

Inherited Metabolic Diseases

Neurometabolic/Intellectual Disability/ X-Linked/ Ornithine Transcarbamylase (OTC) Deficiency



- 1. What are the management strategies for UCP disorders?
- 2. What is the cause for postpartum encephalopathy in cases II:5 and II:6?
- 3. What will be the various components of genetic counselling for the case III:4?
- 4. What is the critical level of ammonia that leads to permanent neurological damage in infancy?
- 5. What is the age of disease onset with total loss of enzyme function?
- 6. Is the genotype strongly follow the phenotype with OTC deficiency?

Plausible tenets:

のないため、

Gene: OTC (Xp11.4); 68,919 bp & 10 Exons

- Second enzyme of the principal pathway used for the detoxification of ammonia
- Transcript (1,522 bps), 3 transcripts (splice variants), 200 orthologues & 2 paralogues
- Protein(354AA, 40 kD) is changed to an active enzyme by fusion of three units of 36-kD by posttranslational modification
- L-citrulline is synthesized by fusion of carbamoyl phosphate with L-ornithine in the mitochondrial matrix
- Citrulline level in <u>plasma is maintained by its synthesis</u> in the intestinal tract through CPS1 and OTC activity and used by renal tubules to form arginine by argininosuccinate synthetase (ASS) and argininosuccinate lyase(ASL).

