The Restoration Act (INGO) is proudly offering virtual seminars on various clinical topics of inborn errors of metabolism, genetics, and neurology in collaboration with the Ministry of Health Kurdistan Regional Government, Directorate General of Health Duhok, Iraqi & Kurdistan Boards for Medical Specialization/Pediatric, University of Duhok College of Pharmacy and Pediatric Department of Medicine, Kurdistan Pediatric Society, Hevi Hospital, and the Iraqi Pediatric Society.

Questions & Answers (Q & A) from:

"Lysosomal Storage Disorders"

Held 29 May 2025

Watch the recorded Virtual Clinical Seminar

Passcode: SNJz4C.Z

Presented by Metabolic Specialist:

Dr. Joshua Baker, DO, FAAP, FACMG

Dr. Baker's written answers to the questions as written/asked during the live seminar:

Q. In the USA, what is the most common type of MPS disease?
A. It use to be MPSI, but now with Newborn screen we are finding a lot more attenuated MPSII patients.

Q. Dr. Baker you state the most common presentation of MPS type 2 is otitis media, do you agree it is important to provide more specialists with this information, especially ENT specialists who may be more commonly caring for these patients?
A. Yes definitely. They need to be educated so we can make sure they are catching everyone at risk and refer those who need diagnosed and managed by a specialist.

Q. You state the GAG in MPS disease you can detect in the blood but in the urine it is more specific and clear. You also stated that Lysosomal Disorders have a very acidic PH. So when we have a GAG and a high PH in the urine and the blood, have you observed any other abnormality in the blood - like liver function test - that will guide us better in testing and investigation?
A. Not that I know of. GAGs are best for diagnosis and monitoring. Other biomarkers are in research currently.

Q. Is there any role for X-Ray studies in the diagnosis of MPS disease?
A. Yes. Depending on the type of MPS there are recommending imaging studies to look for involved bones that may need management by orthopedics.

Q. In case presentation of ASMD, you stated if you are doubting about the diagnosis, in the Newborn Screen you can wait and follow the patient. Is there a reason why we

should not be sending the family for a family segregation study, to confirm any genetic abnormality in the parent, then you can go back and confirm the genetic abnormality in the child/patient?
A. Because a case can look different between family members, you should test ALL at risk family members for possible disease.

Q. If you have a patient with ASMD, and you send or further blood testing and note any form of cytopenia, should we in the beginning try to rule-out malignancy like through bone marrow study. Would we find anything else in the bone marrow that would guide us to diagnosis of ASMD?
A. Yes you should always rule out malignancy

Q. In the patient case study, you observed that they will have hyper (or was it hypo?) dyslipidemia(?). What is the mechanism behind this?
A. The dyslipidemia is deferent based on the lipid type. Low HDL. High LDL and Triglycerides. It is from both abnormal cell wall function from the accumulation of lyso-sphingomyelin and also the liver disease over time.

Q. Is treatment available for ASMD in the USA or not? If treatment is available, do you observe improvement in the patient from this treatment?
A. Yes there is Enzyme Replacement therapy since 2022 and they respond very well to treatment. Unfortunately does not treat the neurologic disease.

Q. A question about Krabbe Disease. We have observed most of the patients have neurological symptoms. And most often our pediatricians are diagnosing this as Cerebral Palsy. Is there anything addition that will specifically guide us to Krabbe Disease, as this diagnosis is difficult in our area/region?
A. Unfortunately this is common and complicated. CP should be static and not changing. Krabbe disease is progressive. So if a child was not born with CP but developed symptoms over time, should look for a lysosomal disease like Krabbe.

Q. Any abnormality to look for if you do a CSF examination in the case of Krabbe Disease?
A. You can do a CSF testing for elevated protein. However, we do not do if we already know the diagnosis.

Q. In Pompee Disease, can one discern if the Cardiomegaly that we observe in the X-Ray is due to the presence of the substance, or due to heart failure?
A. Both typically. Depending on what time it is caught.

Q. If we suspect an LSD, what's the first test we should order in a resource-limited setting
A. An enzyme panel is the cheapest and fastest testing for resource limited setting.

Q. Any gene therapy for these LSDs ?
A. Yes there is Gene Therapy for MPSII, MPSIIIA, and MLD. There are many more in clinical trails that will be moving towards approval soon.

Q. As long as Hunter is X-Linked Recessive so it means mother is the only carrier,will carrier mother has any clinical features to let her do genetic studies?
A. No carriers for Hunter have known to have disease.

Q. What makes Hurler disease more susceptible for CNS involvement than Hunter?
A. Both are at risk depending on type of variant or enzyme activity. We don't fully understand why transplant works well for Hurler but not always for Hunter.

Q. why enzyme therapy fail in reversing neuro signs and symptoms in many LSDs
A. Because it cannot cross the blood brain barrier. Most enyzmes are given IV.

Q. After successful HSCT does the CNS symptoms resolve or remain the same ?
A. Typically plateau is best case scenario. Unlikely to improve CNS once damaged.

Q. Almost all of our Pome patents in Duhok developed significant allergic reactions to ERT Myozyme is it the same in US ?
A. Yes. They often need treatment for this. You can look up Duke immune modulation protocol to help with treatment.

Q. Do you have the ERT for ASMD in your hospital? if yes, what is the outcome for the patients?
A. Yes. They are doing very well. MUCH improvement in organ size, growth, and dyslipidemia.

Q. is there any treatment available in the near future for farber diasease ?
A. There are clinical trials but nothing close to FDA approval that I am aware of at this time.

Q. Regarding the ITI protocol for IOPD, what is the outcome on the patients survival?
A. They do very will with the immune protocol from Duke. Duke has nice published data showing improved outcomes and prolonged survival that you can look up in pubmed.

Q. can enzyme therapy improve skeletal dysplasia or corneal opacity in MPS DISEASE?
A. Skeletal disease – if caught early can improve. For corneal opacity, ERT does not treat since the eye has a protective barrier like the brain. Corneas often need surgery.

Q. Is there any certificate at the end of the seminar?
A. Yes please contact if not received if you met the time requirement.

Q. Thanks for your comprehensive lecture as there is mitochondrial dysfunction in the form of impaired mitophagy so thinking out of the box what about trying to add COQ10 and other mitochondrial cocktail
A. Area of research but nothing published that I am aware of.

Q. Another question GAG is not available in our country so how we can detect pseudo deficiency
A. I am not sure. GAGs are needed. Can you send blood or urine to another country? I think we should discuss with the government if you cannot.

Q. Should asymptomatic children with late-onset lysosomal storage disorder genotypes receive early treatment or only be monitored?
A. Depends on the type of LSD. Would not start treatment until early biomarkers but before symptoms.

Q. What are the earliest red flags in infancy or early childhood that should raise suspicion for LSDs, especially for pediatricians in regions without access to specialized care?
A. Regression is biggest red flag. Or if not neurotype then multisystemic organ disease.

Q. Are there any emerging therapies for the neurodegenerative aspects of MPS
A. Yes there are the enzymes to cross the brain and also gene therapy for many of the neuro MPS disorders in clinical trials.