

# METABOLİK HASTALIKLARIN TANISINDA YENİDOĞAN TARAMA TESTLERİ



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1 Haziran 2004**

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@TANIM

@MATERYAL

@TARİHÇE

@DÜNYA NEREDE, BİZ NEREDEYİZ ?

@TARAMANIN ÖNEMİ

@TARANMASI GEREKLİ HASTALIKLAR

@TEKNOLOJİ

@KALİTE KONTROL

@SONUÇ



“yenidođan taraması sadece bir laboratuvar hizmeti deđil; eđitim, takip, net tanı, tedavi, uzun donem yonetimi iine alan veri deđerlendirilmesinin olduđu bir sistemdir.

# Yenidođan taraması nedir?

## 6 kısımdan oluřan bir sistem

Eđitim, tarama, tanı  
takip, yönetim ve tedavi

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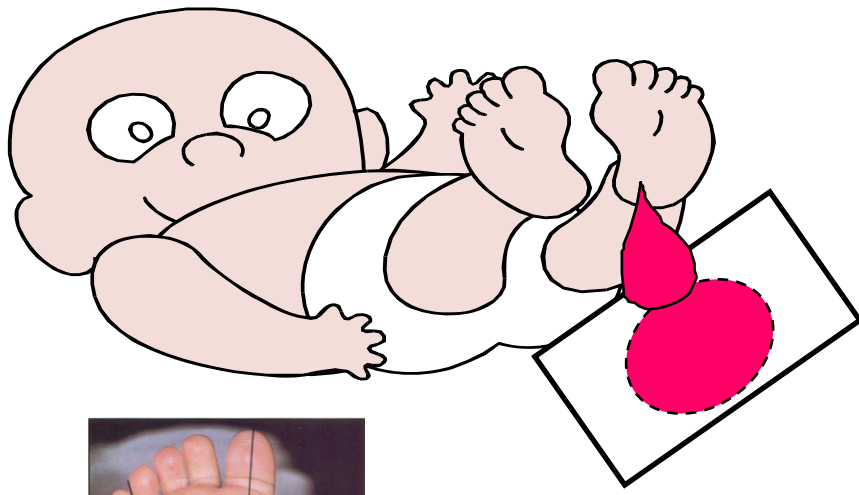
**Eđitim** / anne baba veya doğum yapacak annenin teşhiř edilebilecek hastalıklar konusunda bilgilendirilmesi.

**Laboratuvarda test etme** / doğum sonrası çocuktan alınacak biyolojik materyalin

**Erken tesbit** / klinik belirti vermeden önce genetik defektin tesbiti

**Diagnostic çalıřmalar ve tedavi** / genetik defektin tesbitini takiben

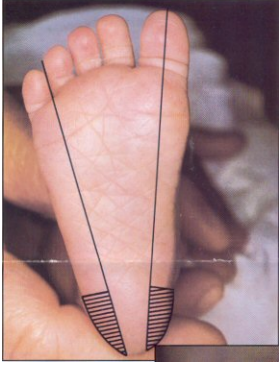
**Önleme** / Mental retardasyon ve erken ölümün önlenmesi en büyük amaç



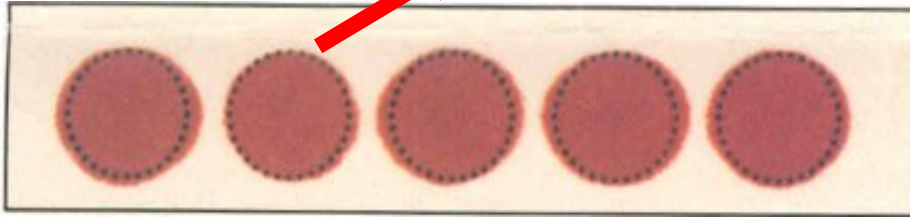
Bir bebekteki toplam kan hacmi  
100-150 ml

Bir EDTA'lı hemogram tüpü  
2,50 ml=2500  $\mu$ L

ANEMİ ?



50  $\mu$ L (PKU, nTSH, G6PD)



4 halka 200 $\mu$ L = PKU, nTSH, Total GAL, Serbest GAL  
GAL1P, GALT, BİOTİNİDAZ, G6PD, MSUD, CK,  
**TMS** için YETERLİ

Örnek alınımı kolay  
Analitlerin çoğu stabil  
Taşıma basit  
Saklamak kolay  
Tam kan matriksi  
Güvenli  
Merkez laboratuvar teknolojisine uygun

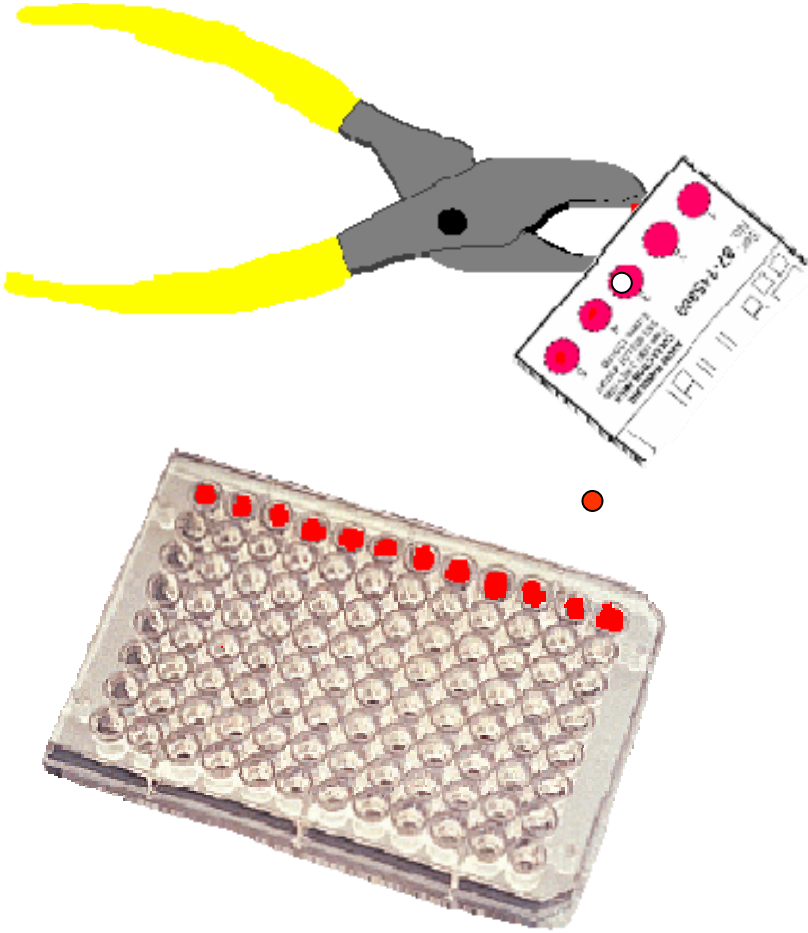


Filtre kağıdı

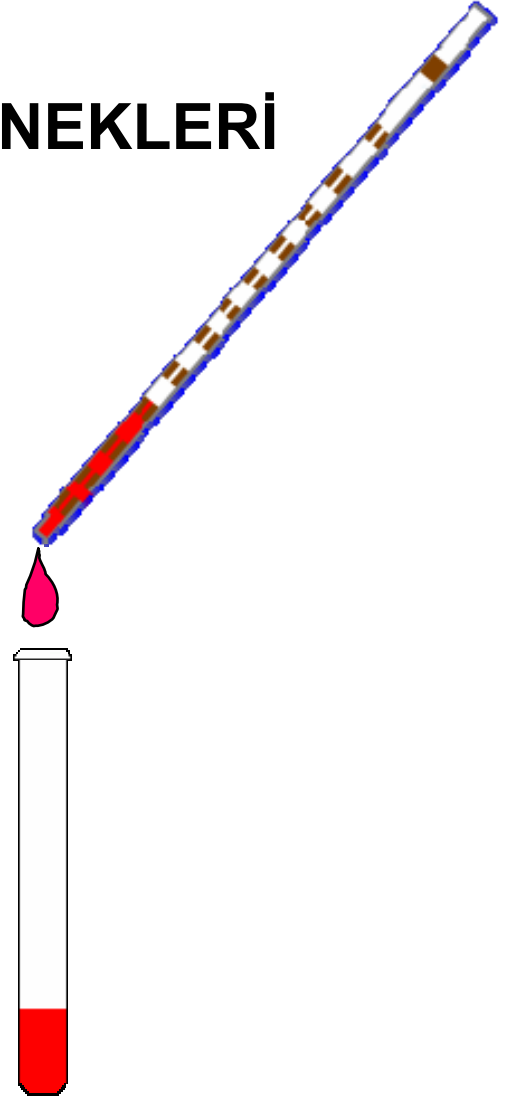
Tam kan

Hematokrit  
Büyükük  
Hacim

# DRIED BLOOD SPOTS-DBS KAĞIDA EMDİRİLMİŞ KAN ÖRNEKLERİ



EŞİT



AYNI DOĞRULUK VE TEKRARLANABİLİRLİĞİ GEREKTİRİR

# **Kağıda emdirilmiş kan örneklerinin Avantajları**

- **Örnek alınımı kolay**
- **Analitlerin çoğu stabil**
- **Taşıma basit**
- **Saklamak kolay**
- **Tam kan matriksi**
- **Güvenli**
- **Sentralize laboratuvar teknolojisine uygun**