Cunical pricedotypes. Simplified denotype and r henotype relationship Sex Treatment of choice for typical Absent Absent Absent Neonatal (floppy, encephalopathy) Male Liver transplantation Fractional Partial Post-Neonatal M>F Preventive - Management: depend upon hyperammonemia, disease stage, and co-morbidity - Preventive - Consequences, if standard treatment not followed: 1. progressive dysfunction of higher cognitive function: delayed milestones, learning disabilities, attention-deficit/hyperactivity disorder, inexplicable cerebral palsy 2. Other neurological features such as headache, migraine Acute NH - \$200 µmol/L rapidly with +/_ dialysis, NH scavenger, stopping catabolism; protect from neurologic damage Chronic dietary protein restriction, medications to stimulate substitute pathway, citrulline/arginine, frequent testing of NH and amino acids levels, untrition supplementations, liver function & neurological evaluation and avoid precipitating factors for catabolic state as fasting and stress & hepatotxic drugs including systemic corticosteroids, Valproate & haloperidol. Anayte ctruline and glutamine Plasma NH, orotic add upuentification profile of anion or catabolic state are external. Anayte ctruline and glutamine rate Specific observations in few UCD VDD - overall incidence has been estimated to be 1 in 10,000 -35,000 births Pregnancy should be managed as a catabolic state, even after delivery
Absent Neonatal (floppy, encephalopathy) Male Liver transplantation Fractional Partial Post-Neonatal M>F Preventive - Management: depend upon hyperanmonemia, disease stage, and co-morbidity - Consequences, if standard treatment not followed: 1, progressive dysfunction of higher cognitive function: delayed milestones, learning disabilities, attention-deficit/hyperactivity disorder, inexplicable cerebral palsy 2. Other neurological features such as headache, migraine Acute NHs - \$200 µmol/L rapidly with +/_ dialysis, NHs acareger, stopping catabolism; protect from neurologic damage Chronic dietary protein restriction, medications, to stimulate substitute pathway, citrulline/arginine, frequent testing of NHs and amino acids levels, nutrition supplementations, liver function & neurological evaluation and avoid precipitating factors for catabolic state as fasting and stress & hepatotxic drugs including systemic corticosteroids, Valproate & haloperidol. Steps for New-born screening (NBS) by dried blood spots (DBS) for OTC deficiency The most important sources of NH3-Alanine and glutamine are internal while guantification, profile of anino acid as a fuel are external. UCD - overall incidence has been estimated to be 1 in 10,000 -35,000 births Pregnancy should be managed as a catabolic state, even after delivery in the asymptomatic carrier. Diagnosis by any one of technique: Technique Comments Argininosuccinate Lyase Specific observations i few UCD Defi
Fractional Partial Post-Neonatal M>F Preventive - Management: depend upon hyperammonemia, disease stage, and co-morbidity - Frectional M>F Preventive - Consequences, if standard treatment not followed: 1. progressive dysfunction of higher cognitive function: delayed milestones, learning disabilities, attention-deficit/hyperactivity disorder, inexplicable cerebral palsy 2. Other neurological features such as headache, migraine Acute NHs- 5200 µmol/L rapidly with +/_ dialysis, NHs scavenger, stopping catabolism; protect from neurologic damage Chronic dietary protein restriction, medications to stimulate substitute pathway, citrulline/arginine, frequent testing of NHs and amino acids levels, nutrition supplementations, liver function & neurological evaluation and avoid precipitating factors for catabolic state as fasting and stress & hepatotoxic drugs including systemic corticosteroids, Valproate & haloperidol. Steps for New-born screening (NBS) by dried blood spots (DBS) for OTC deficiency The most important sources of NH3-Alanine and glutamine are internal while generated by urease-positive bacteria of the gut on dietary amino acids as a fuel are external. UCD - overall incidence has been estimated to be 1 in 10,000 -35,000 births Period comments First case published by Russell and coworkers in 1962 Specific observations in few UCD Pregnancy should be managed as a catabolic state, even after delivery in the asymptomatic carrier. Diagnosis by any one of technique: T
Management: depend upon hyperaminonemia, disease stage, and co-morbidity Consequences, if standard treatment not followed: 1. progressive dysfunction of higher cognitive function: delayed milestones, learning disabilities, attention-deficit/hyperactivity disorder, inexplicable cerebral palsy 2. Other neurological features such as headache, migraine Acute NH ₃ < 200 µmol/L rapidly with +/, dialysis, NH scavenger, stopping catabolism; protect from neurologic damage Chronic dietary protein restriction, medications to stimulate substitute pathway, citrulline/arginine, frequent testing of NH ₃ and amino acids levels, nutrition supplementations, liver function & neurological evaluation and avoid precipitating factors for catabolic state as fasting and stress & hepatotoxic drugs including systemic corticosteroids, Valproate & haloperidol. Steps for New-born screening (NBS) by dried blood spots (DBS) for OTC deficiency Analyte ctrulline and glutamine- regulation, norfie of anino acids as a fuel are external. Alanine and glutamine- regulation, norfie of anino acid & urine organic acid profile Recommended diagnostic test orgen trained to be 1 in 10,000 -35,000 births Specific observations in few UCD First case published by Russell and corver in 1962 Included in the USA NBS panel First beneficial OTC gene therapy trial First beneficial OTC gene therapy trial
