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National Guideline

of Newborn Screening for Care Providers in primary health care centers in Iraq

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Chapter 1

Introduction

Newborn screening (NBS) is intended as a public health program to identify infants with treatable conditions before they present clinically, or suffer irreversible damage.
Metabolic disorders are not easily detected without screening because many of the symptoms are non-specific and look like other more common conditions. Some of the disorders do not show any symptoms at all until after damage has occurred. In some of these cases damage is not able to be repaired. Screening means that metabolic disorders can be diagnosed before a baby gets sick.
The goal of newborn screening is early identification of children at increased risk for selected metabolic , genetic or congenital diseases so that medical treatment can be promptly initiated to avert metabolic crises and prevent irreversible neurological and developmental squeal.
Early identification of these conditions is crucial, as timely intervention can lead to a significant reduction of morbidity, mortality, and associated disabilities in affected infants.

Newborn Screening project in Iraq

This project will participate in reducing the rate of under-five mortality by two-thirds,to meeting Millennium Development Goal 4 in 2015.
The Newborn Screening program has been started on April, 2013 as a pilot project taking two provinces: Baghdad and Karbala as starting provinces.
The preparatory phase for more than one year has focused on capacity building bringing the most updated technology for early identification of two assigned inborn error of metabolism which are, phenylketonuria (PKU) ,Galactosemia(GAL) ,also congenital hypothyroidism(CHT) by Dissociation Enhancement**lanthanidfluoroimmun assay (DELFIA technique) testing blood from a baby's heel prick.**
Sample of blood is collected at appropriate age (72 hours-5days) after delivery and also those who had not screened up to 2 month of age in primary health care centers (PHC) and hospitals that have neonate care units (NICU).

Objective of the Guideline

This guideline is designed to:

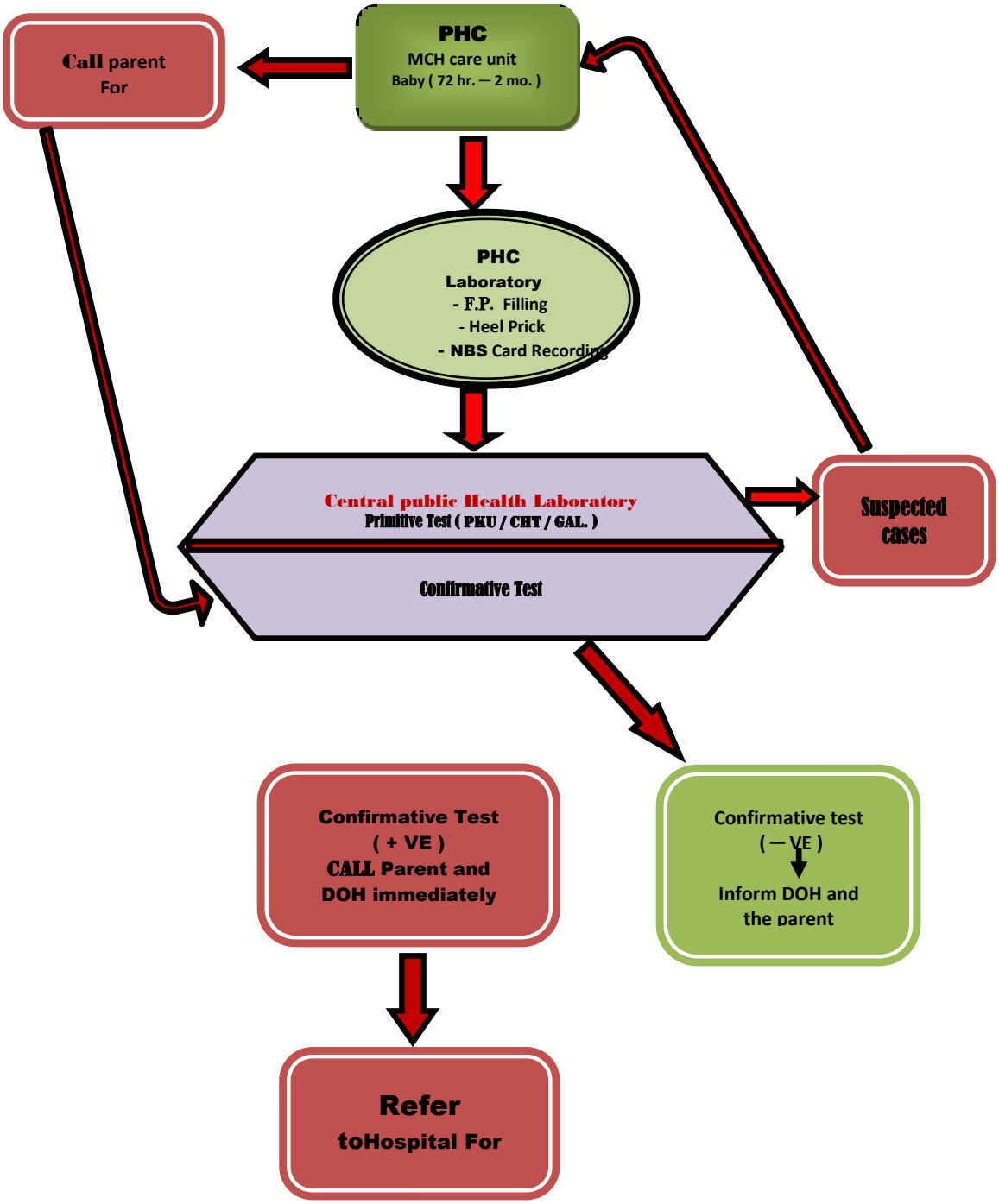
1- providethe general and the specific knowledge about the newborn screening project in Iraq for nurses, neonatologists, pediatrician, physicians, obstetricians, nutritionist and biochemists.
2- Describe the disorders currently included in Iraq screening project.
3- Provide practical manual for everyday use

The concept of newborn screen

The newborn Screening is a public health service. It is done by testing individuals who are not known to have a disease (are asymptomatic) so that they can be identified and treated before problems occur. Screening is the first step in a two-step process. The first screening test indicates a problem MAY BE present (primitive) , and then a second diagnostic test (confirmative) confirms whether or not the problem or disease is present. Newborn screening project is available to all infants and is done shortly after birth, While most infants look perfectly healthy.To test for these diseases, a baby's heel is pricked and a small sample of blood is collected at optimum age (72 hours-5 days) after delivery and those who had not screened up to 2 month of age , The blood is dried onto a newborn screening filter paper (F.P.) aims to detect a certain rare, but serious genetic, congenital and/or metabolic conditions that may be life threatening.

All babies are offered screening for phenylketonuria (PKU), congenital hypothyroidism (CHT), galactosemia.

Organization of newborn screen



Chapter 2

Instruction s for blood sampling & transportation

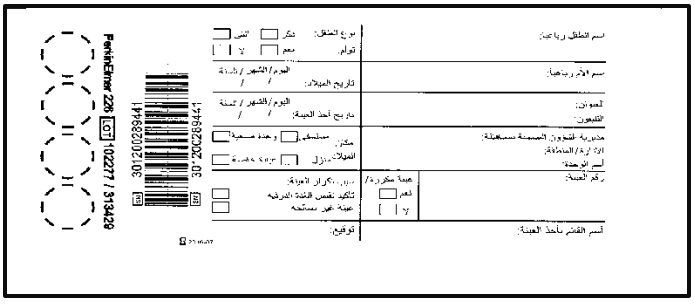
Section A

1- Blood sampling

Before the sample is taken parents are informed about the newborn screening project and the folder(parent Brochure) is handed over to them.
The collection of a blood specimen on the filter paper card is handled by health staff in the primary health centerlaboratory . Prior to the application of the blood to the filter paper they document the required data on the data sheet including general information , on the NBS card and the recording files. After drying, the cardsIs covered by the safety flap after proper drying and before mailing
and transferred to the Central Public Health Laboratory.

2-Time of Blood sampling

The appropriate time for blood sampling is not before72 hours of life up to 5days regardless of the gestational age of the baby. Keeping in mind that the delay in sample might affect the health of baby with irreversible damage(the decision made not to refusing the sampling for a baby up to 2 months age).
The time of blood sampling may influence the results of the screening tests. Very early sampling will lead to a high rate of ‘’false positive ‘results and therefore another sampling in endocrine disorders is needed because there is a TSH surge immediately after birth. In metabolic disorders early sampling may cause false negative results. In case of PKU, the accumulation of the specific amino acid in the blood does not occur UNTIL 36 hours after starting oral feeds, when there clearance via the placenta suddenly stops.The velocity of the rise of the specific amino acid in the blood, therefore, varies depending on the severity of the defect and the protein intake and the same for GAL .



3- How to complete the data on the card

- write inside the appropriate boxes.
- Specify whether this is the first or a consecutive sample by checking the appropriate boxes.
- Check the appropriate box for male or female and for twin.
- Write the PHC name.
- Write the newborn name and 2- the mother name.
- Write the address and contact numbers of parents (mobile phones)

- ❖ Write the place of delivery.
- ❖ Write the date of birth
- ❖ Write the date of sampling
- ❖ Write the name and signature ofSpecimen submitter.

4-How to collect the blood sample Immediately after completion of the data on the card take the blood sample to avoid confusion(especially in twins)before preparing the next card. The most common sampling procedure will be by heel prick.

5- Heel prick

A-Materials

oSterile lancet, with a tip not to exceed 2.0 millimeters in length
• Standardized incision devices are available that produce a 1.0 mm deep incision
• Devices are also available that have been developed specifically for premature infants
oSterile 70% alcohol pads or other appropriate cleansing agent
oSterile gauze pads
oWarm moist cloth or compress
oFilter paper blood collection form with a future expiration date
oGloves
oSupplies for heel stick aftercare as per your institution's policy.

Procedure ***B-***

1. Put on gloves for personal safety
2. Do not touch the circles for blood collection on the filter paper before and after gloves wearing.
3. Place the infant feet lower than the level of the heart (e.g. heart above feet). if possible in order to increase blood flow to the foot.

