

QUESTIONS FOR PHYSICIANS, from ARPKD/CHF Parents

Prenatal/Diagnostic Questions:

- 1) What is the most effective, yet least invasive way to determine an ARPKD/CHF diagnosis? Biopsies of the kidney and liver continue to be performed for diagnostic purposes. When is there an indication for this? What distinguishes ARPKD from ADPKD biopsies? There have been several situations where a biopsy was performed, and a definitive diagnosis was NOT reached. There have been situations where a child has been diagnosed with ARPKD only to later discover they have a different kidney disease. What tests should be done at time of diagnosis?
- 2) Prenatally, many times ARPKD families are given a very grim prognosis or no hope for survival. What is looked at/evaluated besides the amniotic fluid level? What is the best way to predict outcome?
- 3) How successful is prenatal amniotic fluid replacement for low amniotic ARPKD pregnancies? How successful has this procedure been? Is this considered experimental or is it now an accepted medical procedure? Is there anything that can be done prenatally to increase the likelihood of ARPKD newborn survival?
- 4) Some medical literature suggests a C-section should be performed due to the enlarged ARPKD abdomen. Is this necessary?
- 5) At what gestational age, if any, can ARPKD be ruled out completely? If ARPKD/CHF is not present at birth, can it be ruled out, or, at what developmental age can ARPKD/CHF be ruled out completely? Should periodic testing be done on siblings? What sort of test(s) is recommended and up to what age should this be done?
- 6) How often does CHF present prenatally, without any manifestations of ARPKD?

Congenital Hepatic Fibrosis Questions:

- 1) If a child has an esophageal varice rupture should follow up periodic scoping be done? If yes, how often? When is esophageal scoping warranted/necessary? Should scoping be done on an "as needed basis" or as routine maintenance care?
- 2) What are the physiological processes and sequence of symptoms in the progression of CHF and portal hypertension? Can the spleen enlarge before the liver, or does the liver always enlarge first?
- 3) A person can have CHF without ARPKD, but if a person has ARPKD, they always have some degree of CHF. Is it possible for an adult living with ARPKD never to have clinical liver manifestations, or is not enough known about ARPKD/CHF? Does progression of CHF ever stop, or does it continue throughout life?
- 4) Does systemic high blood pressure directly or indirectly affect CHF or portal hypertension?
- 5) What research is being done on Congenital Hepatic Fibrosis and specifically, what does this research entail? How can we promote CHF and ARPKD research?
- 6) Does CHF cause pain, initially or when it progresses and becomes severe?
- 7) What degree of protection do spleen guards provide? Does it allow you to participate in activities such as biking, downhill skiing, roller-blading, etc? How should a spleen protector fit, and be made?

- 8) What degree of caution needs to be taken in regards to airplane travel, due to possibility increasing portal hypertension, resulting from altitude pressure? Does this mode of travel need to be restricted only at stages of severe portal hypertension or should it be limited at any stage of portal hypertension?
- 9) Does the spleen have to be enlarged in order for varices to be present?
- 10) If I live in a rural area and the Emergency Medical System/hospital is 20 minutes away, what can I do, as a parent, to prevent shock if a varice ruptures?
- 11) Is Inderal a good drug of choice for hypertension? What effect does it have systemically? Is it beneficial in lowering portal hypertension, thus reducing the chance of a GI bleed? How routine is its usage? How controversial is it, since it lowers the heart rate? Could it prevent a heart rate from speeding up to effectively respond to a GI bleed and shock, and on the other hand, could levels be too dilute to have any effect on portal hypertension? Are there safe and optimal levels to use?
- 12) Can a lot of severe coughing potentially cause an esophageal varice to rupture?
- 13) Is there any permanent or functional damage to the spleen due to portal hypertension? If so, what sort of symptoms should be looked for? If a hepatic shunt is placed, will the spleen return to normal size?
- 14) What is Caroli's Syndrome? Is it a separate disease, or just part of the CHF spectrum? If it is present, does this mean a more severe case of CHF? What are the complications & precautions in the medical management of Caroli's? What drugs are helpful in preventing liver infections? What are optimal antibiotics?
- 15) What is the most effective shunt treatment, for long-term success, with regard to portal hypertension: TIPS procedure or a selective splenal-renal shunt?
- 16) Does a selective shunt interfere with future transplantation? Does it raise ammonia levels? Does it stress the kidneys?
- 17) Is the TIPS procedure just a bridging to transplantation and therefore not a long-term solution to portal hypertension? Is there a problem with fibrotic obstructions with this procedure? Does it tend to cause more rapid deterioration of liver function? Does it facilitate high ammonia levels?
- 18) What is the cause of elevated ammonia levels? What is the significance and what effect does it have on an individual, both short and long term? What are consequences of elevation? When and how should it be treated?
- 19) Are there any other treatments for portal hypertension, besides shunting? Is there research being done on an Anti-Fibrotic therapy?
- 20) What is the choice treatment for esophageal varices; sclerotherapy or banding?
- 21) What treatment should be pursued, when there is a high protime level, a low INR level, low platelets and low white count? All other liver enzyme levels are well within normal ranges.
- 22) At what stage do you suggest commencing vitamin K supplements for elevated PT levels (protime)? What effect can an elevated PT level have?
- 23) Does Bymphocyte Stimulant (BLYS) stimulate white cells?
- 24) What is the criteria for a liver transplant and the success rate?