 Consequences, if standard treatment not followed: 1, progressive dysfunction of higher cognitive function: delayed milestones, learning disabilities, attention-deficit/hyperactivity disorder, inexplicable cerebral palsy 2. Other neurological features such as headache, migraine Acute NH₃ < 200 µmol/L rapidly with +/_ dialysis, NH₃ scavenger, stopping catabolism; protect from neurologic damage Chronic dietary protein restriction, medications to stimulate substitute pathway, citrulline/arginine, frequent testing of NH₃ and amino acids levels, nutrition supplementations, liver function & neurological evaluation and avoid precipitating factors for catabolic state as fasting and stress & hepatotoxic drugs including systemic corticosteroids, Valproate & haloperidol. Steps for New-born screening (NBS) by dried blood spots (DBS) for OTC deficiency Analyte citrulline and glutamine- levels, unification, profile of anino acid & urine organic acid profile Mecommended diagnostic test Analyte citrulline and glutamine- levels as deficiency organic acid profile Plasma NH₂ orotic acid quantification, profile of anino acid & urine organic acid profile Pregnancy should be managed as a catabolic state, even after delivery in the asymptomatic carrier. Deficiency citrin deficiency Progressive spastic tetraplegia First beneficial OTC gene therapy trial First beneficial OTC gene therapy trial First beneficial OTC gene therapy trial
Acute NH - 5200 µm0/L rapidly with +/_ dialysis, NH scavenger, stopping catabolism; protect from neurologic damage Acute NH - 5200 µm0/L rapidly with +/_ dialysis, NH scavenger, stopping catabolism; protect from neurologic damage Chronic dietary protein restriction, medications to stimulate substitute pathway, citrulline/arginine, frequent testing of NH and amino acids levels, nutrition supplementations, liver function & neurological evaluation and avoid precipitating factors for catabolic state as fasting and stress & hepatotoxic drugs including systemic corticosteroids, Valproate & haloperidol. Steps for New-born screening (NBS) by dried blood spots (DBS) for OTC deficiency Plasma NH, orotic add quantice and glutamice are internal while generated by urease-positive bacteria of hegy or diatery amino acids as a fuel are internal while generated by urease-positive bacteria of anito acid & urine organic add profile UCD - overall incidence has been estimated to be 1 in 10,000 -35,000 births Recommended diagnostic test First case published by Russell and coworkers in 1962 Specific observations in few UCD Deficiency Prograncy should be managed as a catabolic state, even after delivery in the asymptomatic carrier. Diagnosis by any one of technique: Technique Comments Arginase deficiency and, 0TC deficiency differed filterey and the carrier. Diagnosis by any one of technique: Technique Comments Geneticnery differed context and the carrier. Dispecific observations in few UCD Technique Comments
Acute NH3-s200 µmol/L rapidly with +/_ dialysis, NH3 scavenger, stopping catabolism; protect from neurologic damage Chronic dietary protein restriction, medications to stimulate substitute pathway, citrulline/arginine, frequent testing of NH3 and amino acids levels, nutrition supplementations, liver function & neurological evaluation and avoid precipitating factors for catabolic state as fasting and stress & hepatotoxic drugs including systemic corticosteroids, Valproate & haloperidol. Steps for New-born screening (NBS) by dried blood spots (DBS) for OTC deficiency The most important sources of NH3-Alanine and glutamine are internal while generated by urease-positive bacteria of the gut on dietary maino acids as a fuel are external. Analyte citrulline and glutamine Plasma NH3 orotic add quantification, profile of amino acid s version acid profile UCD - overall incidence has been estimated to be 1 in 10,000 -35,000 births Recommended diagnostic test First case published by Russell and coworkers in 1962 Specific observations in few UCD Peficiency Subscinct Lyase Argininosuccinate Lyase Subscinct Lyase Peficiency and, OTC deficiency and, OTC defici