# Topuk kanı toplanmasında kalite güvence

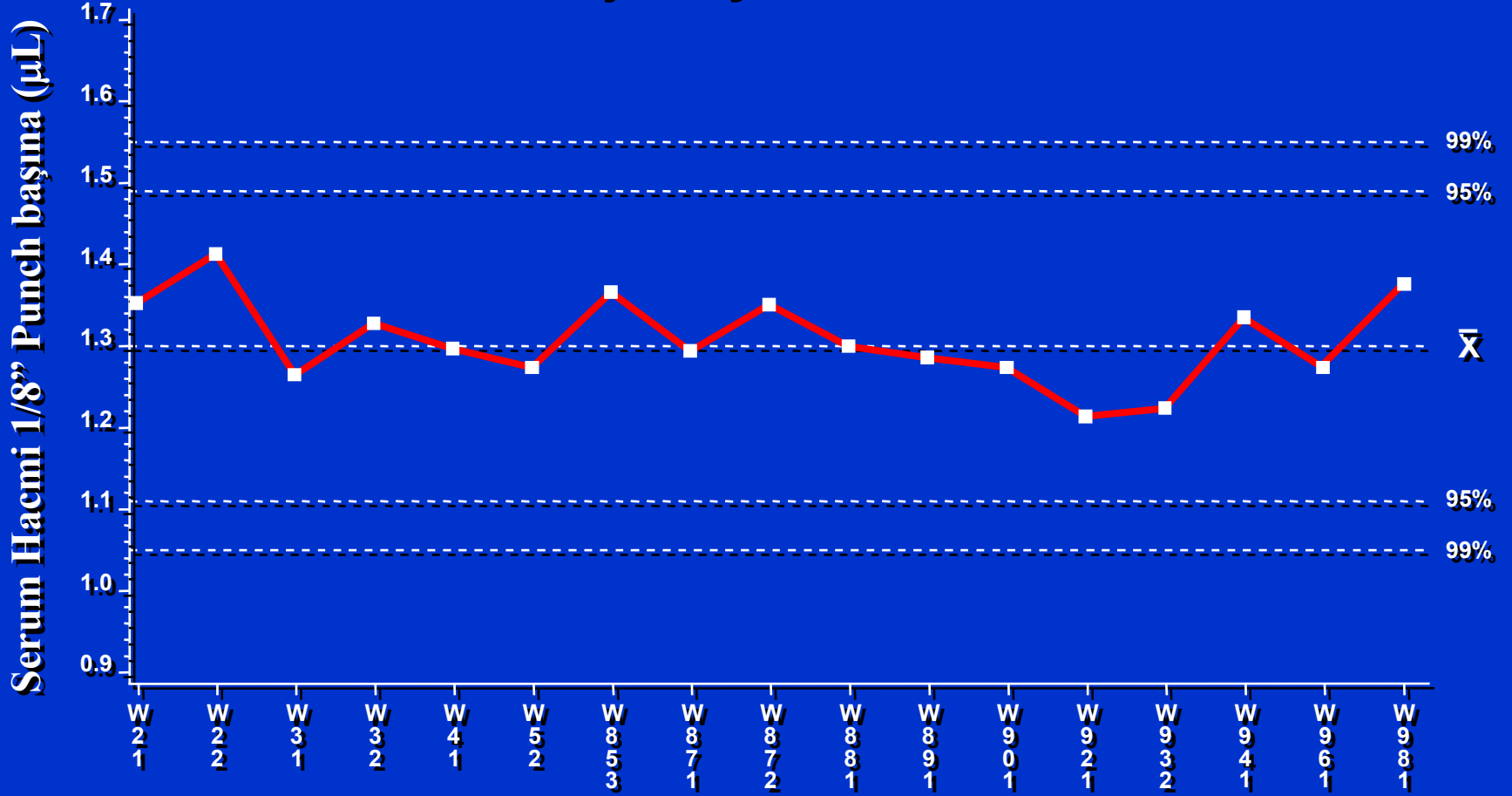


## Filtre kağıdının kalite kontrolü

- Yeni lot numaralarında performans takibi
- Geçmişe dönük lot numaralarının karşılaştırılması
- Gerekli performans kriterlerini karşılayıp karşılamadığının kanıtlanması

# Schleicher and Schuell - Grade 903 Filtre Kağıdı

## 3.2 mm ye düşen serum hacmi



Lot numaralarının kronolojik takibi

# **DBS örneklerinde ölçümü etkileyen değişkenler, filtre kağıdı ile ilgili**

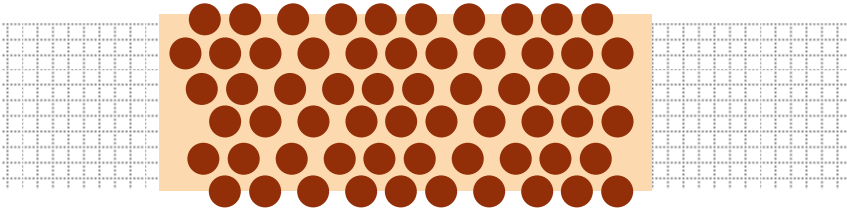
- **Üretim lot numarasında homojenlik**
- **Diğer lot numaraları ile homojenlik**
- **Üretici firmalar arasında değişkenlik**
- **Örnek almada değişkenlik**

# **DBS örneklerinde ölçümü etkileyen diğer değişkenler**

- **Kağıdın saklanması ve kullanımı**
- **Ortamın nemi**
- **Emdirilen kan hacmi**
- **Emdirilen kanın hematokrit düzeyi**
- **Kanın emdirilme süresi**

# DBS

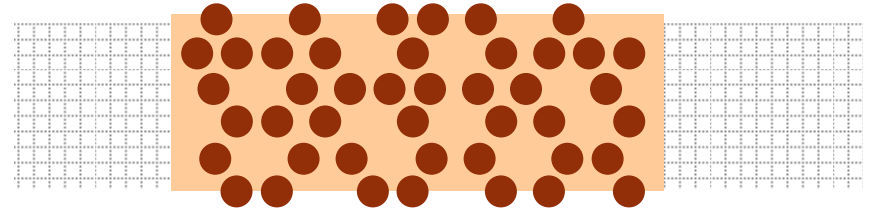
- Filtre kağıdı (Pamuk)
  - Onaylı S&S 903 Lot no.....
  - Kan absorpsiyon spesifikasyonları
    - Hacim / mm<sup>2</sup>
      - Hematokrit



60% hematocrit



2 kısım



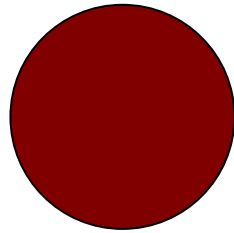
40% hematocrit

# Kağıda emdirilmiş kan örnekleri

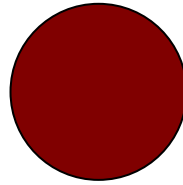
(DBS=dried blood spots)