25) Typically, ARPKD is diagnosed very early in life, resulting in pediatric nephrology referral and care. When should a pediatric GI referral be made for consultation and care? What clinical symptoms or labs would indicate the need for such?

Renal Questions:

- 1) At what sodium blood level is replacement needed? Is there a contraindication in medical management for replacing sodium when some of these children are placed on a low sodium diet? Can sodium replacement pull more fluid into cysts?
- 2) When is there a need for sodium Bicarbonate replacement, what causes such a deficiency? How best to treat a deficiency?
- 3) Why do some children develop rickets with ARPKD?
- 4) When is an MRI indicated for the kidney/liver, what results may be seen that cannot be obtained with an ultrasound? What sort of MRI is best? How invasive is a MRI?
- 5) What invasive procedures/testing should be avoided, if any and why? Some of these children are checked for urinary reflux, where a urinary catheter is inserted. When and why should this testing be done, how valid is it?
- 6) Do ARPKD children become dehydrated during the night from not drinking fluids during their sleeping hours?
- 7) How common are inguinal hernias with these children and what causes them?
- 8) Some ARPKD infants/children have severe or ongoing esophageal reflux problems. Is this from enlarged kidney pressure on the stomach or are there chemical reasons (i.e. poor kidney performance, electrolyte imbalance, etc.)? What are the long-term detrimental effects of reflux? What are the treatments and how successful are they?
- 9) Should dietary infant formulas with phosphorus be avoided? What can phosphorus do and are there drugs to counteract its effects?
- 10) What are the dietary restrictions/suggestions for ARPKD/CHF individuals, and dietary restrictions post-transplant kidney and or liver?
- 11) What effect does caffeine have in ARPKD/CHF and should it be restricted or avoided?
- 12) What are the benefits of utilizing a low protein/soy diet before any renal failure begins, as a preventative measure? What studies have been done on the effect of diet for this disease?
- 13) My son refuses to eat much of anything. We have heard that Captopril may dull the sense of taste. Should we switch BP medications? Do some ARPKD children just lack an appetite, and if so, what can be done about this? Does growth hormone affect appetite?
- 14) Is Suplena low in protein and is it superior to Ensure for additional calories?
- 15) Please rank cow's milk, soy milk and breast milk according to what is superior for ARPKD/CHF individuals and why?
- 16) It seems most deaths from ARPKD occur within the first few months of life. What is the death rate through childhood and adulthood? What is the most common cause of death following the first year of life for ARPKD/CHF individuals?

- 17) Do renal cysts reach a point where they cause pain? If yes, what can be done about the pain?
- 18) When is it necessary to check an erythropoietin level? Is this determined by routine lab work? What causes a low erythropoietin level and what effect would this have?
- 19) What causes white blood cells in the urine and is there ever a "normal" amount in the urine? When is treatment needed and what would that consist of?
- 21) Can you use BP readings as part indicator of what the kidney and liver is doing? Could you have perfect BP readings and have your kidney's fail?
- 22) Does developmental growth affect blood pressure results? The bigger the child, the more hypertension medication needed? Is this why so many need hypertension adjustments, changes, increases the first year of life? Yet, what explains why some ARPKD/CHF individuals can be weaned or completely taken off their BP medication(s), even as disease progression continues?
- 23) In the general population there are ways of lowering a person's blood pressure without medications, like weight loss, exercise, low salt diet. Are these effective with PKD?
- 24) For children who do not have high blood pressure, how often should they have their pressures checked? Except in emergency medical situations, can a rise in blood pressure occur suddenly for an ARPKD/CHF individual with a normally stable BP, or does a rise occur slowly, over an extended amount of time?
- 25) What are the long-term side effects (10 years or more) for commonly used blood pressure medications in the pediatric population?
- 26) What hypertensive drugs are most effective in treating ARPKD? Is there any evidence to the theory that Capoten, in particular, may retard cyst growth, more so than other ACE inhibitors, such as Prinival and Vasotec, as the study concerning this was done specifically with Capoten.
- 27) If a blood pressure is consistently in the 95% range, is this considered adequate? What BP percentile range is most effective in preventing further kidney damage in ARPKD kidneys?
- 28) When should growth hormones be introduced? Only when growth is below the fifth percentile? What factors should be evaluated? Can growth hormones accelerate cyst growth? What are the pros and cons of usage? Are there any long term side effects from using the growth hormone with this particular kidney disease? How does parathyroid and PTH (parathyroid hormone) for deficient growth come into play?
- 29) When the creatinine level starts to rise, is it usually a steady, continual rise, or can it stop rising and remain steady for years?
- 30) How spaced should nephrology visits be made, and ultrasounds of the kidneys and lab work be done, if everything is stable?
- 31) Does ARPKD affect learning at all? Is the brain affected by the disease process other than as a result of floating chemistry levels? What are floating chemistry levels?
- 32) I've heard toilet training takes longer because of the enlarged kidneys and constant pressure on the bladder, so a child doesn't always know when they have to go, or feel the urge and that even older children have a problem staying dry at night. Is this true and what can be done? Is there an optimal way to toilet train for both day and evening dryness?
- 33) What would cause an elevated phosphate and low calcium level to stabilize and is this typical for ARPKD individuals?