Acute NH ₂ - 5200 µmol/L rapidly with +/_ dialysis, NH ₃ scavenger, stopping catabolism; protect from neurologic damage Chronic dietary protein restriction, medications to stimulate substitute pathway, citrulline/arginine, frequent testing of NH ₃ and amino acids levels, nutrition supplementations, liver function & neurological evaluation and avoid precipitating factors for catabolic state as fasting and stress & hepatotoxic drugs including systemic corticosteroids, Valproate & haloperidol. Steps for New-born screening (NBS) by dried blood spots (DBS) for OTC deficiency The most important sources of NH3-Alanine and glutamine are internal while generated by urease-positive bacteria of the gut on dietary amino acids as a fuel are external. Analyte citrulline and glutamine tradition profile of amino acid & urine organic acid profile Recommended diagnostic test UCD - overall incidence has been estimated to be 1 in 10,000 - 35,000 births Pregnancy should be managed as a catabolic state, even after delivery in the asymptomatic carrier. Pregnancy should be managed as a catabolic state, even after delivery in the asymptomatic carrier. Diagnosis by any one of technique: Technique Argininosuccinate Lyase Disease Deficiency Specific observations Analyte citruline in the USA NBS panel Frist beneficial OTC gene therapy trial Presence of pathological variant disease First beneficial OTC gene therapy trial Argininosuccinate Lyase Trichorrhexis Nodosa
Chronic dietary protein restriction, medications to stimulate substitute pathway, citrulline/arginine, frequent testing of NH ₃ and amino acids levels, nutrition supplementations, liver function & neurological evaluation and avoid precipitating factors for catabolic state as fasting and stress & hepatotoxic drugs including systemic corticosteroids, Valproate & haloperidol. Steps for New-born screening (NBS) by dried blood spots (DBS) for OTC deficiency The most important sources of NH3-Alanine and glutamine are internal while generated by urease-positive bacteria of the gut on dietary amino acids as a fuel are external. Analyte citruline and glutamine-to-glutamate ratio Plasma NH, orotic acid acid & urine organic acid profile of amino acid & urine organic acid profile organical acid profile organical acid acid acid acid acid acid acid acid
acids levels, nutrition supplementations, liver function & neurological evaluation and avoid precipitating factors for catabolic state as fasting and stress & hepatotoxic drugs including systemic corticosteroids, Valproate & haloperidol. Steps for New-born screening (NBS) by dried blood spots (DBS) for OTC deficiency The most important sources of NH3-Alanine and glutamine are internal while generated by urease-positive bacteria of the gut on dietary amino acids as a fuel are external. Analyte citrulline and glutamine to-glutamate ratio Plasma NH, orotic acid quantification, profile of amino acid as a fuel are external. UCD - overall incidence has been estimated to be 1 in 10,000 -35,000 births Recommended diagnostic test First case published by Russell and coworkers in 1962 Specific observations in few UCD Included in the USA NBS panel Specific conservationa is few UCD First beneficial OTC gene therapy trial Substantial liver disease First beneficial OTC gene therapy trial Substantial liver disease
as fasting and stress & hepatotoxic drugs including systemic corticosteroids, Valproate & haloperidol. Steps for New-born screening (NBS) by dried blood spots (DBS) for OTC deficiency Analyte ctrulline and glutamine- to-glutamate ratio Plasma NH, orotic add quantification, profile of amino acid & urine organic acid profile Recommended diagnostic test UCD - overall incidence has been estimated to be 1 in 10,000 -35,000 births Recommended diagnostic test Age of disease onset with absent gene expression - 2nd to 3rd day of life First case published by Russell and coworkers in 1962 Included in the USA NBS panel Specific observations in few UCD Pregnancy should be managed as a catabolic state, even after delivery in the asymptomatic carrier. Diagnosis by any one of technique: Technique Comments disease Perficiency, citrin deficiency and, OTC deficiency and, OTC deficiency trial Substantial liver disease Trichorrhexis Nodosa
Steps for New-born screening (NBS) by dried blood spots (DBS) for OTC deficiency Analyte citrulline and glutamine reinternal while generated by urease-positive bacteria of the gut on dietary amino acids as a fuel are external. Analyte citrulline and glutamine reinternal while generated by urease-positive bacteria of the gut on dietary amino acids as a fuel are external. UCD - overall incidence has been estimated to be 1 in 10,000 - 35,000 births First case published by Russell and coworkers in 1962 Included in the USA NBS panel First beneficial OTC gene therapy trial First beneficial OTC gene therapy trial
Steps for New-born screening (NBS) by dried blood spots (DBS) for OTC deficiency Analyte citrulline and glutamine to glutamine to glutamine to glutamine and glutamine are internal while generated by urease-positive bacteria of the gut on dietary amino acids as a fuel are external. Analyte citrulline and glutamine to glutamine toglutamine to glutamine to glutamine to gluta
Steps for New-born screening (NBS) by dried blood spots (DBS) for OTC deficiency The most important sources of NH3-Alanine and glutamine are internal while generated by urease-positive bacteria of the gut on dietary amino acids as a fuel are external. Analyte citrulline and glutamine-to-glutamate ratio Plasma NH, orotic acid quantification, profile of amino acid & urine organic acid profile Recommended diagnostic test UCD - overall incidence has been estimated to be 1 in 10,000 -35,000 births Age of disease onset with absent gene expression - 2nd to 3rd day of life First case published by Russell and coworkers in 1962 Deficiency Specific observations in few UCD Included in the USA NBS panel Peficiency (trin deficiency on C) Substantial liver disease Diagnosis by any one of technique: First beneficial OTC gene therapy trial Argininosuccinate Lyase Trichorrhexis Nodosa Substantial liver disease Biochemical Random urinary sample - Orotic acid exerction ≥20 umol/mmol creatinine)*