1 inch =25,4 mm  
1/8 inc=3,2 mm  
3/16 inc=4,76 mm  
1/4 inc=6,35 mm

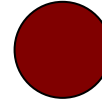
Vol / inc<sup>2</sup>



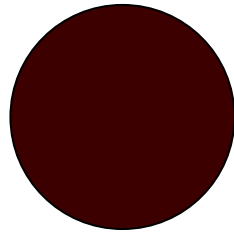
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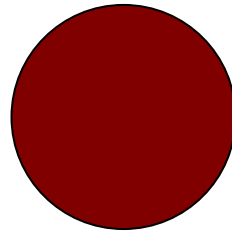
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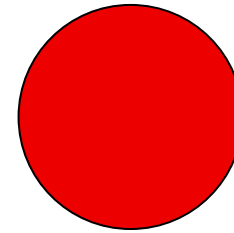
Vol / inc<sup>2</sup>



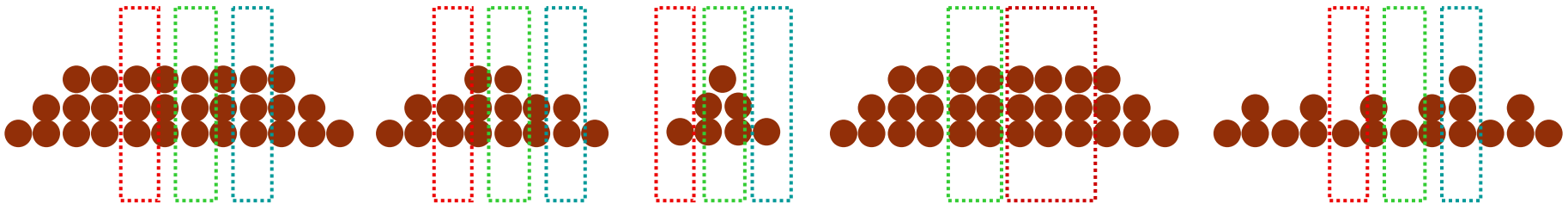
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>



NEDEN???

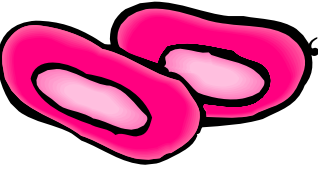


# DBS

- $1/8 < 3/16 < 1/4$
- İdeali hangisi ?
- **Cevap: 1/8**
- Örnek sarfı az , tekrar koyma , çift veya daha çok örnek çalışma olanağı var



# NCCLS Standard



## “Blood collection on Filter Paper for Neonatal Screening Programs, Approved Standard”

**LA4-A3, Vol. 17, No. 16**

**Authors:**

W. Harry Hannon, Ph.D.

James Boyle

Brad Davin

Anne Marsden

Edward R.B. McCabe, M.D., Ph.D.

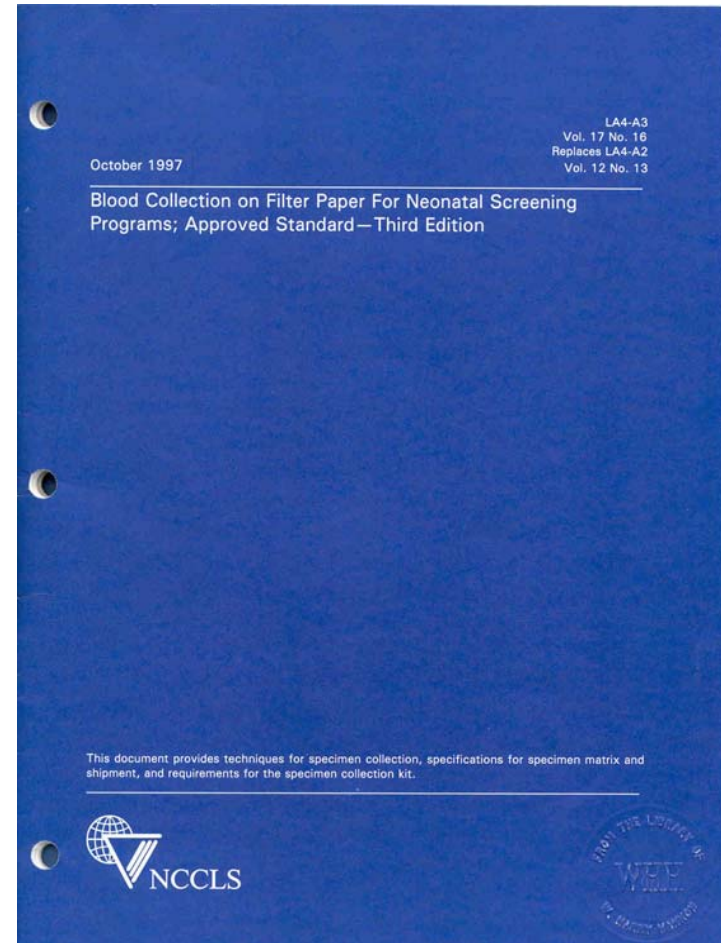
Marion Schwartz, R.N., M.S.N.

George Scholl

Bradford L. Therrell, Jr., Ph.D.

Martin Wolfson

Freda Yoder



**W. Harry Hannon, Ph.D**





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## Robert Guthrie, M.D., Ph.D.

Basit, ucuz PKU tayini testi,  
Guthrie testi 1960 lı yıllarda bulunmuş  
Yenidoğan tarama konusuna ilk adım



30,000 bireyin mental retardasyondan  
korunduđu biliniyor.

Sponsored: National  
Meeting on Tandem Mass  
Spectrometry Use in  
Newborn Screening

Madison, WI

September 10-11, 2001



Enhancing the Implementation  
of Tandem Mass Spectrometry  
for Newborn Screening Laboratories

September 10-11, 2001  
Marriott - Madison West  
Madison, Wisconsin

Hosted by the



Wisconsin State  
Laboratory of Hygiene

**1960**

**PKU**

**Kongenital hipotiroidi**

**Biotinidaz eksikliđi**

**Galaktozemi**

**GALT**

**G6PD**

**MSUD**

**CK**

**Homosistinüri**

**CAH**

**SCD (hemoglobinopatiler)**

**Metabolik tarama (açil karnitin profil ,aminoasid profil)**

**Mutasyonel analizler**

**2000**

## **Amerika USD**

**51 farklı tarama programı var , zorunlu testler**

**PKU**

**CH**

**GAL**

**Bir kısım bölge 40 hastalık tararken bazıları 8 in altında test tarıyor.**

**CH dünyada görülme sıklığı : 1/3.000**

## **AMERİKA**

**Kübada : 1970 tarama başlangıcı**

**Costa Rica da: 1990 tarama başlangıcı**

**Guatemela: 1986**

**Uruguay: CH, ve PKU**

**Argentin & Brazilya: bazı bölgeler geniş tarama , bazı bölgeler kısıtlı , kanun yok**

**Kolombiya, Ekvator, Paraguay, Peru, Venezuela: yeni başlangıç aşamasındalar**

## **ASYA**

**Ekonomik ve sosyal koşullar kötü**

## **JAPONYA %100**

**PKU, MSUD, HCY, GAL, CAH**  
**Bazı bölgelerde MS/MS**

## **TAIWAN**

**CK, PKU, HCY, GAL, CAH, G6PD**

## **SİNGAPUR, HONG KONG**

**CH, G6PD**

## **KOREA**

**PKU, CH 1991**

## **AVRUPA**

Avrupa konseyinde 46 ülke var,  
PKU, CH, BIO, CAH, GAL

CF, MCAD

+

MS/MS (Almanya, Hollanda, Belçika)

**TÜRKİYE (Sağlık Bakanlığı)**

1/3.000 -1/4.500 PKU 1.481.000 doğumun %59 taranıyor; recall %5 PKU için Guthrie testi  
1/2600 CH  
63.000 ilk 5 yaş ölüm, 48.000 (0) yaş grubu 28.000 neonatal  
Bunun %52 si 1. gün ölüyor.

**YUNANİSTAN** 24 yıldır G6PD, 20 yıldır PKU, CH  
1994/1996 Galaktozemi taranmış ancak  
durdurulmuş finans problemi, sadece özel kurumlar yapıyor

**AFRİKA** CH

**ORTA DOĞU** CH

İsrail, İran, Umman, Birleşik Emirlikleri CH dışında hizmet alımı  
**Kral Faysal (Riyad) MS/MS**

# ÜLKEMİZ

1/3.000 -1/4.500 PKU 1.481.000 doğumun 48.000 (0) yaş grubu 28.000 neonatal

Bunun %52 si 1. gün ölüyor

Gerikalanının %59 taranıyor; recall (geriçağırma) %5 PKU için

1/2600 CH

630.000 ilk 5 yaş ölüm.