4. Warm the heel to increase blood supply to the area by massage or by covering the puncture site for three to five minutes with a warm, moist towel which has been run under tap water at a temperature of not more than 42oC.

5. Cleanse the puncture site with sterile alcohol pad and allow the heel to air dry.

6. Puncture the heel with a single use sterile lancet.
   The best area for heel puncture is toward the sides of the heel as shown in the cross hatched areas in the photo to the left. *Do not* puncture on the posterior curvature of the heel, or on a previous puncture site.

7. Wipe away the first drop of blood with a sterile gauze pad.
8. Allow another large drop of blood to form.
9. Apply very gentle intermittent pressure with the thumb.
10. Avoid excess squeezing or milking as it contaminates the blood sample with tissue fluid.

11. Allow the blood drop to touch one side of the filter paper circle and let the blood soak through the paper to completely fill the circle.

12. Do not press the paper against the puncture site(will interrupt blood flow).
13. Do not apply successive drops of blood to the same circle.
14. After blood collection, elevate the foot above the body and gently press the puncture site with a sterile gauze pad or cotton swab until the bleeding stops.
15. Check for adequacy of the blood sample after finishing.(**a Valid Specimen**) as shown below

6-**Identification of inadequate samples (invalid specimen*)***

1-The blood did not completely soak through filter paper
2 -The blood sample appears layered, clotted supersaturated scratched or abraded.
3-Specimen exhibits serum rings or appears diluted, discolored or contaminated.
4-The blood is scanty and not sufficient.
5-The data on the card is incomplete.

7-Drying of the blood sample

The blood sample on the filter paper will be dried for 3 hours in the special shelf(Rack) available on every PHC.Direct exposure to heat and moisture has to be strictly avoided.

Exposure to humid heat will destroy the enzyme galagtose-1-Phosphateuridyltransferase (GALT).This will cause false positive result in the screening for classical galactosemia.

Newborn screening blood spot check

After the card has dried, check your collection against these examples. Any cards that look like the 'not acceptable' examples should be recollected.

GOOD SAMPLE

All circles filled, blood soaked from back of card, one application with no over-layering of blood, sample dried in air for 4 hours

ACCEPTABLE SAMPLE

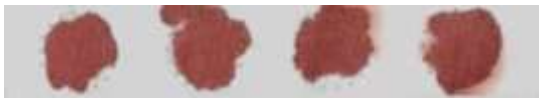
It is not essential to fill all circles if collection is difficult or causes unnecessary trauma to the baby or parents. Three good spots are usually sufficient.

Small misalignments with the circles or slight over or under filling is acceptable.

NOT ACCEPTABLE

misalignments with the circles or slight over or under filling is not acceptable**.**

Insufficient blood: not enough circles.



Contaminated sample: another liquid has been in contact with the card *e.g.* TPN, water, urine, tea, coffee, *etc*

Sample not dried properly: not air dried for 4 hours, card placed in plastic bag.

Serum rings: not wiping alcohol from heel before puncture, card contaminated with alcohol, hand

lotion or water, excessive squeezing to collect sample

Back

front

Clotted or layered: filling card from both sides, touching paper to blood several times

Section B

Transfer of samples to the laboratory

When the blood on the card is dry, kept in a nylons envelopand immediately transported from the PHC to the district and then/ or directly to the Central Public Health Laboratory(CPHL) to start the analytical procedures.

A written record is kept of each incident of non-compliance with the specimen or documentation protocol.

A copy of the record of sample or documentation non-compliance is sent the DOH,CPHL, district and the fourth copy remain in the PHC. The data entered into the Central Public Health Laboratory health information system.

Chapter 3

Laboratory methods in newborn screening – principles and pitfalls

A-Primitive test

1 -Neonatal n TSH(time resolved fluoroimmunoassy)

The DELFIA Neonatal nTSH assay is a solid phase, two site fluoroimmunometric assay based on the direct sandwich technique in which two monoclonal antibodies (derived from mice) are directed against two separate antigenic determinate on the n TSH molecule . standards, control and test specimen containing nTSH are reacted simultaneously with immobilized monoclonal antibodies directed against a specific antigenic site on the B nTSH subunit and europium-labeled monoclonal antibodies (directed against a different antigenic site located partly on the B subunit and partly on the alpha subunit) in assay buffer . The assay buffer elutes nTSH from the dried blood spot on the filter disks.
The complete assay requires only one incubation step.Enhancement solution dissociates europium ions from the labeled antibody into solution where they form highly fluorescent chelates with components of the enhancement solution . The fluorescence in each well isthen measured. The fluorescence of each sample is proportional tothe concentrationof sample is proportional to the concentration of nTSH in the sample .

2- Neonatal phenylalanine

Phenylalanine kit makes use of a fluorescent ninhydrin method. The Neonatal
The procedure is a modification of the fluorometric procedure published by McCaman and Robins in 1962 .The assay is based on the enhancement of a phenylalanine –ninhydrine reaction product by the dipeptide , L-leucyl-L-alanine . A succinate buffer is used to optimize the fluorescence and increase specificity. The copper reagent is used to further enhance the reaction and reduce background. This method measures phenylalanine quantitatively in the presence ofother amino acids . The fluorescence is read using anexcitantion wavelength of 390 nm and an emission wavelength of 486 nm.

3-Neonatal Total Galactose

The Neonatal total Galactose kit makes use of a fluorescent galactose oxidase method
The assay measures total galactose , i.e. both galactose and galactose -1- phosphatethe following scheme summarizes the reaction that occur during the test procedure.

GAL-1-P + H2O --- AP ---------- GAL + P

GAL + O2 ----- GOD-- GHD + H2O2

-HPPA+H2O2-- POD -- HPPA- - dimer + H2O2

GAL –1-P = Galactose – 1- phosphate
AP = Alkaline phosphatase
GAL = Galactose
P = Phosphate
GAO = Galactose oxidase
GHD = D- galactose-hexadialdose
POD = Peroxidase
HPPA = 3 –(p-hydroxyphenyl)propionic acid

B-confirmative test

1) TSH & FreeT_4:The principle of the test is depend on the ELFA (enzyme linked fluorescenent assay) method by using venous blood sample.

2) PKU Phenylketonuria : The principle of the test is depend on Electrospray ionization tandam mass spectrometry coupled in series and separated by a collision cell . Every molecule to be analyzed has to be ionized first by applying a high voltage

3)Galactosemia: The principle of the test depend on the measurement of the enzyme activity GALT (galactose 1-p uridyltransferase) by kinetic methods using spectrophotometer.

public Health Laboratory

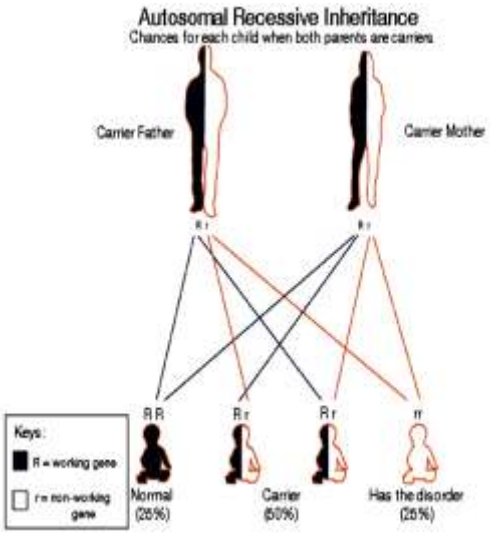
Chapter 4(Core conditions)

Galactosemia (GAL)

Galactosemia is a rare genetic metabolic disorder that is inherited in an autosomal recessive manner. It is an inborn error of carbohydrate metabolism characterized by elevated levels of galactose and its metabolites due to enzyme deficiencies involved in its metabolism. Galactose is the sugar found mainly Milk contains a sugar called lactose, and during digestion, lactose is broken down into the sugars glucose and galactose. Glucose can immediately be used as a source of energy by the body, but galactose needs to be further broken down before it can be utilized.
The birth incidence of classic galactosemia is about 1 per50,000- 60,000 in the Caucasian population .

galactosemia Essentials

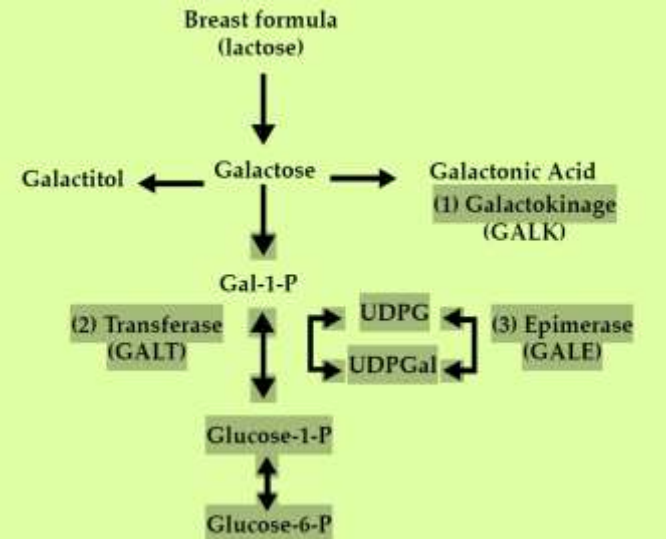
- ***Neonatal Emergency: 50% will die in the first 7-10 days usually from gram-negative sepsis. Acute liver disease can produce a coagulopathy and vitreous hemorrhage. Incidence: 1:60,000***
- ***Screening Test: GALT test (quantitative enzyme assay); Second tier: Hill test (free galactose and galactose-1-phosphate) is done on every infant with abnormal GALT test. *Confirmatory Tests: Enzyme assay GALT, RBC gal-1-phosphate***
- ***Validity: >99% found on 1st specimen, unless transfused***
- ***Treatment: Lactose restricted diet***
- ***Outcome: Somewhat diminished IQs as a group, verbal and motor dyspraxia in 60%, ovarian failure in 80% of females and post-natal growth delay during childhood.***



PATHOPHYSIOLOGY

Dietary galactose is most commonly ingested as lactose, the principal carbohydrate of human milk and most non-soy commercial infant formulas; it is hydrolyzed to glucose and galactose in the intestine. After absorption, galactose is metabolized by several enzymes including galactokinase and galactose-1-phosphate uridyltransferase (GALT).