34) For urinary tract infections, what is the best prophylactic antibiotic for long term use and how long can these be used for?

35) "Our son sweats excessively, even when it is not hot" and from another parent, "my son wants to consistently wear light clothing, even no pajamas or coat during the winter months, he always seems warm". Is this due to the enlarged organs which generate extra heat, or a disease effect, caused by the disorder, or possibly a hormonal imbalance?

36) Do hormones affect ARPKD/CHF? Does adolescence, with all its numerous hormonal changes, cause a decline in kidney function or affect liver function? Are boys affected differently than girls with ARPKD/CHF? Possibly, do females have more liver involvement early on where as boys present with more kidney involvement? If so, could this be hormonally related? Because of the adrenal glands location, could hormone production from these glands affect polycystic kidneys? Could increased or decreased hormones be the reason for high blood pressure, short stature, and the inability to concentrate urine and conserve sodium in some of these individuals? Can altered levels of estrogen, testosterone, epogen, renin, angiotensin I and II, etc, in any way be responsible for progression of ARPKD/CHF. Could the endocrine and exocrine systems be affected or involved? Can hormones be measured and monitored to examine their effects on the disease process? If hormone excretions are abnormal in the ARPKD/CHF population, could hormone treatment potentially alter outcomes for the ARPKD/CHF population?

36) Can kidney failure happen suddenly, or is there usually a slow decline in function? What is the typical progression?

Transplantation Questions:

1) Why are kidneys sometimes removed prior to transplant and sometimes not? What are the pros and cons of each? Should PKD kidneys be routinely removed before placing a new kidney to alleviate cystic infections after transplant?

2) What is the ideal placement of a new kidney? Can placing a new kidney under the liver on the right side, near the ovary, create childbearing problems?

3) If a liver transplant is required, does it have to be from a cadaver or as the parent, can I donate a lobe of my liver? Does the age of the recipient make a difference for the type of liver transplant surgery chosen? What is the success rate of Split Liver transplants? Is the spleen removed at the time of transplant? If it remains, does it return to normal size and functioning?

4) When the time comes for a kidney transplant, how much liver disease has to be present before a liver transplant would be necessary as well? I heard that the liver could regenerate, so could a partially affected/diseased liver be surgically removed?

5) What has come out of the "Chimerism" concept? Does it look feasible for long-term transplant candidates who have had very few rejection episodes?

6) What is the current status of the usage of hu5C8 protein to replace anti-rejection drugs? What are the new immunosuppression medications?

7) What are the long term survival rates for a kidney/liver transplant, specifically on ARPKD/CHF patients?

8) How many kidney/liver transplants can a person have? Is there more rejection, infections, and complications with each subsequent transplant?

9) Do you suggest doing a donor bone marrow transplant before the liver transplant, to help head off rejection? If so, is it more effective to do it before transplantation or after?

- 10) Can excessive transfusion of blood, as a result of variceal bleeds, be detrimental to the kidneys and could it also cause problems with transplantation because of the antibodies?
- 11) Is it beneficial to do a double transplant (kidney & liver) so that antibodies are in response to the same donor, verses doing separate transplants, (at different time intervals), from two different donors?
- 12) When can an infant be transplanted for either/both a kidney or liver?
- 13) What indicates a kidney or liver transplant should be performed? What abnormal lab values, clinical manifestations, parameters would demonstrate transplantation should occur and when is there a benefit in waiting verses performing a transplant as early as possible?
- 14) Cysts do not form in transplanted kidneys, but does CHF continue after kidney transplant? Once an ARPKD/CHF individual has both a kidney/liver transplant, does this mean they are rid of the disease?

Miscellaneous Questions:

- 1) When can we expect clinical trials for Dr. Ellis Avner's drug to begin, what will be the number of participants? What are the determining factors for selection to participate? How long will the clinical trials last? Will it have an effect on CHF? Would it possibly reverse existing cysts or hepatic fibrosis, or just retard progression?
- 2) What clinical drugs currently being developed/drug tested may have an effect on ARPKD, and CHF? What is the time frame and process, for drug development, clinical trials, to market availability?
- 3) Can the epidermal growth factor be measured, is this a hormone, or influenced by such?
- 4) Will our ARPKD daughter be able to have children of her own? Will she be passing the disease to her own children?
- 5) What substances/chemicals are particularly troublesome to ARPKD/CHF? What over-the-counter medicines may I give my child with ARPKD/CHF for the common cold, flu, nasal congestion or general aches and pains? Is Motrin a drug of choice for fever?
- 6) Guidelines for physical activity, what should be avoided?
- 7) Does ARPKD/CHF place our children at greater risk for developing tumors? What is the potential for CHF developing into liver cancer?
- 8) When do you think growing organs for human application will be available?