# Newborn Screening in Europe; results of a survey

Loeber JG<sup>1</sup>, Zabransky S<sup>2</sup>  
<sup>1</sup>RVM, Bilthoven, The Netherlands;  
<sup>2</sup>Unikinderklinik, Homburg/Saar, Germany

## TÜRKİYE

Veri = biraz

Nüfus = 65,78 mil

Doğum hızı = 1406/bin

Tarama hızı = ?

Lab = ?

Finans = ?

PKU = p (kısmi)

CH = p

GAL = p

G6PD = p

AA = p

MCA = p



Since the 1960's neonatal blood spots have been used to detect the number of diseases

20. Until recently there was no structure in European countries. This is a first attempt of the International Society for Neonatal Screening.

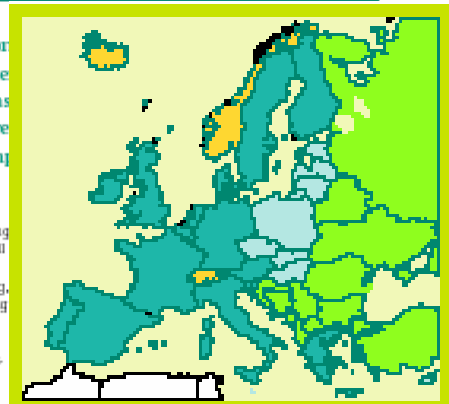
There are several ways to determine which countries belong to Europe. Here the list of member countries of the Council of Europe has been chosen.

In November 2001 the first ISNS European regional meeting, called "Euroscreening", was held in Germany. This meeting aimed to get acquainted with the key persons from each country and to exchange ideas for harmonisation and optimisation of procedures, both analytically and pre/post-analytically. A questionnaire was developed concerning diseases screened for, methods and cut off limits used and prevalences and recall rates noted.

### Method

The questionnaire consisted of the following topics:

- 1) How many annual births
- 2) Which panel of diseases, methods and results
- 3) How many laboratories in the country
- 4) How is the programme funded



Council of Europe member countries

EU EFTA  
 future EU other

As is expected, PKU and CH are screened for everywhere. Other diseases depend on the genetic make up of the population per country and the technical developments. With the implementation of MS/MS as a screening tool these data will have to be updated regularly in the coming years.

methodologies and their quality aspects; 3. the ways parents and professionals are educated concerning the aims of each screening programme including legal and ethical aspects.

European recommendations will attempt to bridge the present large gaps both within and between countries.

ISNS must collect similar data from other regions as well to obtain an overview on global level and to identify where screening programmes should be initiated or further developed.

Table 1: Population and neonatal screening data (2002)

Country	Screening	Population (million)	Perinatal death rate (per 1000 live births)	Screened neonates (thousand)	Lab. units	Recall rate (%)
Austria	yes	8,240	5.9	200	1	100
Belgium	yes	10,230	7.0	170	1	100
Denmark	yes	5,280	4.5	100	1	100
Finland	yes	5,270	7.0	100	1	100
France	yes	64,560	10.0	100	1	100
Germany	yes	82,120	10.0	100	1	100
Greece	yes	11,230	10.0	100	1	100
Ireland	yes	3,780	8.0	100	1	100
Italy	yes	57,230	10.0	100	1	100
Japan	yes	127,230	10.0	100	1	100
Netherlands	yes	16,230	7.0	100	1	100
Norway	yes	4,230	7.0	100	1	100
Portugal	yes	10,230	10.0	100	1	100
Spain	yes	40,230	10.0	100	1	100
Sweden	yes	8,230	7.0	100	1	100
Switzerland	yes	7,230	7.0	100	1	100
Turkey	yes	65,230	10.0	100	1	100
UK	yes	57,230	10.0	100	1	100
USA	yes	265,230	10.0	100	1	100
Total		800,230	8.0	100	1	100

Table 2: Screening programmes in European countries (2002)

Country	PKU	CH	GAL	CF	GCD	GD	MSU	GSD	var	total	lab	recall
Austria	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	1	100
Belgium	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	1	100
Denmark	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	1	100
Finland	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	1	100
France	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	1	100
Germany	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	1	100
Greece	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	1	100
Ireland	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	1	100
Italy	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	1	100
Japan	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	1	100
Netherlands	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	1	100
Norway	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	1	100
Portugal	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	1	100
Spain	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	1	100
Sweden	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	1	100
Switzerland	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	1	100
Turkey	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	1	100
UK	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	1	100
USA	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	1	100
Total	250/250	250/250	250/250	250/250	250/250	250/250	250/250	250/250	250/250	250/250	250	100

Table 3: Organized Neonatal Screening (ONS)

Country	Screening	Lab	Method	Recall rate (%)	Prevalence
Austria	2000/01	1	MS/MS	100	100
Belgium	1998/99	1	MS/MS	100	100
Denmark	1998/99	1	MS/MS	100	100
Finland	1998/99	1	MS/MS	100	100
France	1998/99	1	MS/MS	100	100
Germany	1998/99	1	MS/MS	100	100
Greece	1998/99	1	MS/MS	100	100
Ireland	1998/99	1	MS/MS	100	100
Italy	1998/99	1	MS/MS	100	100
Japan	1998/99	1	MS/MS	100	100
Netherlands	1998/99	1	MS/MS	100	100
Norway	1998/99	1	MS/MS	100	100
Portugal	1998/99	1	MS/MS	100	100
Spain	1998/99	1	MS/MS	100	100
Sweden	1998/99	1	MS/MS	100	100
Switzerland	1998/99	1	MS/MS	100	100
Turkey	1998/99	1	MS/MS	100	100
UK	1998/99	1	MS/MS	100	100
USA	1998/99	1	MS/MS	100	100
Total	250/250	250	MS/MS	100	100



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# **WILSON & JUNGNER KRİTERLERİ, 1968**

**Taranan metabolik hastalık ciddi sonuçlar doğurmalı  
(ölüm, fiziksel, mental handikap)**

**Kabul edilen bir tedavi protokolü olmalı / önlenebilir  
(genetik danışmanlık olmalı)**

**Hastalık, klinik semptomlar belirgin olmadan önce  
asemptomatik bir dönem içermeli**

**Basit, güvenilir, uygun maliyette, hassasiyet ve özgüllüğü  
yüksek, topluma uyarlanabilir bir testi var ise taranmalı**