The galactose metabolic pathway (figure) with multiple enzymatic steps is shown.



Galactose Metabolic Pathway

CLINICAL FEATURES

Patients can present with feeding problems, failure to thrive, hepatocellular damage, bleeding, and sepsis in untreated infants.
In approximately 10% of individuals, cataracts are present.
Failure to thrive is the most common initial clinical symptom of classic galactosemia . Vomiting or diarrhea usually begins within a few days of milk ingestion .
Jaundice of intrinsic liver disease may be accentuated by the severe hemolysis occurring in some patients.
Cataracts have been observed within a few days of birth.
There appears to be a high frequency of neonatal death due to E. coli sepsis in patients with classic galactosemia.
The association of jaundice and hemorrhagic diathesis in the first 2 weeks of life is a clinical presentation in which galactosemia must be considered. Coagulopathy may also be present in galactosemia with little evidence of liver disease.
Galactosemia also causes learning and language problems in children, bone mineral density problems and ovarian failure in girls.

DIAGNOSIS.

Laboratory tests Two screening tests are used to detect galactosemia in a two-tiered sequence:

1-Galactose (Hill Test): Slight elevations (up to 1. 20 mg/dL) can occur in normal neonates, but galactose metabolites are greatly elevated in infants with galactosemia if they are receiving a lactose-containing formula or breast milk. The Hill test is a fluorometric chemical spot test that measures galactose and galactose-1-phosphate. Liver disease may also cause an elevation of galactose metabolites. All infants with an abnormal GALT or who have been transfused will be screened with the Hill test.

2- GALT activity: The enzyme test depends upon fluorescence produced by the normal galactose enzyme cascade in red blood cells. A temporarily abnormal result (diminished or absent fluorescent activity) is found in 1:2,000 infants. The test may be persistently abnormal if the enzyme activity is <50 percent of normal. It does not differentiate milder variants from severe defects. All infants are screened with the GALT test.

Results		**Likely causes**	**Health care provider action**
GALT Test	**Galactose Metabolites**	• Severe galactosemia • Variant galactosemia • False positive	POSITIVE: Potential Neonatal Emergency. Consult with pediatric metabolic specialist. Contact parents and obtain serum confirmatory test for galactose- 1-phosphate uridyl-transferase. Interrupt breast or mammalian milk formula and initiate powder-based soy formula. Report lab tests, diagnosis and treatment to DOH.
<3.5 u/dL	≥20 mg/dL		
<3.5 u/dL	<20 mg/dL	• Severe galactosemia with little lactose intake • Variant galactosemia • Other enzyme defects in red blood cells • Improperly handled sample (heat damage or transit delay)	
Elevated Galactose, Normal GALT (Inconclusive)		(same as above)	Inconclusive: Contact parents and obtain repeat dried blood spot specimen testing. Most often repeats will be normal. If galactose is still elevated on repeat, refer to pediatric metabolic specialist.

Treatment

1-Referral of suspected disease,

2-excludeGalactose&Lactose from diet

3- Supportive treatment for liver, renal and CNS complications(Antibiotics, Plasma, IVF, Vitamins.)

4 -Continue on Galactosefree milk&diet when the disease is confirmed.

5- Refer to regional center where Pediatric specialist-and dietitian with the biochemist support.

Long term management

- **Review in outpatient (follow up):**
  - every 3months in first yearprovided they are well,
  - every 4months in second year ,
  - every six months till 14 years and
  - annually after 14 years and more frequent in adolescence especially in girls to check pubertal growth.

- **Diet;**

Milk and breast milk are not allowed on the modified diet.

1-Breast feeding, Cow's milk Milk or Diary product are contraindicated .Soy based is alternative.

If there is liver disease, give MCT Casein hydrolyzed protein such as Pregstemil till resolution of liver disease.2-

3-Food such as Offal, legumes, pulses, fruit are insignificant source of galactose compared to endogenous production of galactose and there is no evidence to restrict these foods.

4-Soy formula provides adequate Calcium in infancy. But after 1year Soy decrease and need to supplement Ca otherwise its depletion cause decrease in bone density Ca preparation to be used(.Ca lactate,100mg,300mg) ,Ca gluconate 1gm,SandoCal 400mg Ca and SandoCal 1000mg Ca

5-Adequacy of diet checked annually by die titian.

6-There is no need to restrict galactose from diet of normal pregnant mother with previous affected baby because it does not harm the fetus.

7-Many medications contain lactose, it should be checked, but in most it is insignificant in comparison to endogenous production of galactose and it is only for short period.

Monitoring of the following :

1-**Measurement of Red cell galactose-1 phosphate to measure dietary compliance every 3months in first year**

every 4months in second year , every six months till 14 years and annually after 14 years

(for the time being we measure Red cell total galactose Acceptable level – .Acceptable level – up to 9mg/100ml

2- Checking development

3-Cognitive problems during schooling using standard test for development

4 -Many children need speech therapy

5-Additional help at school because of ataxia, intention tremor.

6-Opthalmological slit lamp for cataract every 6months until 3years and thereafter annually.

7-Growth assessment, which is normal if proper diet is adequate and proper

8-Osteoporosis –satisfactory Ca, some do bone density for regular checking.

9-Pubertal development in girls, because hypergonadotrphichypogonadism occur in most girls and mostly are infertile but this complication is not seen in boys.

Following milk formula

Trade Name	Manufacturer	Formula
Infrosoy	Cows and Gate	Lactose free +Soy
Weysoy	SMA	Lactose free +Soy
Prosobee	Mead Johnson	Lactose free+Soy
Pralys Soy	Farlys	Lactose free+Soy
Isomil	Abbott	Lactose free +Soy
MCT Peptide	SHS	Liver disease –MCT-Lactose free
Pregestmil	Mead Johinson	sever liver disease 0.8mg lactose/100ml
Enfamil	Mead Johnson	Lactose 3mg/100ml not first choice
Al1/0	Nestle	Lactose 10mg/100ml, not first choice
Galactomin	Cows and Gate	Lactose 13mg/100ml not first choice.

Fruits and vegetables.

There is some galactose in some fruits and vegetables. Laboratory analysis has shown that free galactose content in fruits and vegetables varies with the variety, ripeness, time in storage and the type of processing

Some clinics allow all fruits and vegetables in the diet forgalactosemia for these reasons:

1- *The amount of galactose in any of the analyzed fruits or vegetables is much less than what is found in milk or cheese*

Fruits and vegetables 2-40 mg galactose/100 g of food Milk 2000-2500 mg galactose/100 g Cheddar cheese 600 mg galactose/100 g

2- *The amount of galactose in fruits and vegetables is less than the amount that our bodies make in a day(endogenous galactose production)*

PROGNOSIS

Despite an early galactose-free diet, long-term complications have been noted in older children and adults with classic galactosemia because of endogenous galactose production. These include speech problems, poor intellectual function, neurologic deficits (predominantly extra pyramidal findings with ataxia), and ovarian failure in females. Thus, the need for regular monitoring and evaluation is important.

Counseling with galactosemia:-

Galactosemia does not present the same in all children. Many have varying degrees of symptoms, and some do not display difficulties. Speaking with parents about their child's galactosemia is often a challenge. They want their child to be like other children. Try and be sensitive to this issue an Therapiesincluding physical, speech, andoccupational have been shown toincrease the child's motor planning,processing, and integration skillsSome Therapists.

Include:

•**Breathing:** Advise the child to take a deep breath if speech is erratic

•**Tracing:** Allow the child to trace letters repeatedly

•**Repetition:** repeat exercises several times to enhance muscle memory

•**Functional Training:** practice exercises that mimic everyday movements

•**Modeling:** place the children next to peers so that they can model behavior

•**Sensory Table:** use of sensory table to work with different mediums convey a sense ofnormalcy, reminding them that learning is an individualized process.

Parents also experience their child's frustration and can also feel frustrated themselves. In order to keep remedies consistent, ask parents what they have observed at home and what strategies they use.

Communication

•**Pace:** break topics down slowly

•**Pitch:** change the tone of your voice when describing opposite concepts

•**Pictures:** use a visual aids, pictures, or sign language when possible

•**Praise:** provide positive feedback

•**Patience:** maintain patience Lesson Planning

•**Packets:** provide note packets for the week and distribute them prior to lessons

•**Peers/Partners:** place students next to peers or assign partners so they canemulate their behavior.

•**Prioritize:** provide subject folders for assignments and an outline of expectations/goals

•**Prompt:** tell the students when their turn is **c**oming up

Phenylketonuria (PKU)

Hyperphenylalaninemia Essentials

- It is the most frequent inherited disorder of amino acid metabolism (prevalence 1:10 000).
- It is due to partial or complete inactivity of hepatic phenylalanine hydroxylase enzyme, result in consequent increase in phenylalanine in blood and tissues causing structural and functional abnormalities of brain resulting in progressive neurological impairments (due to its interference with the processes of myelination, synaptic sprouting and dentritic pruning in developing organism in addition to its inhibition of neutral amino-acids transport which limit the production of neurotransmitters)
- In 1-3% of infants with hyperphenylalaninemia, the defect resides in 1 of the enzymes necessary for production or recycling of the cofactor BH_4
- If these infants are misdiagnosed as having PKU, they may deteriorate neurologically despite adequate control of plasma phenylalanine because In addition to action of BH_4 as a cofactor for PAH, BH_4 is also a cofactor for other enzymes, which are involved in the biosynthesis of neurotransmitters (dopamine and serotonin)

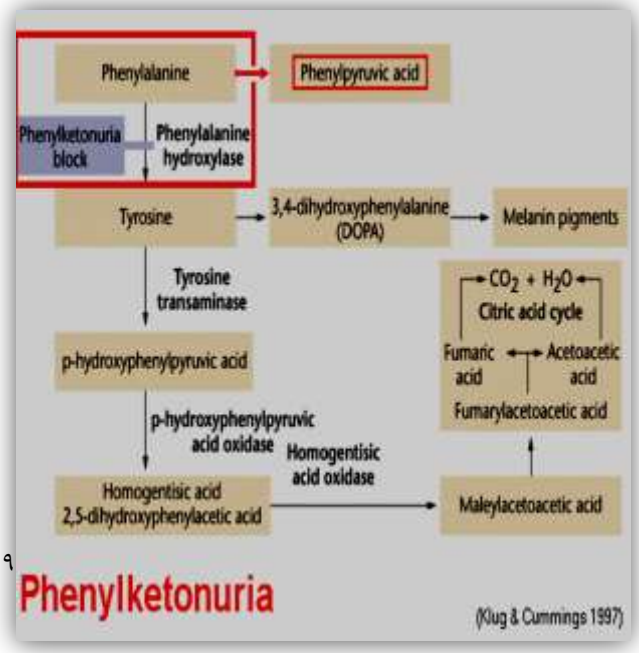
Pathophysiology

- classic "inborn error of metabolism"
- autosomal recessive disease characterized by mutations in the liver
enzyme, phenylalanine hydroxylase, encoded by the PAH gene PAH converts phenylalanine to tyrosine
(reaction requires O2 and co-factor BH4)

- HPA or non-PKU hyperphenylalaninemia are related disorders of phenylalanine hydroxylation involving several enzymes necessary for the synthesis and recycling of co-factor for PAH, tetrahydrobiopterin (BH4)

Clinical Manifestations

The affected infant is normal at birth, Profound mental retardation develops gradually if the infant remains untreated. Cognitive delay may not be evident for the 1st few months .