Steps for New-born screening (NBS) by dried blood spots (DBS) for OTC deficiency Analyte citrulline and glutamine- to-glutamate ratio Plasma NH ₃ orotic acid quantification, profile of amino acid & urine organic acid profile Recommended diagnostic test Alainia and glutamine are internal while generated by urease-positive bacteria of the gut on dietary amino acids as a fuel are external. UCD - overall incidence has been estimated to be 1 in 10,000 -35,000 births Age of disease onset with absent gene expression - 2nd to 3rd day of life First case published by Russell and coworkers in 1962 Deficiency Specific observations in few UCD Deficiency Specific observations terraplegia Pregnancy should be managed as a catabolic state, even after delivery in the asymptomatic carrier. Diagnosis by any one of technique: Argininosuccinate Lyase Deficiency and, OTC deficiency Substantial liver disease First beneficial OTC gene therapy trial Random urinary sample - Orotic acid excretion ≥20 umol/mmol creatinine)*
Analyte citrulline and glutamine- to-glutamate ratio Plasma NH ₃ orotic acid guantification, profile of amino acid & urine organic acid profile Recommended diagnostic test generated by urease-positive bacteria of the gut on dietary amino acids as a fuel are external. UCD - overall incidence has been estimated to be 1 in 10,000 -35,000 births Age of disease onset with absent gene expression - 2nd to 3rd day of life First case published by Russell and coworkers in 1962 Specific observations in few UCD Pregnancy should be managed as a catabolic state, even after delivery in the asymptomatic carrier. Deficiency Resource the rapy trial Specific observations in few UCD Pregnancy should be managed as a catabolic state, even after delivery in the asymptomatic carrier. Diagnosis by any one of technique: Included in the USA Argininosuccinate Lyase Substantial liver disease Diagnosis by any one of technique: First beneficial OTC gene therapy trial Substantial liver Argininosuccinate Lyase Substantial liver disease Implements disease Argininosuccinate Lyase Trichorrhexis Nodosa Implemental Random urinary sample - Orotic acid excretion ≥20 umol/mmol creatinine)*
Analyte citrulline and glutamine- to-glutamate ratio Plasma NH3 orotic acid quantification, profile of amino acid & urine organic acid profile Recommended diagnostic test the gut on dietary amino acids as a fuel are external. UCD - overall incidence has been estimated to be 1 in 10,000 -35,000 births Specific observations in few UCD Argininosuccinate Lyase Progressive spastic tetraplegia Pregnancy should be managed as a catabolic state, even after delivery in the asymptomatic carrier. Deficiency Specific observations Progressive spastic tetraplegia Diagnosis by any one of technique: Argininosuccinate Lyase Substantial liver disease disease 1. Molecular Presence of pathological variant acid excretion >20 umol/mmol creatinine)*
Commended diagnostic test External. UCD - overall incidence has been estimated to be 1 in 10,000 -35,000 births Age of disease onset with absent gene expression - 2nd to 3rd day of life First case published by Russell and coworkers in 1962 Deficiency Specific observations in few UCD Included in the USA NBS panel Argininosuccinate Lyase Substantial liver disease Diagnosis by any one of technique: First beneficial OTC gene therapy trial First beneficial OTC Substantial liver disease Trichorrhexis Nodosa
UCD - overall incidence has been estimated to be 1 in 10,000 -35,000 births Age of disease onset with absent gene expression - 2nd to 3rd day of life First case published by Russell and coworkers in 1962 Specific observations in few UCD Pregnancy should be managed as a catabolic state, even after delivery in the asymptomatic carrier. Included in the USA NBS panel Argininosuccinate Lyase Deficiency, citrin deficiency and, OTC deficiency and, OTC deficiency and, OTC deficiency and, OTC deficiency argininosuccinate Lyase Trichorrhexis Nodosa Substantial liver disease Diagnosis by any one of technique:
UCD - overall incidence has been estimated to be 1 in 10,000 -35,000 births expression - 2nd to 3rd day of life First case published by Russell and coworkers in 1962 Specific observations in few UCD Pregnancy should be managed as a catabolic state, even after delivery in the asymptomatic carrier. Included in the USA NBS panel Argininosuccinate Lyase Deficiency, citrin deficiency and, OTC deficiency Substantial liver disease Diagnosis by any one of technique: Technique Comments 1. Molecular Presence of pathological variant acid excretion ≥20 umol/mmol creatinine)*
First case published by Russell and coworkers in 1962 Specific observations in few UCD Pregnancy should be managed as a catabolic state, even after delivery in the asymptomatic carrier. Deficiency Specific observations Arginase deficiency Progressive spastic tetraplegia Included in the USA NBS panel Argininosuccinate Lyase Deficiency, citrin deficiency and, OTC deficiency Substantial liver disease Diagnosis by any one of technique: I. Molecular Presence of pathological variant acid excretion ≥20 umol/mmol creatinine)*