**Metod tanımlayıcı olmalı ve ayırıcı tanıya götürmeli,  
test tekrarına gerek duyulmamalı**

**Hastalık taranan toplumda belirli bir sıklıkta görülmeli**

# *De opsporing van aangeboren metabole aandoeningen :*

- *Fenylketonurie*
- *Hypothyreoidie*



**Province of ANTWERP**

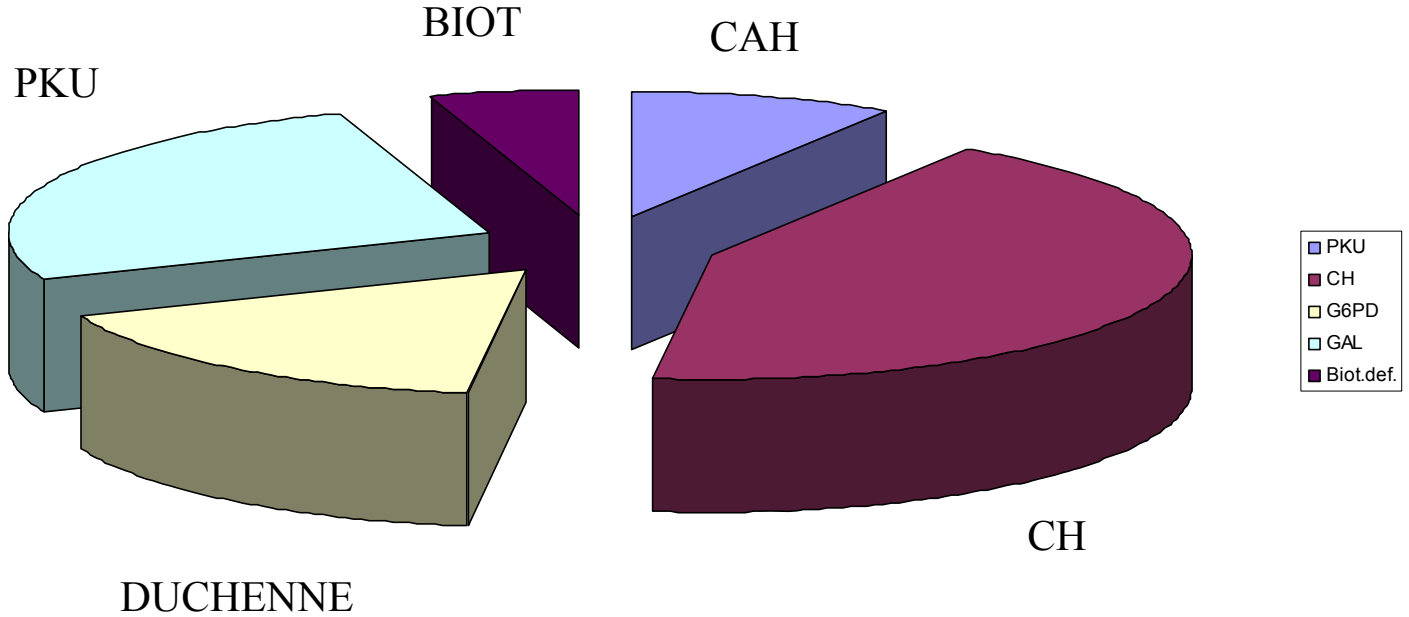
**PCMA Lab.  
BELÇİKA**

**22.000 bebek/yıl**

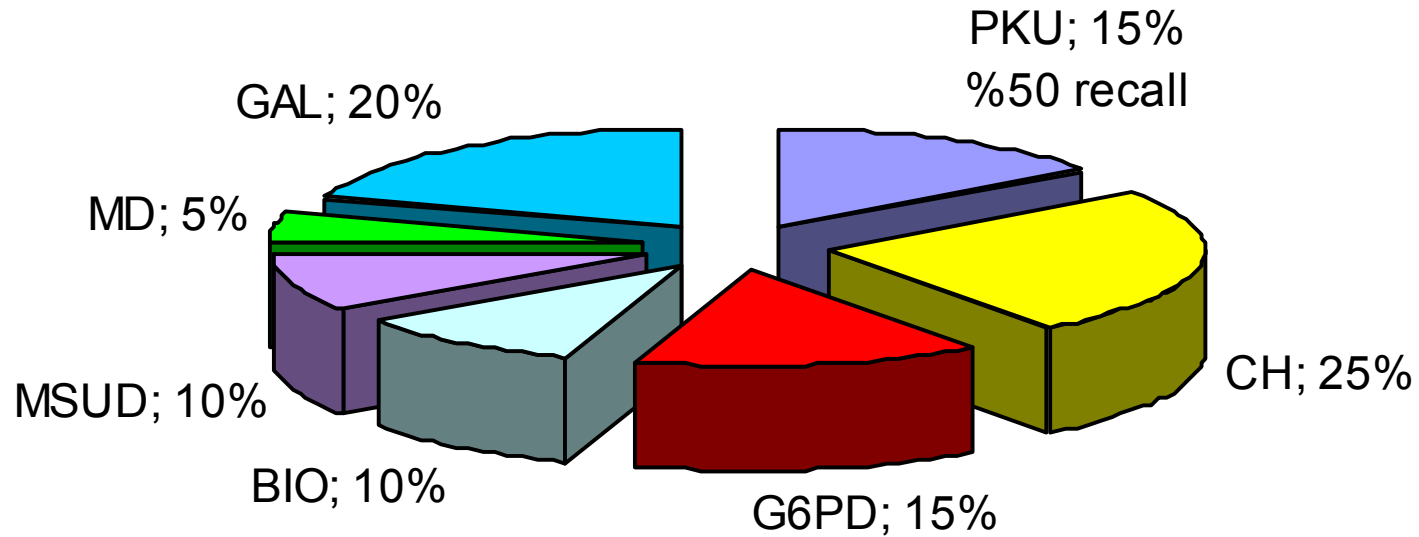


Ministerie van de  
Vlaamse Gemeenschap

# Yenidoğan tarama (Antwerp / BELÇİKA / PCMA)



# Selektif Yenidođan Taraması (topuk kanı)

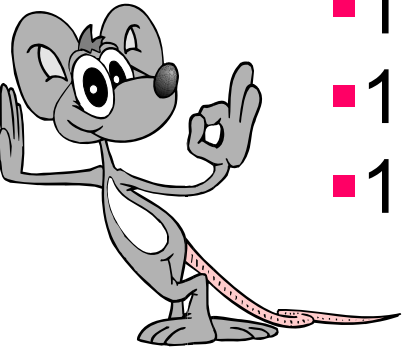


# Yaklaşık 1600 Yenidoğan tarama sonuçları (selektif tarama)



- 20 G6PD defekti
- 1 Biotinidaz defekti, 1 kısmi defekt
- 1 MSUD
- 1 Galaktozemi
- 2 PPA
- 1 MMA
- 1 hiperfenilalaninemi
- 1 Wolman's hast
- 1 Ducheen MD
- 1 CH

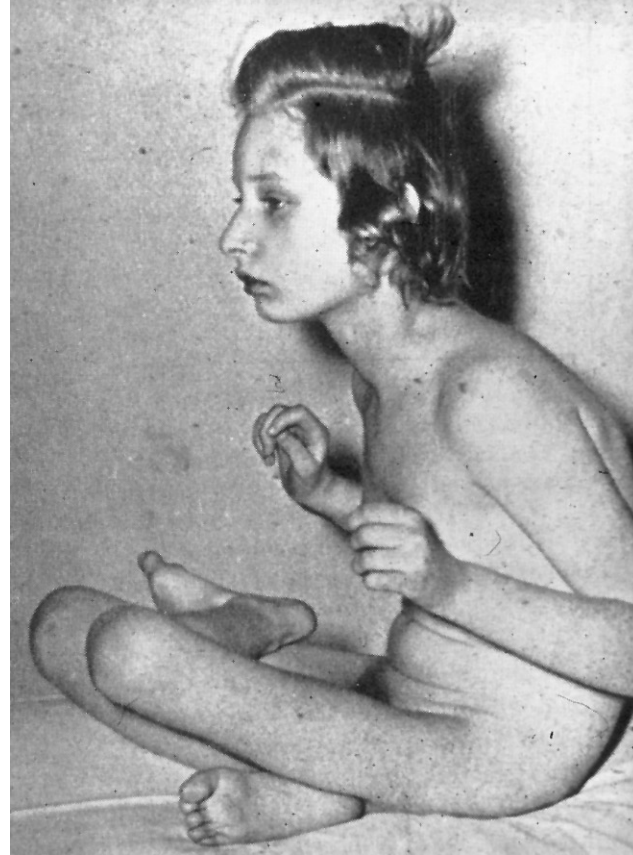
**1 / 53 hastalık**  
**Selektif tarama**