In untreated patients, 50-70% will have an IQ below 35, and 88-90% below 65. Only 2-5% of untreated patients will have normal intelligence. Vomiting, sometimes severe enough to be misdiagnosed as pyloric stenosis, may be an early symptom.Older untreated children become hyperactive withautistic behaviors, including purposeless handmovements, rhythmic rocking, and athetosis. The infants are lighter in their complexion thanunaffected siblings.

Some may have a seborrheic or eczematoid rash, which is usually mild and disappears as the child grows older.These children have an unpleasant odor ofphenylacetic acid, which has been described as musty or mousey.Neurologic signs include seizures (≈25%), spasticity, hyperreflexia, and tremors; more than 50% have EEG abnormalities. Microcephaly, prominent maxillae with widely spaced teeth , enamel hypoplasia, and growth retardation are other common findings in untreated children.

The clinical manifestations of classic PKU are rarely seen in those countries in which neonatal screening programs for the detection of PKU are in effect.

*Plasma phenylalanine is not detectably elevated in cord blood. It starts rising within 24 hours after birth and often reaches 1,200 µM/L or more within a few days. The screening test is often abnormal within 24 hours and almost uniformly abnormal within 48 hours of birth***.**

Table (***)Acceptable phenylalanine blood levels at different ages in children with phenylketonuria***

Age group (Years)	**Phenylalanine (mmo/L)**
0-2	0.2-0.4
2-4	**up to** *0'5*
4-8	**Up to** ***0.6***
8-1	**up to I .O**
Over 10	**Upto1 2**

Variant forms of PKU (Hyperphenylalaninemia)

Several intermediate forms of hyperphenylalaninemia

occur in which the plasma phenylalanine levels are lower than in classic PKU (180–1,200 µM/L).
In these cases, mental retardation is variable and in the milder variants is completely absent.
In infancy, these patients can mimic severe PKU , and for adult women the risk of maternal PKU syndrome increases in proportion to the plasma phenylalanine.

.Clinical Manifestations in infants with cofactor deficiency

Usually they are identified during screening programs for PKU because of evidence of hyperphenylalaninemia. Their plasma phenylalanine levels may be as high as those in classic PKU or in the range of milder forms of hyperphenylalaninemia.
However, the clinical manifestations of the neurotransmitter disorders differ greatly from those of PKU.
Neurologic symptoms of the neurotransmitter disorders often manifest in the 1st few months of life and include extra pyramidal signs with choreoathetotic or dystonic limb movements, axial and truncalhypotonia, hypokinesia, feeding difficulties, and autonomic problems. Mental retardation, seizures, hyper salivation, and swallowing difficulties are also seen.
Definitive tests can differentiate these variant forms of PKU . In view of the severity of this group of diseases, all infants with persistently abnormal levels of phenylalanine must have testing by special blood and urine tests for biopterin abnormalities. Information regarding this testing is provided through the metabolic consultants.

Maternal PKU and Hyperphenylalaninemia

Women with significant hyperphenylalaninemia have an increased risk of miscarriage and their offspring (who usually do not have PKU) may have intra-uterine growth retardation that persists postnatally. More than 90 percent of infants of untreated mothers with classical PKU have microcephaly, mental retardation, and/or congenital heart defects. They have a transient elevation of phenylalanine (240–1,200 µM/L) that falls to normal within 24 hours. A screening test on the mothers of infants with transient hyperphenylalaninemia, particularly if the infant's sample was collected in the first 24 hours after birth, is recommended. A phenylalanine restricted diet begun prior to conception, (at least 3 months) and during pregnancy can often prevent damage to the fetus; every effort should be made to keep blood phenylalanine levels below 6 mg/dL (360 µmole/L) throughout the pregnancy. All women with hyperphenylalaninemia who are of childbearing age should be counseled properly as to the risk of the just described congenital anomalies in their offspring

Diagnosis (laboratory test):

Hyperphenylalaninemia above the cut off value of screening (usually in range of 2-2.5 mg/dl) is usually diagnosed through mass screening of newborn infants .The method of choice is tandem massspectrometry (MS/MS), which identifies all forms of hyperphenyalaninemia with a low false-positive rate, and excellent accuracy and precision. The addition of the phenylalanine/tyrosine molar ratio (greater than or equal to 3) has further reduced the number of false-positive resultsIn infants with

positive results from the screen for hyperphenylalaninemia, diagnosis should be confirmed by quantitative measurement of plasma phenylalanine concentration.
Identification of phenylketones in the urine by ferric chloride may offer a simple test for diagnosis of infants with developmental and neurologic abnormalities in countries and places where such programs are not in effect Once the diagnosis of hyperphenylalaninemia is established, additional studies for biopterin metabolism should be performed to rule out biopterin deficiency as the cause of hyperphenylalaninemia.
one of the tests used is BH4 loading test.(An oral dose of BH4 (20 mg/kg) normalizes plasma phenylalanine in patients with BH4 deficiency within 4 to 8 hr. The blood phenylalanine should be elevated (>400 µmole/L) to enable interpretation of the results.) This may be achieved by discontinuing diet therapy for 2 days before the test or by administering a loading dose of phenylalanine (100 mg/kg) 3 hr before the test. In BH4-responsive PKU due to PAH deficiency, phenylalanine levels may decrease during the BH4 loading test but increase later even with BH4 supplementation.

Results	**Likely causes**	**Health Care Provider Actions**
Phenylalanine >190 µM/L, Phe/Tyr >3.0 • Mild elevation of Phenylalanine • Abnormal level of phenylalanine • Substantial elevation of phenylalanine possibly with elevated phe/tyr ratio	• PKU possible • Variants forms of PKU • Mother has PKU • False positive • Transient hyperphenylalaninemia	-Obtain repeat dried blood spot specimen testing within 48 hours -Obtain repeat dried blood spot specimen testing immediately -Obtain quantitative plasma amino acids -Consult with and refer to pediatric metabolic specialist -Report confirmatory lab results, diagnosis and treatment to DOH.

Treatment

The goal of therapy is to reduce phenylalanine levels in the plasma and brain. It is generally accepted that infants with persistent (more than a few days) plasma levels of phenylalanine >6 mg/dL (360 µmole/L) should be treated with a phenylalanine-restricted diet. Because phenylalanine is not synthesized endogenously, small amounts of phenylalanine should be added to the diet to prevent phenylalanine deficiency(the fasting morniglevele< 1,6 mg /dl.shoud be avoided) Dietary deficiency of this amino acid is manifested by lethargy, failure to thrive, anorexia, anemia, rashes, diarrhea, and even death; moreover, Tyrosine becomes an essential amino acid in this disorder and its adequate intake must be ensured.
In 2001, the National Institutes of Health Consensus Development Panel recommended that plasma phenylalanine levels to be maintained between 2 and 6 mg/dL in neonates through 12 yr of age and between 2 and 15 mg/dL in older individuals. The fact that brain development continues in adolescence and even in adulthood, lower plasma phenylalanine levels (2-10 mg/dL) have been encouraged strongly after 12 yr of age. Blood phenylalanine (phe) levels should be obtained at periodic intervals to monitor the efficacy of therapy in patients with PKU.

The recommended of phe blood level interval is ：

- Weekly for infants <1 year of age,

whose nutritional requirements change

- frequently as a result of rapid growth

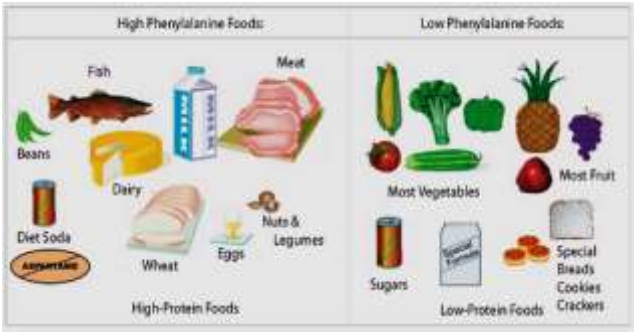
- Every 2 weeks from 1 to 12 years of age
- Monthly after 12 years of age
- Twice weekly during pregnancy

Frequency of clinical monitoring:

- Every 1 – 3 months
- Every 3 months
- Every 4 months
- Every 6 months
- Every year
- Every 2 – 4 weeks

The duration of diet therapy is also controversial. Discontinuation of therapy, even in adulthood, may cause deterioration of IQ and cognitive performance. The current recommendation from the 2001 National Institutes of Health Consensus Development Panel is that all patients be kept on a phenylalanine-restricted diet for life. Oral administration of tetrahydrobiopterin (BH4), the cofactor for PAH, may result in reduction of plasma levels of phenylalanine in some patients with PAH deficiency. Plasma levels of phenylalanine in these patients may decrease enough to allow for considerable modification of their dietary restriction.(At a dose of 10 mg/kg/day, it reduces phenylalanine levels in up to 50% of patients.) some of the classical PKU patient may not benefit of drug therapy and if It is important to aggressively treat the usual childhood illnesses to prevent tissue catabolism and consequent elevated blood Phenylalanine levels. During an illness or infection, it is important to maintain the formula intake as much as possible. The continuation of formula is to help prevent the breakdown of muscle protein during illness that will increase the level of phenylalanine in the blood. However, if a child refuses to drink formula, then whatever clear liquid the primary care physician recommends is appropriate. Parents need to contact the primary care physician for management of the illness before calling the PKU staff. Long-term care of these patients is best achieved by a team of experienced professionals (physician specialist, nutritionist, neurologist, geneticist, and psychologist) in a regional treatment center.