First case published by Russell and coworkers in 1962 Specific observations in few UCD Pregnancy should be managed as a catabolic state, even after delivery in the asymptomatic carrier. Included in the USA NBS panel Argininosuccinate Lyase Deficiency, citrin deficiency and, OTC deficiency Substantial liver disease Pregnancy should be managed as a catabolic state, even after delivery in the asymptomatic carrier. First beneficial OTC gene therapy trial Argininosuccinate Lyase Argininosuccinate Lyase Substantial liver disease Technique 1. Molecular Presence of pathological variant acid excretion ≥20 umol/mmol creatinine)*
by Russell and coworkers in 1962DeficiencySpecific observationsArginase deficiencyProgressive spastic tetraplegiaDiagnosis by any one of technique:Included in the USA NBS panelArgininosuccinate Lyase Deficiency, citrin deficiency and, OTC deficiencySubstantial liver diseaseTechniqueFirst beneficial OTC gene therapy trialArgininosuccinate Lyase Trichorrhexis NodosaTrichorrhexis NodosaBiochemical reatinine)*
coworkers in 1962 Arginase deficiency Progressive spastic tetraplegia Included in the USA NBS panel Argininosuccinate Lyase Deficiency, citrin deficiency and, OTC deficiency Substantial liver disease First beneficial OTC gene therapy trial Argininosuccinate Lyase Deficiency, citrin deficiency and, OTC deficiency Substantial liver disease
Included in the USA NBS panelArgininosuccinate Lyase Deficiency, citrin deficiency and, OTC deficiencySubstantial liver diseaseDiagnosis by any one of technique:First beneficial OTC gene therapy trialArgininosuccinate Lyase Argininosuccinate LyaseSubstantial liver diseaseIMolecularPresence of pathological variant2.Biochemical acid excretion ≥20 umol/mmol creatinine)*Andom urinary sample - Orotic acid excretion ≥20 umol/mmol creatinine)*
Metaded in the OSA Argininosuccinate Lyase Substantial liver Technique Comments NBS panel Deficiency, citrin disease disease 1. Molecular Presence of pathological variant First beneficial OTC deficiency Trichorrhexis Nodosa Trichorrhexis Nodosa Image: Comments of the pathological variant
First beneficial OTC gene therapy trial Deliciency, cu m disease 1. Molecular Presence of pathological variant Argininosuccinate Lyase Trichorrhexis Nodosa Trichorrhexis Nodosa acid excretion ≥20 umol/mmol creatinine)*
First beneficial OTC gene therapy trial deficiency Intervention Random unitary sample = Orote acid excretion ≥20 umol/mmol creatinine)*
gene therapy trial Argininosuccinate Lyase Trichorrhexis Nodosa creatinine)*
with (DTX301) was Deficiency 3. Enzyme activity Fail to detect carrier status
done on Simon associated with cholestasis *Alternately in older cases, presence constant biochemical characteristics
Smith in August Citrullinaemia type-II Gastrointestinal symptoms of OTC deficiency as elevated ammonia, elevated glutamine and low-to-
2017 & Failure to thrive and normal citrulline, and high Orotic acid after an allopurinol challenge test
Constis sourcelling components with case III.4
<u>Genetic counselling components with case III:4</u> Understand family's psychological condition \rightarrow first confirm the disease \rightarrow define the disease course and its management \rightarrow discuss future treatment including
Genetic counselling components with case III:4 Understand family's psychological condition→ first confirm the disease → define the disease course and its management → discuss future treatment including Gene therapy surveillance guidelines → haploinsufficiency and stress phenomenon → antenatal diagnosis in the subsequent pregnancy
<u>Genetic counselling components with case III:4</u> Understand family's psychological condition \rightarrow first confirm the disease \rightarrow define the disease course and its management \rightarrow discuss future treatment including Gene therapy surveillance guidelines \rightarrow haploinsufficiency and stress phenomenon \rightarrow antenatal diagnosis in the subsequent pregnancy
Genetic counselling components with case III:4 Understand family's psychological condition → first confirm the disease → define the disease course and its management → discuss future treatment including Gene therapy surveillance guidelines → haploinsufficiency and stress phenomenon → antenatal diagnosis in the subsequent pregnancy Thought Riveting:
Genetic counselling components with case III:4 Understand family's psychological condition → first confirm the disease → define the disease course and its management → discuss future treatment including Gene therapy surveillance guidelines → haploinsufficiency and stress phenomenon → antenatal diagnosis in the subsequent pregnancy Thought Riveting: Image: Ima

What is the crucial role of tertiary protein structure in the success of gene therapy?

For a low resource center, what could be the best NBS strategy for detecting the UCD?

Does ammonia have teratogenic effects at the early embryonic stage, especially on the neuroectodermal growth plate and synaptogenesis?