# PKU yenidođan taraması öncesinde

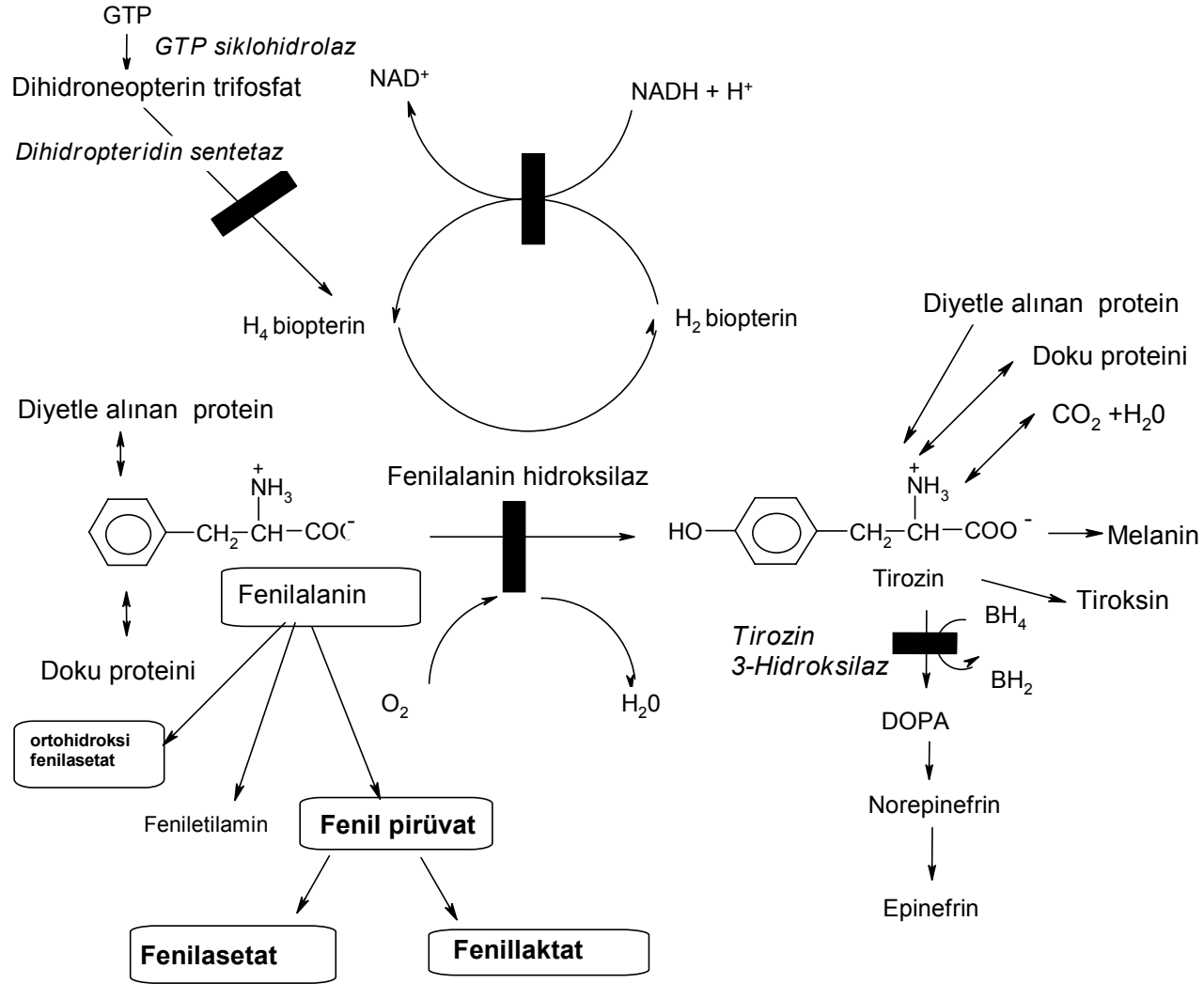
Prevalans

1/5.000-1/20.000



Mental retardasyonun önlenimi





\* Tedavi edilmemiş olan FKU da çerçeve içine alınan metabolitler birikir.

■ Enzim eksikliğinin olduğu bölgeleri göstermektedir.



*Lizin veya lizil peptidler*

**BIOTİN**

**BIOTİNİDAZ**

**Holokarboksilaz sentetaz**

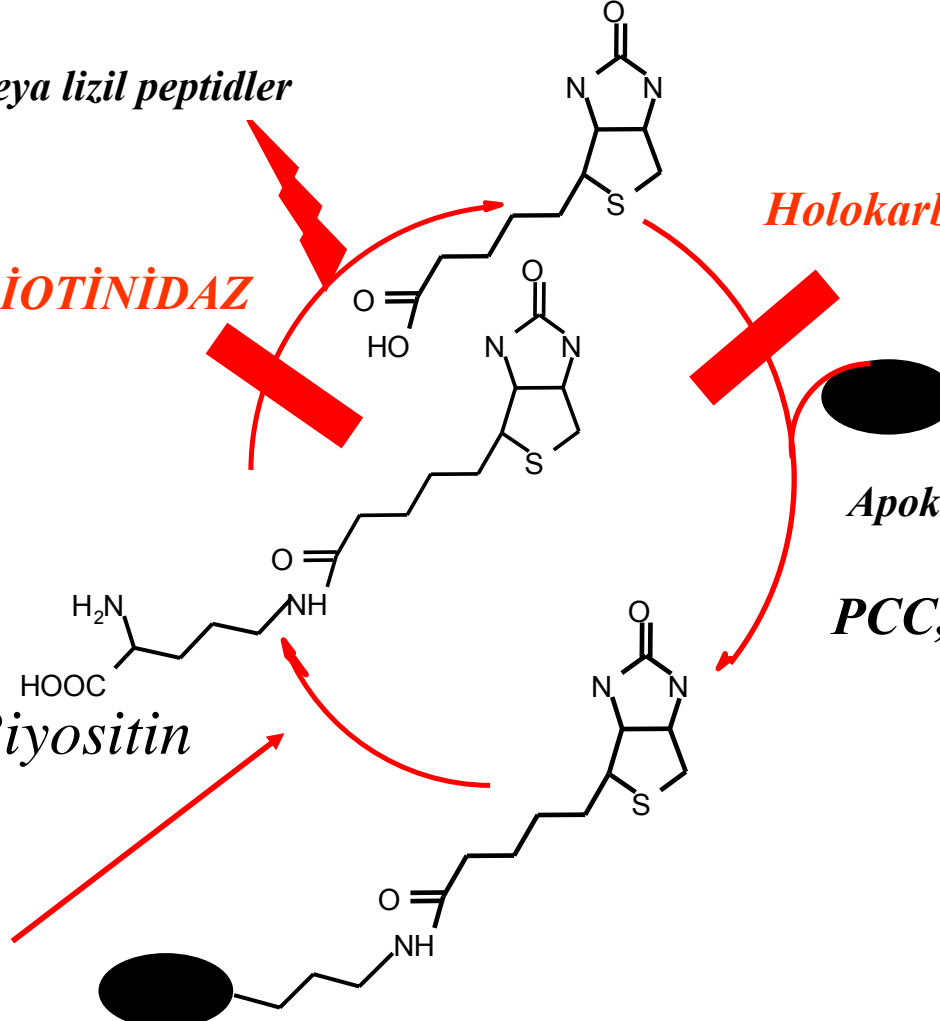
**Apokarboksilazlar**

**PCC, MCC, PC, ACC)**

**Biyositin**

**Proteolitik yıkım**

**Holokarboksilazlar**



# Biotinidaz eksikliği

- Autosomal resessif yenidoğan hastalığı
- Klinik gecikme CSF da laktat artışı
- Neurologic symptomlar
- Deri ve saç problemleri
- Biotin desteği: etkin, ucuz ve kolay
- Hassasiyet %100, özgüllük %99,9
- Tam yetmezlik prevalans 1:38,000\*