Nutritional aspect of diet management



1- Formula; for babies, phenylalanine free formula is safe and can mix with breast feeding or artificial ,and parents can introduce solid with lowphenylalanine.if plasma level of phenalanaline exceed 15 mg/dl breast milk withdially monitoring* Formula for older children and adult continue to have protein substitute formula but can have it between the meals or snacks it acts as essential substitute for life.

2- Foods that are not allowed:

♦ All meats such as: beef, lamb, ham, bacon, chicken, fish and fish products, organ meats (liver, heart, kidney), etc.
♦ Eggs
♦ All dairy products including: cheese, milk, yogurt, ice cream, pudding, etc.
♦ Nuts and seeds
♦ Legumes
♦ **Ordinary** breads, flour cakes, and biscuits (made with yeast and/or gluten)
♦ Soya-Foods (meat substitutes)
♦ Any food containing **aspartame** such as: diet sodas, diet jams, diet, Medication **contains aspartame** lemonades, etc.

3-Foods that are restricted (these must be weighed at given amounts):

Each weighed amount provides 50 mg of phenylalanine which equal to 1gm of protein.

The body cannot function properly without the amino acid phenylalanine, but it can only be given in very small amounts to the child with PKU. To achieve this we give a measured amount of phenylalanine every day. These are called **exchanges**. Every child will have a set number of exchanges every day and the number will generally not change even as the child gets older and bigger. The exchanges are provided from foods such as breakfast cereals, potatoes and potato products such as chips and crisps

Sample of exchang

♦ Potato chips	30 grams
♦ Potatoes: boiled, mashed, roasted, etc	80 grams
♦ Broccoli	30 grams
♦ Peas: fresh, frozen, etc.	25 grams
♦ Spinach: boiled, steamed, etc	. 25 grams
♦ Corn on the cob	55 grams
♦ Cereals (depending on type)	10-20 grams
♦ Rice: white or brown	45 grams

The number of exchanges was given to the baby or child needs is estimated on the blood tests that are taken regularly. It may seem cruel to prick the finger or heel regularly, but in fact this is the only way we can tell how much phenylalanine is in the blood.

4-Foods that are allowed (monitor these foods-do not allow excessive use):

♦ Fruits: apples, oranges, bananas, melons, grapes, grapefruit, peaches, strawberries
♦ Vegetables: french beans, carrots, cauliflower, celery, cucumbers, lettuce, radishes, tomatoes

5- "Free" foods:

♦ **Desserts/Sweeteners:**
• Corn syrup, honey, sugar, molasses
• Candy and gum with allowed ingredients (no aspartame)
• Frosting
• Popsicles
♦ **Fats:**
• Oil, lard, bacon drippings
♦ **Beverages:**
• Apple juice
• Carbonated beverages (soda) without aspartame
• Coffee and instant tea's

Breakfast

Low protein all-purpose packing mix , cornflake, fruit juice with almond or vanillaa

Lunch

mall portion of rice cakes, grapes, apple souce lemonade ,
low protein vegetable soup.
Snack PKU formula and piece of FRUIT.

Dinner

Egg plant salad, ,veg shish kabab baked potato broccoli or mushroom, pepper stuffed with sweet potato or carrot Then phenylketonuria formula. Families need to change their life style though it is difficult, and need the child to eats with the family Records of phenylalanine in diet in baby food PKU formula ,baking and cooking ingredient and use common scales like cup, spoon
and kitchen scale in grams

Approximate daily requirements for selected dietary components and amino acids in infancy and childhood

dietary components and amino acids	Birth to 12 mo (mg/kg)	1-10 year ((mg/kg)
Phenylalanine	1-5 mo : 47-90 6-12 mo :25-47	200-500
"Histidine	16-34	
Tyrosine	1-5 mo: 60-80 6-12 mo: 40-60	25-85 (mg/kg)
Leucine	76-150	1000
Isoleucine	1-5 mo: 79-110 6-12 mo: 50-75	1000
Valine	1-5 mo: 65-105 6-12 mo: 50-80	400-600
Methionine	25-45	400-800

Cyst(e)ine "	15-50	400-800
Lysine	90-120	1200-1600
Threonine	45-87	800-1000
Tryptophan	13-22	60-120

Energy	1-5 mo: 108 kcal/kg 6-12 mo: 98 kcal/kg	70-102 kcal/kg
Carbohydrate	Kcal X 0.5÷4=g/day	Kcal X 0.5÷4 =g/day
Total protein	1-5 mo: 2.2 g/kg 6-12 mo: 1.6 g/kg	16-18
water	100 ml/kg	1000 ml
Fat	Kcal X 0.35÷9=g/day	Kcal X 0.35÷9=g/day

Notes to be consider before starting the interview:

a-Preparation for the appointment, because there are a lot of ground to be covered.

b-Ask family member or friend to come, because it is sometime difficult to remember all the information given during the interview.

C-Write the questions from most important to least important one that need to be answered by the specialist?

1-How did my child get PKU?
2-How can we manage PKU?
3-Are there any medication to treat this disease?
4-What foods are absolutely forbidden?
5-How much formula will the child needs?
6-What happen if my child eats food that my child is not supposed to eat?
7-Is this condition is temporary or long standing?
8-Will my child stay on this special diet for life?
9-Are there brochures or other printed material that I can take with me?
10-What websites do you recommend?
11-If I have another child, will he or she has PKU*?*
12-Did something I did or did not during pregnancy cause this to happen?

What does the specialist want to know from the parents?

1 Has your child has any symptoms that concern you?
2-Do you have any questions about your child s diet?
3-Are you having any difficulty concerning the diet?
4-Has the growth and development of your child been normal?

What other measure might help?

1-Learn from other families who they have PKU.
2-Try to get menu planning –idea from dietitian.
3-Try to eat out in some restaurant that serves low protein diet
4-Financial aid for sports and special activities
5-Let the child to manage with diet as early as possible like cereal, fruit, vegetables, given as snacks and ought to be measured*.*
Make Grocery list and Child with PKU meal within whole family and not trying to make separate meal even if the child does eat anything Serve whole family with low phenylalanine soup Be prepared for picnic trips and you can have: Dehydrated fruit sweet, like raisin , crackers, fruit shish kabab*,*

Counseling

The most important patient instructions are those related to dietary interventions. These need to be reviewed at each clinic visit. Extensive support is required at the time of the initial diagnosis of PKU. Parents should be reassured that their child will not be mentally retarded and can be expected to grow and develop like all other children. As children grow older, education needs to continually emphasize the adverse consequences of loss of metabolic control. Parents should be assisted in educating the child to gradually participate in his or her own care, including mixing formulas, doing blood tests, and completing diet records. In the case of patients taking tetrahydrobiopterin (BH4), the importance of taking the medication on a daily basis should be emphasized.

Individual Education Plan (IEP) with PKU

An IEP is a written statement of an educational program designed to meet a child's individual needs. An IEP sets reasonable and attainable learning goals for a child with PKU. Children with PKU have a legal right to these plans and it is important that they be followed at school. Teachers should work with parents, to decide on a plan that meets the specific needs of each child with PKU.

Ask parents if they want to send in a batch of low-Phe treats that can be frozen so they are available for class celebrations . Serve fresh fruit. If a child with PKU eats food with Phe, it is not a medical emergency. Just be sure to notify the parent at the end of the day.

and vegetables instead of baked goods at parties. This can make food choices easier for children with PKU.

.If a child doesn't finish his or her food or formula during the school day or eats food with Phe, tell the parent. This is important so they can adjust the child's dinner for that night or meals for the next day to balance out the child's Phe intake and maintain the child's Phe levels within the recommended range.

Some children take a new prescription drug, known as Kuvan (sapropterindihydrochloride), to treat their PKU. Changes in behavior could indicate the drug is not working, so it is important to notify parents.

Psychologists in many hospital metabolic clinics are available to discuss behavioral changes and symptoms in children with PKU.

Organize class activities that highlight the differences among people to show that there are many things, not just PKU, that make people different.

Allow older children with PKU to write a report or give a presentation to classmates about the disorder. This can help the child to feel confident among peers.

Congenital hypothyroidism

CHT essentials

- ***Ncidence :*** 1:3,000 newborns
- ***Screening test:*** T4 (thyroxine) and TSH (thyroid stimulating hormone)
- ***Validity:*** 90% identified on 1st screen, 10% on 2nd screen
- ***Causes:*** Thyroid dysgenesis: 85%; hereditary inborn error of thyroid hormone biosynthesis: 15%
- ***Treatment:*** L-thyroxine normalize T4 by 2 weeks of age; TSH by 1 month
- ***False positives:*** Early collection within 24 hours of birth; premature or ill infants
  Outcome: Can be normal, but depends on severity of thyroid deficit, days to treatment and adherence to treatment. Infants with just a 2-week delay in reaching a serum T4 >10 ug/ dL may have up to a 10 point drop in IQ.16

Congenital hypothyroidism: (CH) occurs in infants who are born without the ability to produce adequate amounts of thyroid hormone. The incidence is 1:3,000 worldwide . There is a 2:1 female/male ratio, explanation unknown. Infants with Down's syndrome have increased risk of CH (1:140 newborns).

