, palpatable**,** echogenic kidneys. **d)** Significant hypertension is common, with or without normal renal function; aggressive treatment may be needed with multiple antihypertensive medications. **e)** Decline in renal fu**n**ction variable, usually early in life, yet ESRD sometimes does not occur till adulthood. **f)** Glomerular Filtration Rate (GFR) may improve the first 6 months of life. g) Increased thirst with large amounts of dilute urine. h) White blood cells in urine without infection is common. **i)** Bed-wetting common in school age children due to a concentrating defect and large volume output. **j)** Increased risk of dehydration with prolonged fevers and sweating. **k)** Low stature not uncommon, and approximately 25% have failure to thrive, exact cause unknown. **l)** Many have an enlarged liver (hepatomegaly) and enlarged spleen (splenomegaly). **m)** All have microscopic liver changes. **n)** Most liver labs and enzymes remain normal, even with clinical manifestations. **o)** As fibrosis progresses clinical symptoms become more pronounced and may include: upper GI bleed (vomiting of copious amounts of blood due to esophageal varices-- life threatening), or lower GI bleed (varies in stomach or elsewhere resulting in tarry stools). Both require prompt, proper care. **p)** Possible petechiae (due to low platelet count), and high PTT (from abnormal liver function/production). **q)** Cholangitis can occur due to bile sluggishness/status; ascending cholangitis is life-threatening and requires aggressive IV antibiotics. **r)** Caroli's Syndrome/Disease may or may not be present, but provides increased risk of cholangitis that *decreases* with age. **s)** Those patients with primary kidney involvement should have periodic GI consultations.
Adolescent, Adult and other Important Findings	**a)** ARPKD/CHF is occasionally diagnosed in adolescence and adulthood; clinical course of these patients is not well documented at this time, but it appears fibrosis tends to advance and CHF clinical findings become more prominent with age including those with early kidney transplant with no apparent liver involvement. **b)** Because of improved healthcare, the pediatric population is now living into adulthood. **c)** There are no guidelines to predict prognosis or outcomes. **d)** Due to progression and changing typical kidney shape, some mistakenly are diagnosed with ADPKD. A CT scan can effectively visual collecting tubules which are always involved. **e)** There are a few documented cases of liver cancer associated with CHF. **f)** Clinical findings may suggest other diseases and should be ruled out: MODY type 5, ADPKD, cystic dysplastic kidneys, glomerulocystic kidney disease, medullary sponge kidney and nephronophthisis.

***Autosomal Recessive Polycystic Kidney Disease and Congenital Hepatic Fibrosis.**

DIAGNOSTIC TESTS AND FINDINGS

Ultrsonography (has largely replaced IVPs for diagnosing PKD)	**1) Kidney** **a)** Always bilateral involvement a) Presence of precaliceal tubular ectasia or bilateral renal cysts in children **b)** Loss of corticomedullary differentiation **c)** Massive renal enlargement in patients diagnosed the first year of life **d)** Kidneys become smaller relative to body size in all with ARPKD; size stabilizes at 4-5 yrs of age unlike ADPKD. **e)** Macroscopic cysts appear in childhood and in adolescence, sometimes resulting in ADPKD diagnosis; cysts change the typical kidney shape **f)** Adult patients presenting with renal insufficiency from ARPKD do not have markedly enlarged kidneys and may have only a small number of cysts **g)** Increased echogenicity and irregular contour **h)** Finding consistent with calcifications may be present	**2) Liver** **a)** Most patients have increased hepatic echogenicity **b)** Dilated intrahepatic bile ducts (the ADPKD liver shows normal ducts and normal echotexture with/without presence of cysts**)** c) With severe portal hypertension, spontaneous shunting may occur or blood flow may reverse.	**3) Spleen** **a)** Splenomegaly may be present
IVP/EUG (Intravenous Pyelography)	**1) Kidney** **a)** Enlarged kidneys **b)** Findings may suggest medullary sponge kidney (collecting duct ectasia) and calcifications may be present		
CT (Computerized Tomographic Scanning)	**1) Kidney** **a)** Enlarged kidneys, cysts **b)** Increased parencymal echogenicity **c)** Medullary calcifications **d)** Bilateral renal parenchymal	**2) Liver** **a)** Tiny biliary liver cysts **b)** Intrahepatic and less commonly extrahepatic bile duct dilatation	**3) Spleen** **a)** Splenomegaly **b)** Splenic hilar varices
MRI (Magnetic Resonance Imaging) and MRC (Magnetic Resonance Cholangiography)	**1) Kidney** **a)** Kidney enlargement, enlarged cysts **b)** Reniform but 'lumpy humpy bumpy' shape **c)** Homogeneously grainy renal parenchyma **d)** Normal renal pelvis and normal calyces **e)** By RARE-MR urography a hyperintense, linear radial pattern is seen in the cortex and medulla which represents the characteristic microcystic dilatation of collecting ducts in ARPKD **f)** To confirm a diagnosis of ARPKD, RARE-MR urography seems to be a non-invasive imaging tool that shows directly microcystic dilated water-filled collecting ducts	**2) Liver** **a)** Dilated intrahepatic bile ducts consistent with Caroli Syndrome/Disease **b)** Intrahepatic bile duct stones	
Amniocentesis/ Genetic Testing/ Pre-implantation	**1)** Amniocentesis cannot provide an ARPKD/CHF diagnosis and direct genetic testing is not available. Prenatal diagnosis of ARPKD/CHF, on the basis of haplotype and mutation analysis is possible when previously affected sibling and disease free parental analysis are available. Pre-implantation genetic diagnosis is also available. For more information: http://www.arpkdchf.org/information/testing/index.htm).		

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