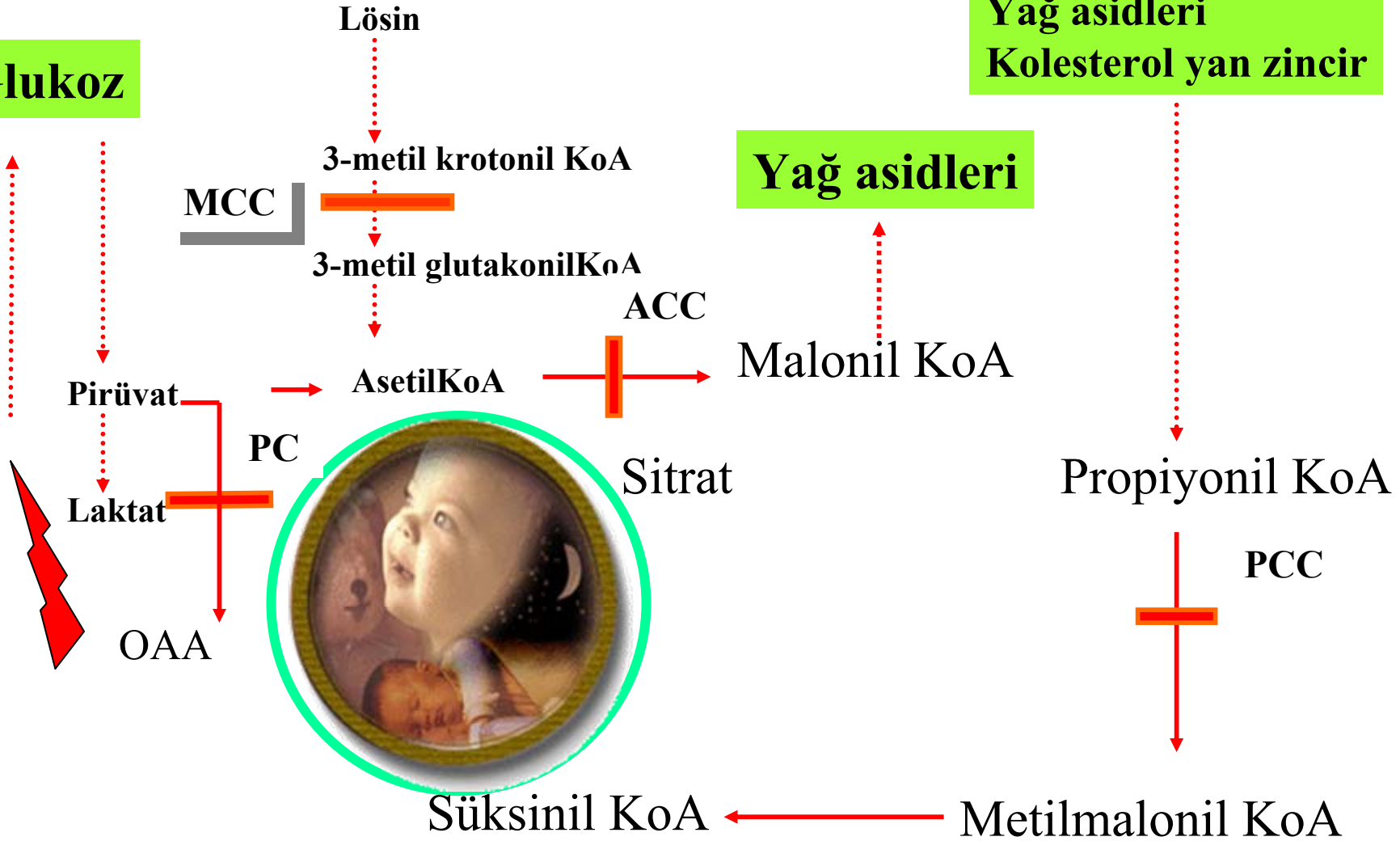
*\*(Demirkol M et al: 29th EMG meeting, London 1996)*



**Glukoz**

**Valin**  
**İzolösin**  
**Metiyonin**  
**Treonin**  
**Yağ asidleri**  
**Kolesterol yan zincir**

**Yağ asidleri**



# Kongenital hipotiroidizm



İnsidans 1/4000

Tiroid hormon sentezinde yetersizlik

Tarama testi: neonatal TSH ölçümü

Cut off: 20 mU/L

**Protokol**

*20-50 retest (3 kez)*

*Yeni örnek istenir*

*50-100 arası değerlerde doktor aranır*

*>100 değerlerde ilgili hekim pediatrik endokrinolog ile görüşme ve tedavi hemen tedaviye geçilir.*

**MR , gelişme geriliği**

**1:**



***ENZİM: galaktokinaz***

**2:**



***ENZİM: galaktoz-1-fosfat üridil transferaz (G-1-PUT veya GALT)***

**3:**



***ENZİM: UDP-glukoz epimeraz***

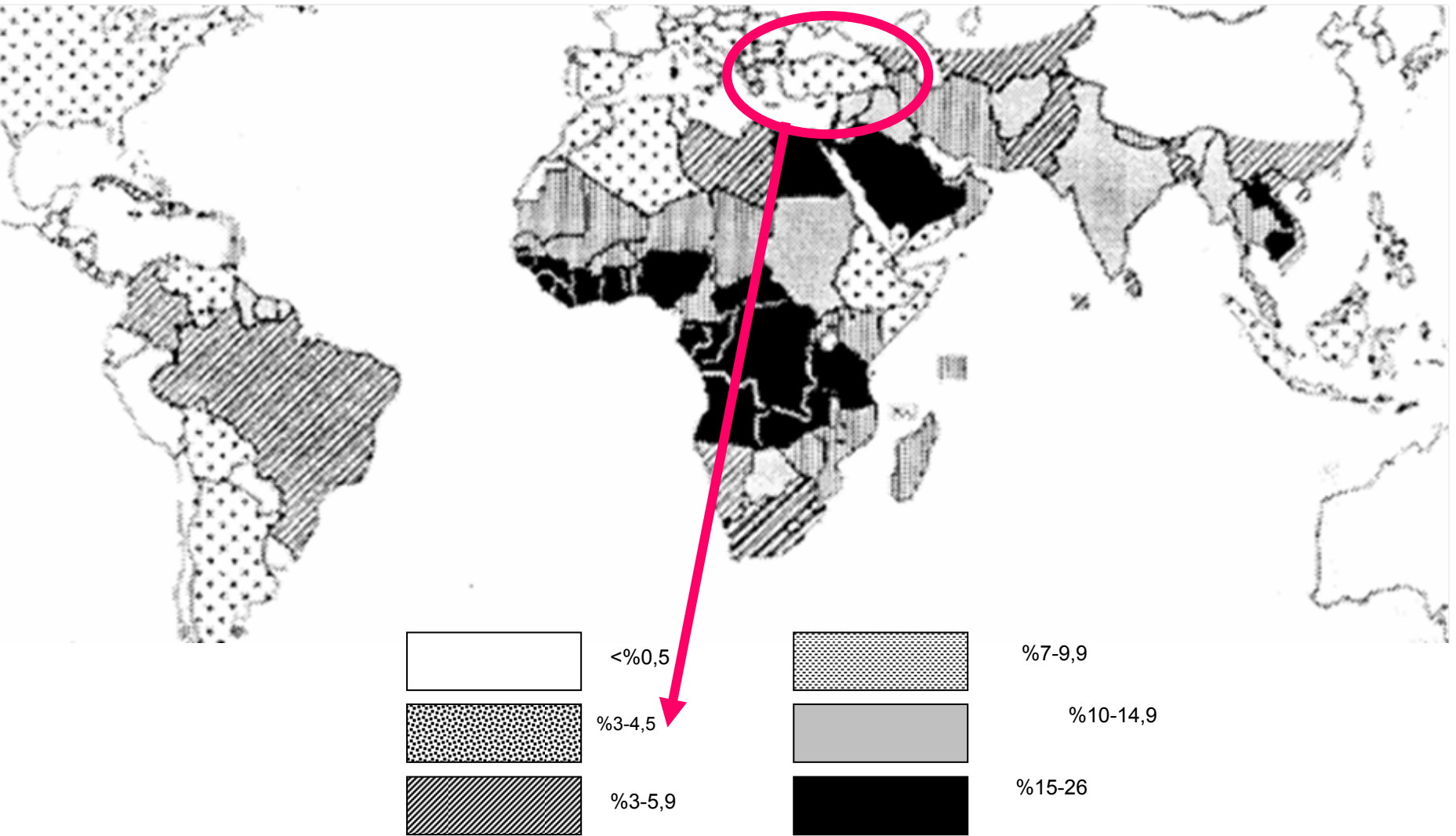
**Net sonuç**



Prevalans

1/25.000-1/30.000

# G6PD



# TANININ DOĞRULANMASI

- MS/MS teknolojisi taramadır!
- Tanı konulması:
  - GC-MS ile organik asid analizleri PA?  
MMA? METH? ARGİNİNOSUKSİNİKASİDÜRİ?
  - Likid kromatografi amino asid analizleri ile
  - Doku enzim analizleri
  - Moleküler genetik analizler
- Eğer ileri araştırma yapamayacaksan  
TARAMA YAPMA !!!!





@TANIM

@MATERYAL

@TARİHÇE

@DÜNYA NEREDE, BİZ NEREDEYİZ ?

@TARAMANIN ÖNEMİ

@TARANMASI GEREKLİ HASTALIKLAR

@TEKNOLOJİ

@KALİTE KONTROL

@SONUÇ

# GELECEĐE BAKIŐ

HASTALIĐIN ÖNLENİMİ  
OLMALI

# MS/MS versus NBS

- MS/MS is not supplemental or comprehensive screening.
- Comprehensive and supplemental screening may include MS/MS.
- MS/MS is not a disease classification, category, or group of disorders.