Clinical features

Deficiency of thyroid hormone in an infant may result in mental retardation and other signs of brain damage if it is not diagnosed and corrected by 3 –4 weeks of life.
Many infants with CH may appear clinically normal before 3 months of age, by which time some brain damage has usually occurred. Laboratory test results are the only reliable means of diagnosing CH in the newborn. When symptoms or signs are present, they may include prolonged neonatal jaundice, constipation, lethargy and poor muscle tone, feeding problems, a large tongue, puffy face, large fontanels, distended abdomen and umbilical hernia. Approximately 10 percent of cases will have other congenital abnormalities,

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usually cardiac defects. Persistence of severe, untreated hypothyroidism resulted in severe mental impairment. Since thyroid deficiency can occur at any age, normal tests in the newborn period do not exclude deficiency in an older infant or child.

Causes of congenital hypothyroidism

The most common causes are total or partial defect of fetal thyroid development (digenesis or ectopic)(80-85%) or (dyshormonogenesis) 15%. Less commonly, hypothyroidism is induced by maternal medications (antithyroid drugs or excess iodine), or maternal autoimmune thyroid disease 2%.

Diagnosis

When the infant's physician is notified that screening results are abnormal, blood should be collected by venipuncture as soon as possible to confirm the abnormal screening results. In the case where the T4 is low and TSH is elevated, treatment can be started as soon as the serum is obtained, pending final confirmation. If the serum thyroid function tests confirm hypothyroidism, further diagnostic studies, such as a thyroid ultrasound examination or scan and latralview X-ray to the knee to assess skeletal maturation, may be performed to determine the type, age of onset and severity of hypothyroidism.

Generally, these studies do not change management and so are optional. (see table Bellow)

Results	Likely causes	Health Care Provider Actions
T4 low/TSH elevated	• Hypothyroidism probable • False positive(2nd screen)	-POSTIVE: Notify parents, and obtain confirmatory serum specimen. Ensure specimen is tested at GPH laboratory with established neonatal reference ranges. Consult with pediatric endocrinologist. Report lab tests, diagnosis and treatment to DOH .
T4 low/TSH >100 and ≤200 µUI/mL, 0–11 hrs.	•Prematurity hypothyroidism possible •False positive(2nd screen)	Medical consultant contacts practitioner by phone requesting further testing.
T4 low/TSH normal (on two specimens unless premature)	•Thyroid binding globulin (TBG) deficiency • False positive(2nd screen) • Pituitary gland problem with secondary hypothyroidism •Prematurity (2nd screen)	Medical consultant contacts practitioner by phone requesting further testing.
Normal T4/mildly elevated TSH	•subclinical hypothyroidism	Medical consultant contacts practitioner by phone requesting further testing.

Thyroid function in premature infants: In premature infants,there is a physiological reduction in blood T4 levels; TSH levels are not elevated in this situation. These cases need special observation to ensure that the low T4 levels rise into the normal range as the matures, but this may take several weeks.

/

Subclinical hypothyroidism : defined by a normal total or free T4 level and a mildly elevated TSH (typically 5–10 mU/L), is common in children, but there is currently no consensus on management.

Management:

The main treatment for CH is thyroid hormone replacement. It is safe and easy to take. If it is begun immediately after your child is diagnosed, *physical examination, X ray of lateral knee to assess bone age. serum confirmation*, treatment can prevent many or all of the effects of CH. If damage to the brain and nerves happens because treatment is delayed, it is usually permanent and cannot be reversed.

1. **Medication**

   L-thyroxine is a synthetic form of thyroid hormone (but its chemical structure is identical to thatproduced by the normal thyroid gland). This is given in tablet form once daily to all babies with CH. L-thyroxine tablets are small and can be crushed into food or dissolved into a small amount of formula, juice or other liquid.

- The starting dose of oral levothyroxine should be 10-15 mcg/kg/day, with a maximum dose of 50 mcg/day. The objective of treatment is to normalise TSH within the first month. The dose of levothyroxine may need to be reduced if TSH is suppressed or if the baby is showing signs of overtreatment.
- Recommended dose of oral thyroxin(25-50microgram/day for term) and(8-10ug/kg/day for preterm). lower doses for infant with coexisting symptomatic cardiac disease.
- Low T4 and slightly elevated TSH managed by repeating the tests and clinical observation.
- Re-examination and Recheck T4, TSH should be done:

- 2–4 wk after initial treatment is begun
- Every 1–2 mo in the first 6 mo
- Every 3–4 mo between 6 mo and 3 y of age
- Every 6–12 mo from 3 y of age to end of growth

- General guidelines for dosage during 1st year are as follows;
- 0-6months 25-50microgramm/day or 8-10ug/kg/day
- 6-12months 50-75microgram/day or 6-8ug/kg/day.
- The dose is individualized for each patient according to clinical response and lab response since excessive and inadequate treatment are determinable to neurological development.
- Maintenance of T4/OrT3 in high or in normal range and normal longitudinal growth have been found more useful than TSH regulating therapy.

is important to give the child the correct amount of L-thyroxine. Giving a child more than he or she needs can cause body functions to speed up. Some of the signs that occur when a child takes too much L-thyroxine are:

- **Rapid heart rate**
- **Diarrhea**
- **Lack of sleep**
- **Shakiness**

Soy-based formulas and iron supplements can reduce the amount of thyroid hormone that baby absorbs from the pills. Separate the time of administer baby's thyroid medication by at least one hour from the time you feed soy formula or iron medication.

2. Monitoring

A child will need regular visits to the doctor to check his or her weight, height, development and overall health. The child will also likely need regular blood tests to check the level of thyroid hormone. Blood tests are usually done every one to three months until age one, and then every two to four months until age three. They can usually be done less often after age three.

3. Developmental Evaluation

Your doctor may suggest a formal evaluation of your child's development. If your child show delays in certain areas of learning or speech, extra help can be arranged. Early intervention programs are available in most states to provide services to children before they reach school age.

4. Babies with CHT are more likely to have associated anomalies, particularly congenital heart defects and hearing loss and require careful neonatal examination and follow up. A complete history, including maternal thyroid status (previous history of thyroid dysfunction, maternal anti-thyroid medications), maternal diet (e.g. vegan or other low iodine diet) and family history should be obtained

5 -Thorough neurological development should be made on each follow up visits

6 -Coordination between the neonatal screening programmer, primary physician and

endocrinologist about the children with hypothyroidism periodically till age 4years to verify that the child is still followed.

Diagnostic possibilities exist:

It can be made by good history, examination, appropriate tests (as shown in algorithm below)

1-Low T4,high TSH,75% are agenesis of thyroid gland. Inadequate gland or ectopic.

If thyroid gland is enlarged-dysharmonogenesis or maternal drugs.

If sever elevation of TSH –Thyroid scan – and treatment commenced immediately.

2-Low T4 and normal TSH due to low TBG.

.Secondary hypothyroidism due to hypothalamic or pituitary dysfunction which occur in1/60,000

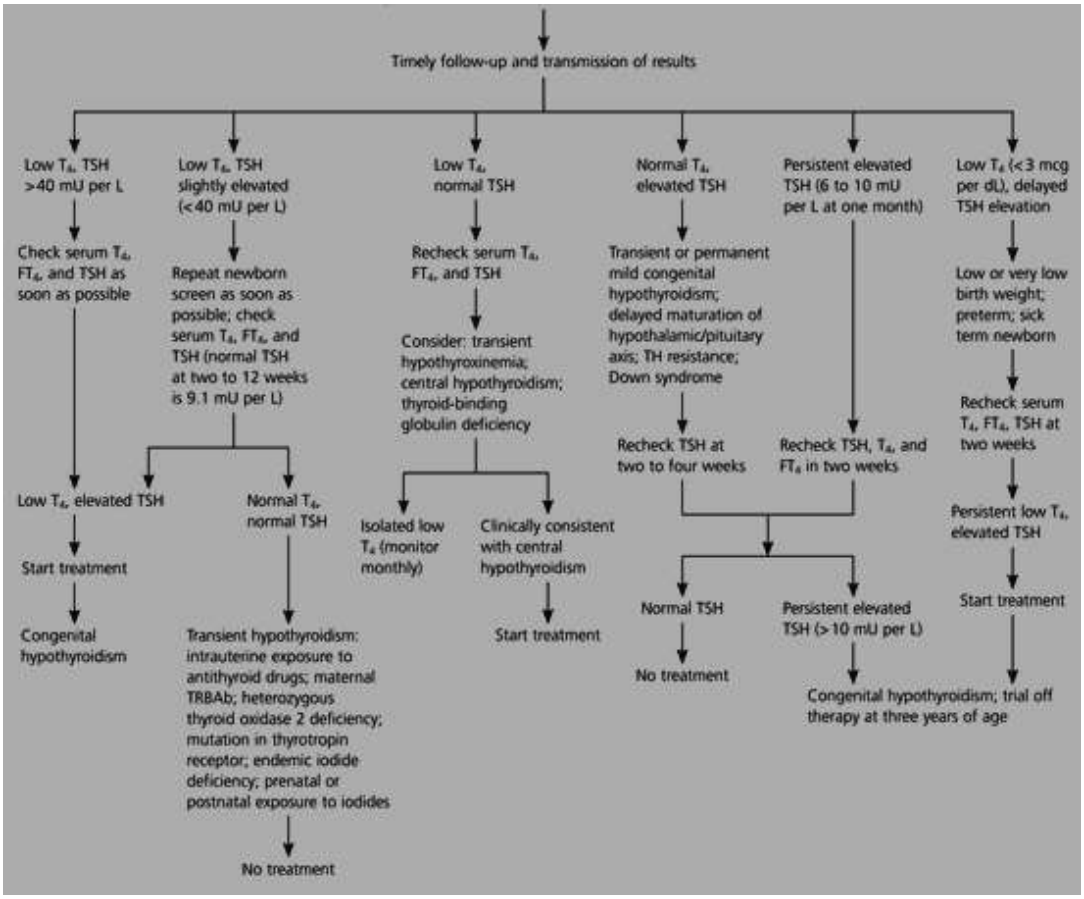
Repeat testing and need for test for pituitary function and treatment started once the results are available unless have symptoms of hypothyroidism treatment started immediately.

3-Normal T4 and high TSH, they are not detected by screening unless T4 decrease by 10% ,the infants with dysplastic gland have such results and become hypothyroid in infancy.

- **(6-8% OF THE DIAGNOSED CASES ARE IDENTIFIED BY SECOND SCREEN ANNUALLY)**

4-Low T4 in LBW,TSH is not elevated or slightly above upper limit by screening program . As stress is removed or the nutrition is improved thyroid function return to normal, Thyroxin is not necessary and not recommended.

- **Note Premature have the same incidence of hypothyroidism as in full term**.



Defects of TBG (Thyroid Binding Globulin)

- They are not associated with clinical disease and they do not require treatment.
- They are discovered accidently by low or high T4 confusing with hypo or hyperthyroidism.
- It is X-linked occur only in male the gene defect on short arm of X-chromosome.
- Defect of TBG occur in 1/2800 new-born males and 36% of them have TBG below 1mg/l and complete deficiency <5ug/l occur less frequently.
- Affected patients have low T4, normal or low freeT4 and TSH, The hypothyroidism is excluded by low or absent TBG.

Counseling

Q. What will happen if my baby misses a dose of thyroxin or vomits up one of the tablets?

A. No harm is done if only one or two doses of thyroxin are missed. It is, of course, important that the tablets are administered regularly, so make sure that you obtain a repeat prescription from your doctor when your supplies are getting Low
.
Q. Can treatment be stopped at any stage, e.g. on reaching adult life?
A. In permanent Congenital Hypothyroidism, it is not possible to stop treatment. Thyroxin must be taken regularly throughout life, even when physical growth has ceased.
Q. Will any problems occur when my child has immunizations or has to take other medication?
A. No. Children with hypothyroidism can have the usual immunizations QUESTIONS AND ANSWERS for new born with congenital hypothyroidism?
and take other medication without any problem.

Q. What are the side effects of thyroxin treatment?
A. Because the treatment of hypothyroidism involves replacement therapy with a natural hormone, no side effects occur if the dosage is appropriate.
If, however, too much thyroxin is given, the effects will be the same as those that occur with an overactive thyroid gland, viz., rapid pulse, loss of weight, restlessness, over activity, etc.

Q. What are the risks of a further child in the family having hypothyroidism?
A. The risks depend on the cause. Most cases of Congenital Hypothyroidism are due to absent, ectopic or hypoplastic thyroid glands. These problems are not inherited and the risk of a subsequent child having a similar condition is very small. The likelihood of a baby being born with an absent or malformed thyroid gland in the general population is about one in 3000. This risk may be slightly higher when there is already one affected child in the family, but it is not a substantial risk.

Q. When a person with hypothyroidism has children of his or her own, what risk do the children face of having the same condition?
A. There is only a low risk that the children of a congenitally hypothyroid mother or father will have the same problem. In general, this applies to all the types of Congenital Hypothyroidism. Even with permanent dyshormonogenesis due to an enzyme deficiency, the risk remains low, unless the affected person happens to marry
Someone who either has the same condition or is a carrier of it.
Q. Is a child with hypothyroidism more likely to get other diseases later in life?
A. No. With regard to the risk of contracting other disease later in life, hypothyroid children are no different from the normal population.

Special Circumstances: Babies Born Preterm Or For In Hospital Specialist Unites

Some babies will be in hospital when their blood spot sample is due to be taken. This section highlights the needs of babies who are cared for in neonatal units (this includes Pediatrics Intensive Care Units, Neonatal Intensive Care Units, Special Care Baby Units, cardiac units, surgical units, transition wards, etc.), preterm babies born at less than 32 weeks (less than or equal to 31 weeks + 6 days) and those who experience multiple blood spot samples taken from the heel.

NO	Action	Reasoning
1-	Babies admitted to neonatal units are likely to have multiple blood samples taken. Blood spot screening should be coordinated with other tests when possible. Venipuncture or venous / arterial sampling from an existing line is an alternative. This is providing the sample is not contaminated with EDTA and the line is cleared of infusate.	To minimize the number of invasive procedures.
2-	Babies less than 5 days of age should have a single circle blood spot sample taken on admission/prior to blood transfusion to screen for SCD. The blood spot card should be marked 'Pre-transfusion'. Complete the details on the blood spot card	The screening test for SCD cannot be done on samples from babies who have received a blood transfusion
3-	The 'Pre-transfusion' blood spot card should be stored with the baby's medical records in line with local protocols and dispatched to the newborn screening laboratory together with the routine day 5 sample if the baby has received a blood transfusion in the interim. (In Northern Ireland, the 'pre-transfusion' sample is to be sent directly to the screening laboratory). If the baby is transferred to another unit before the day 5 sample has been taken, ensure pre-transfusion blood spot card accompanies the infant. Details of newborn sampling should be documented and included in transfer information.	• The single circle blood spot sample taken and marked as 'Pre-transfusion' can be discarded if the baby does not receive a blood transfusion. • To ensure new unit is aware that pre-transfusion sample has been taken
4-	The routine blood spot sample (four spots) should be taken on day 5 and in exceptional circumstances between day 5 and day 8 for all babies regardless of medical condition, milk feeding and prematurity. For the purpose of screening, date of birth is day 0	To enable timely detection of abnormal results and initiation of Appropriate treatment.

	(some IT systems record date of birth as day 1). Complete the details on blood spot card	

5-	When a baby has had a blood transfusion, either intrauterine or in the newborn period, before the day 5 blood spot, another sample (four spots) is needed 72 hours (3 days) after the last blood transfusion. In the event of multiple blood transfusions an initial screening sample should be sent by day 8 at the latest. (For intrauterine transfusion count date of birth as date of transfusion). The date of the last blood transfusion before the blood spot must be recorded on the card and on discharge / transfer notifications.	• To enable metabolite concentrations to return to pre-transfusion levels. • To ensure all babies are screened by day 8 regardless of blood transfusion status. • To reduce the chance of the baby missing newborn blood spot screening. • To permit appropriate interpretation of results.
6-	For SCD, a pre-transfusion sample is the preferred option for sickle cell screening. When a preterm baby has not had a pre-transfusion sample taken, the laboratory may forward the routine 5-8 day sample to the DNA laboratory for analysis as failsafe	To ensure all babies are screened for SCD.
7-	An assessment of the baby's level of distress and ability to tolerate handling must be made before initiating comfort measures. Where appropriate for the baby's condition, analgesia and comfort measures may be used	To reduce the pain/discomfort of the procedure.
8-	Inform parents of any outstanding screening tests, and record this in the PCHR. Advise parents which healthcare professional will be responsible for completing the blood spot screening for their baby and approximately when it will occur. Provider organizations should ensure failsafe arrangements for notifying screening status when the care of babies is transferred. This includes babies who are transferred in the neonatal period. The screening status of the baby is to be recorded on an auditable IT system and in the discharge/transfer documentation	To ensure that all babies are screened.

Finger Foods

PEELED FRUITS	Weight (g)	mg Phe
Apple wedges	10	1
Banana chunks	10	4
Cantaloupe chunks	10	3
FRESH OR CANNED		
Peaches	10	2
Pears	10	1
Plums	11	2
Fresh Strawberries	10	1
VEGETABLES		
Fresh, Frozen, or Cooked		
Carrot coins or sticks	10	3
Asparagus spears	10	6
Summer squash, seeded	10	4
Winter squash, cubed	10	5

VEGETABLES	Amount	Weight (g)	mg Phe
Green Beans	½ cup	34	17
Beets, sliced, cooked	¼ cup	43	21
Broccoli Flowerettes, raw	¼ cup	20	17
Cauliflowerettes	¼ cup	25	18
Cabbage shreds (green)	¼ cup	5	2
Cucumber slices, peeled	¼ cup	36	8
Lettuce, Iceberg	¼ cup	29	12
Mushrooms, raw	¼ cup	18	14
Bell peppers, raw	¼ cup	35	10
Pickles, dill	1 medium	60	11
Tomatoes, raw	½ cup	40	9
Turnip sticks, cubes, raw	½ cup	33	6

LOW PROTEIN SNACKS	Amount	mg Phe
LoProfin Crackers	5	5
Aproten, Cream Filled Wafer		
Vanilla	3	8
Chocolate	3	17
LoProfin, Cream Wafers		
Chocolate/Orange/Vanilla	4	2

SNACKS	Amount	mg Phe
Goldfish, original	5	9
Saltine Crackers	1	13
Ritz Crackers	1	10
Graham Cracker	½ full sheet	24
Marshmallow, mini	1/3 c = 13 g	5
Fruit Snacks, Betty Crocker	1 packet	3
Fruit Roll-ups, Betty Crocker	1	3
Potato Chips, plain or BBQ	3	15
Doritos, Ranch/ Nacho Cheeser	8	30
Pringles, Original/ BBQ	3	16
Pretzels, Rold Gold, tiny twists	3	23

FRUIT	Amount	Weight (g)	mg Phe
Fresh, canned, or frozen			
Blueberries	¼ cup	36	9
Canned	¼ cup	64	16
Cranberries	¼ cup	24	3
Sauce	¼ cup	70	3
Grapefruit, segments			
Fresh	¼ cup	43	9
Canned	¼ cup	48	9
Guava	1/3 guava	30	1
Kiwi, med, peeled	½ kiwi	38	11
Mango, sliced	¼ cup	48	6
Mandarin Orange	¼ cup	62	13
Orange, segments	½ orange	90	19
Papaya, cubed	¼ cup	35	7
Pineapple Chunks			
Fresh	¼ cup	38	5
Canned	¼ cup	45	6
Raisins, seedless	1 Tbsp	9	6
Raspberries			
Fresh	¼ cup	31	11
Frozen	¼ cup	63	16
Tangerine segments	½ tangerine	42	9

LOW PROTEIN PASTA	Weight (g)	mg Phe
ALL PASTA IS MEASURED DRY		
Aglutella, Spaghetti	60	20
Aglutella, Macaroni	60	20
Aproten, Spaghetti	56	17
Aproten, Ditalini	62	19
Cambrooke, Elbow Pasta	60	7
Cambrooke, Spaghetti	60	5
Dietary Specialties, Elbows	60	7
Ener-G Macaroni	57	5
Ener-G Spaghetti	57	5
LoProfin Spaghetti	56	6
LoProfin Macaroni/Penne	56	6

CEREALS	Amount	Weight (g)	mg Phe
Cheerios , plain	¼ cup	10	4
Cheerios, Honey Nut	¼ cup	10	53
Cocoa Krispies	¼ cup	10	25
Cocoa Puffs	¼ cup	8	15
Corn Chex	¼ cup	8	27
Corn Pops	¼ cup	8	15
Froot Loops	¼ cup	7	19
Honeycombs	¼ cup	6	16
Kix	¼ cup	6	20
Rice Krispies	¼ cup	7	23
Trix	¼ cup	8	19
Very Berry Kix	¼ cup	8	15

15 mg Phe equals 1 food equivalent

University of Utah, Metabolic Clinic April 2004

PKU list of foods:

Foods that are not allowed:

- All meats such as: beef, lamb, pork, ham, bacon, chicken, fish and fish products, organ meats (liver, heart, kidney), etc.
- Eggs
- All dairy products including: cottage cheese, cheese, milk, yogurt, ice cream, pudding, etc.
- Nuts and seeds
- Legumes
- **Ordinary** breads, flour cakes, and biscuits (made with yeast and/or gluten)
- Soya-Foods such as TVP (meat substitutes)
- Any food containing **aspartame** such as: diet sodas, diet jams, diet lemonades, etc.

Foods that are restricted (these must be weighed at given amounts):

Each weighed amount provides 50 mg of phenylalanine

Foods:	**Amount allowed:**
Potato chips	30 grams
Potatoes: boiled, mashed, roasted, etc.	80 grams
Broccoli	30 grams
Peas: fresh, frozen, etc.	25 grams
Spinach: boiled, steamed, etc.	25 grams
Corn on the cob	55 grams
Cereals (depending on type)	10-20 grams
Rice: white or brown	45 grams
Crackers and Snack foods	Varies
Cookies and desserts	Varies

For specific questions about foods for the PKU diet please contact the CRC dieticians.

Foods that are allowed (monitor these foods-do not allow excessive use):

- Fruits: apples, oranges, bananas, melons, grapes, grapefruit, peaches, strawberries
- Vegetables: french beans, carrots, cauliflower, celery, cucumbers, lettuce, radishes, tomatoes

"Free" foods:

- **Desserts/Sweeteners:**
  - Corn syrup, honey, sugar, molasses
  - Candy and gum with allowed ingredients (no aspartame)
  - Frosting
  - Hunt's® Lemon Pudding (canned)
  - Popsicles

- **Fats:**
  - Oil, lard, bacon drippings
  - Salad dressings-Catalina (Kraft), Italian
- **Beverages:**
  - Apple juice
  - Carbonated beverages (soda) without aspartame
  - Gatorade®
  - Kool-Aid®
  - Lemonade (not diet)
  - Tang
  - Strawberry Quik® (powder only)
  - Coffee and instant tea's


Aim for Healthy Choices
Choose the Foods Closest to the Bull's-Eye
Steak
Milk
Regular Pasta
Rice
Refried Beans
Vegetables
Corn
Pork Chops
BEST
Juices
Fruits
PHENYL-FREE
Chicken
Peas
FOODS
Bread
Eggs
Nuts
Low Protein Breads and Pastas
Potatoes
French Fries
Cheese
They are BEST for YOU
Peanut Butter
Hamburger

وزارة الصحة مشروع غربلة حديثي الولادة

كارت أخذعينة الدم
دائرةصحة ----------
قطاع الرعاية الصحية الأولية ----------
مركز الرعاية الصحية الأولية ----------

اسم الطفل الرباعي ----------
تأريخ الولادة ----------

تأريخ أخذ العينة ----------
-
رقم العينة التسلسلي ----------

- **(ملاحظة : يحتفظ بالكارت لحين الحصول على نتيجة الفحص التوكيدي)**

تأريخ مراجعة مختبر الصحة العامة المركزي ---------- اسم وختم مدير المركز الصحي----------

التغذية الإسترجاعية (مختبر الصحة العامة المركزي)

المرض المشتبه به ----------
تأريخ إجراء الفحص التوكيدي ---------- إسم
وختم القائم بأخذ العينة ----------

تأريخ وجهة الإحالة ----------إسم وتوقيع مدير المركز الصحي ----------

التغذية الاسترجاعية (مستشفى الأطفال)

إسم وختم الطبيب المعالج ---------- الإجراءات المتخذة ----------
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نتيجة الفحص التوكيدي ----------
الإجراءات المتخذة ----------

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- Guidelines on newborn screening and therapy for congenital hypothyroidism have been released by the American Academy of Pediatrics
- SYMPOSIUM ON 'DIETARY MANAGEMENT OF DISEASE'
  The dietary management of phenylketonuria
  By JENNIFER COUTTS, Royal Manchester Children's Hospital, Pendlebury,
  Manchester M27 IHA

- Newborn screening sample collection guidelines
  Detailed information about the newborn screening program, including correct sample collection techniques, can be found in the e-learning tool available at:
  www.vcgs.org.au/pathology/nbs

- Florida
  Newborn Screening Guidelines
  2012

- PRESENT NEWBORN SCREENING FOR PHENYLKETONURIA
  Frances E. Doughertyl* and Harvey L. Levy2
  IDivisionofGenetics, Scottish Rite Children's Medical Center, Atlanta,
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- The Northwest Regional Newborn Screening Program Oregon Practitioner's Manual Oregon Health & Science University Cary Harding, MD Stephen L. LaFranchi, MD Gregory Thomas, MD Michael Wall, MD Oregon Health Authority Public Health Michael R. Skeels, PhD, MPH Cheryl A. Hermerath, MBA, DLM (ASCP), RM (NRM) Lindsey Caudle, RN, BSN Becky J. Whittemore, MN, MPH, FNP 9th Edition, 2010

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  Implementation date: 1 April 2013

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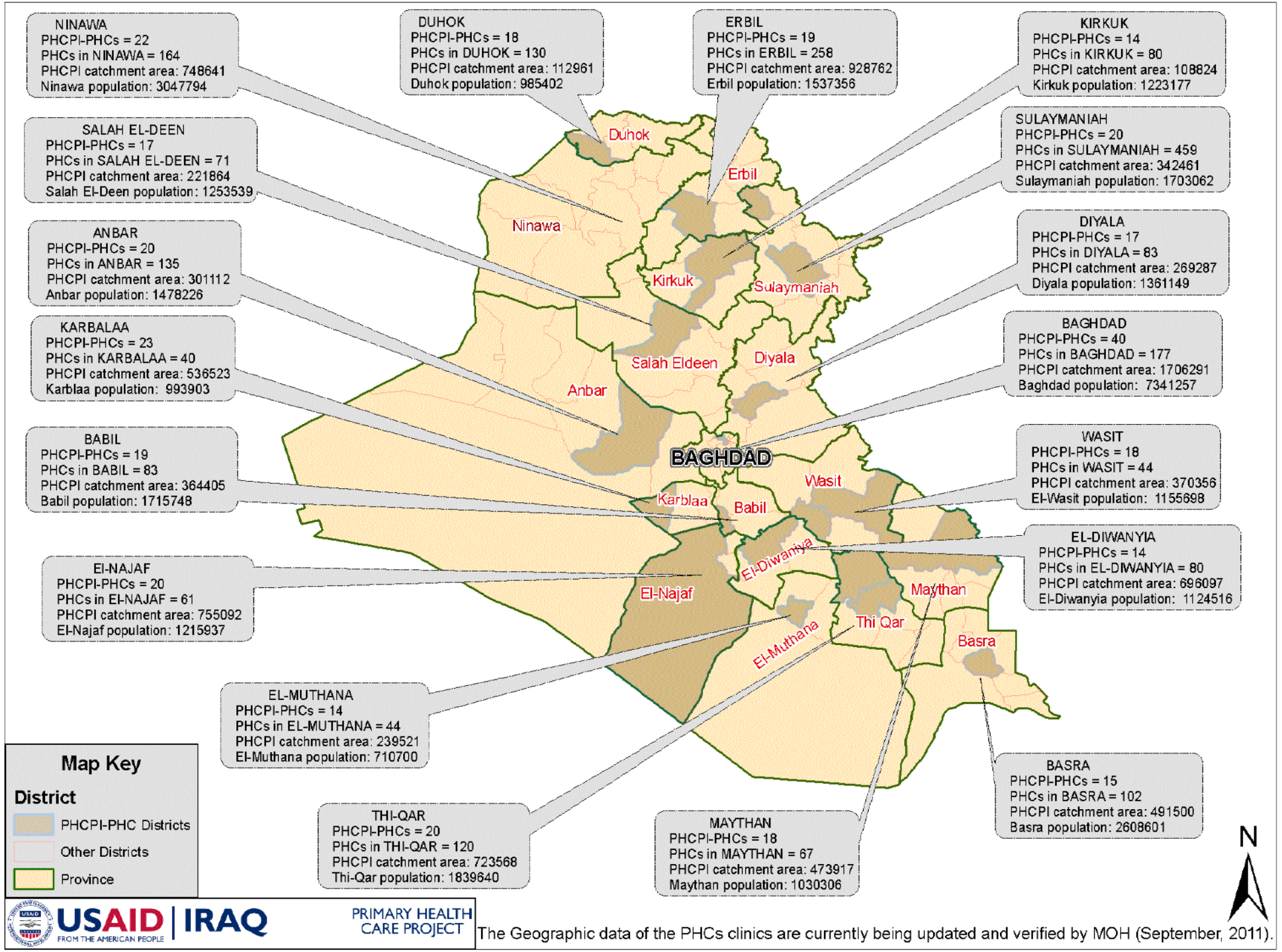
Primary Health Care Project In Iraq
http://phciraq.org/
www.usaid.gov

PHCPI-PHCs population mapped to IRAQ population



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PRIMARY HEALTH CARE PROJECT

The Geographic data of the PHCs clinics are currently being updated and verified by MOH (September, 2011).