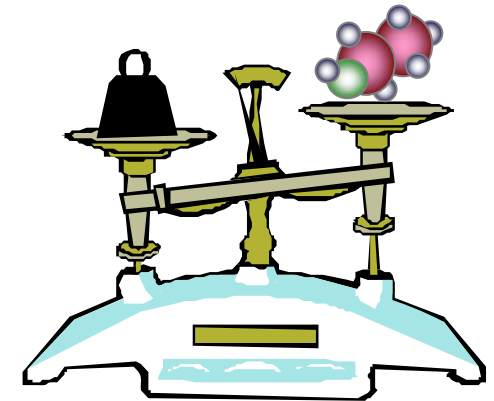
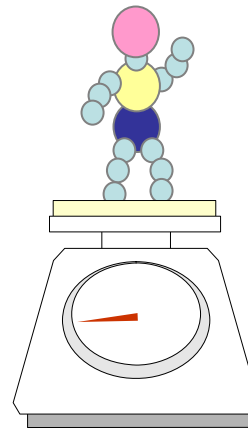
# MS/MS

**210.000.000 Euro**

**13.000 Euro speed fact**

**10.000 Euro yıllık bakım**

- MS/MS is one type of mass spectrometer that is used in newborn screening to detect and quantify numerous compounds in blood in a highly selective manner based on mass, structure, and charge without the need for chromatography.



# Yenidoğan taramasında MS/MS ile saptanabilen hastalıklar

---

## Açıl karnitin Profili:

MCAD, SCAD, V/LCAD, LCHAD, TFP, CPT I/II, CAT  
GA I & II, Malonic Acidemia, 3-MCC, SKAT, IBDH, 2MBDH  
deficiency, Propionic/Methylmalonic/Isovaleric Acidemia

## Amino Acid Profile:

PKU, MSUD, Tyrosinemias, Methioninemias

Citrullinemia, Argininosuccinic Aciduria, Hyperornithinemia  
(?), Hyperglycinemia (?) Argininemia (?)

# Organik asidemilerde açıl karnitinler:

## Acylcarnitine species

## Disorder to be considered

C3↑

PA, MMA, MCD

C4 ↑

IBCD, (SCAD, MAD)

C5 ↑

IVA, 2MBCD (MAD)

C5:1 ↑ (with C5-OH)

SKAT, 3-MCC

C5-OH ↑

3-MCC, HMGL, SKAT,  
MCD, 3-methyl-  
glutaconyl hydratase def

C3-DC ↑

MA

C5-DC ↑

GA-I

C6-DC ↑ (with C5-OH)

HMG

# YAO defektlerinde açıl karnitinler

## Açıl karnitinler

## Düşünülmesi gereken hastalıklar

C0 ↓ (with low AC)

Transporter defect

C4 ↑

SCAD-, MAD

C5 ↑ (with C4)

MAD

C6 ↑ (with C8; C10:1)

MCAD

C8 ↑

MCAD

C10 ↑ (with C8, C10:1)


MCAD

C10:1 ↑ (with C8)

MCAD

C14:1 ↑

VLCAD+

 60%  
asemptomatik

**MS/MS**



**MASS SCREENING**

**GC/MS**



**SELECTIVE SCREENING**  
**Confirmatory test**





@TANIM

@MATERYAL

@TARİHÇE

@DÜNYA NEREDE, BİZ NEREDEYİZ ?

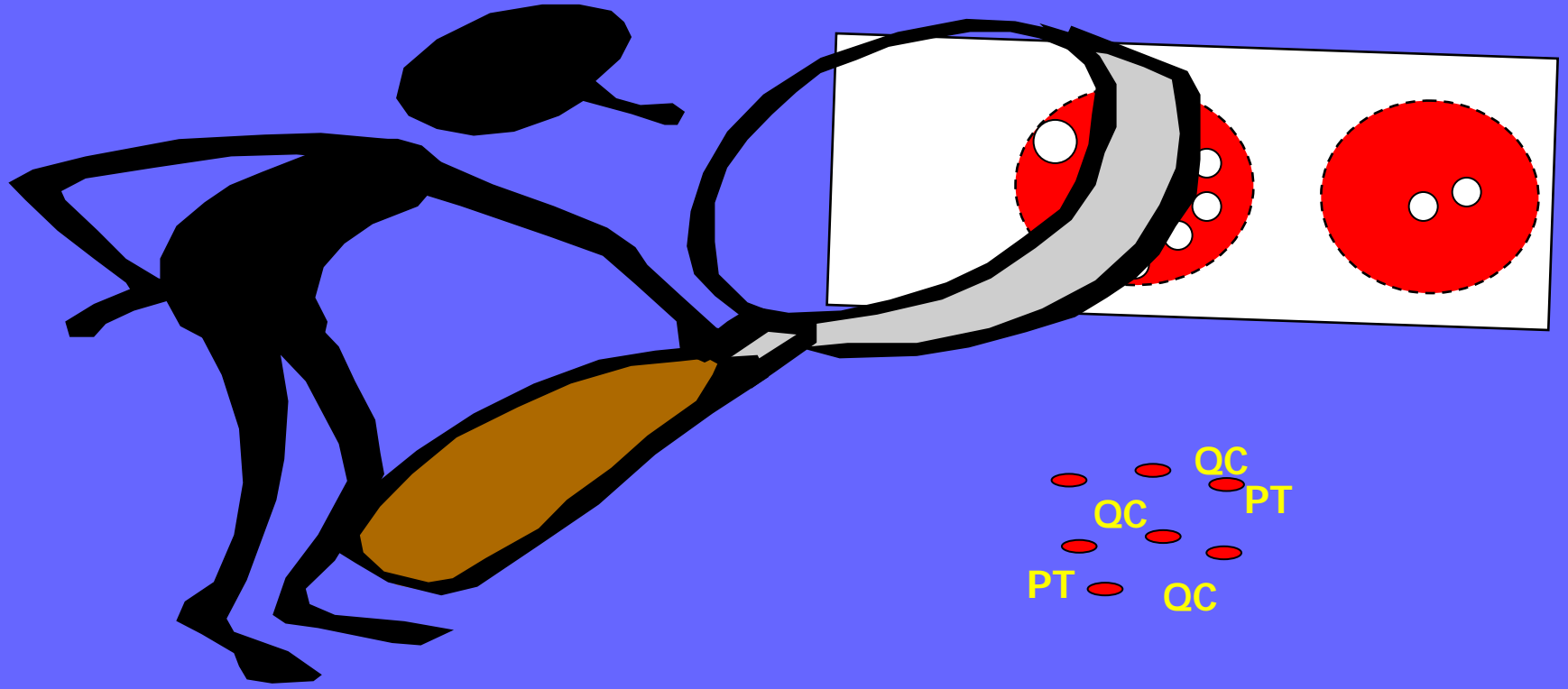
@TARAMANIN ÖNEMİ

@TARANMASI GEREKLİ HASTALIKLAR

@TEKNOLOJİ

@KALİTE KONTROL

@SONUÇ





## **KALİTE KONTROL PROGRAMLARI**

**CDC** (center for disease control)

**DGKC** Deutsche vereinte gessellschaft für kliniche chemie  
und laboratoriummediin

**TAIWAN** interlaboratory QA program for G6PD



## Newborn Screening Quality Assurance Program

### Quarterly Report

Year: 2003 Quarter: 2

Lab: 773

- [Quarterly Report Newsletter](#)
- [Specimen Certification](#)
- [Data Verification](#)
- [Overall Statistics](#)
- [Frequency Distributions of Clinical Assessments](#)

[Main Menu](#)[Back](#)[Help](#)

Analyte	Specimen 2311		Specimen 2312		Specimen 2313		Specimen 2314		Specimen 2315	
	Result	Code	Result	Code	Result	Code	Result	Code	Result	Code
T4										
TSH	8.8	1	6.9	1	61.2	2	63.9	2	7.6	1
Phe	4.7	2	1.9	1	0.6	1	8.5	2	0.6	1
Gal	8.1	1	31.4	2	4.0	1	4.5	1	5.2	1
17-OHP										
Leu	6.4	2	0.4	1	0.0	1	0.0	1	0.0	1
Met										

Analyte	Specimen 2391		Specimen 2392		Specimen 2393		Specimen 2394		Specimen 2395	
		Code		Code		Code		Code		Code
GALT										

Codes: 1 = Within normal limits 2 = Outside normal limits

Analyte	Specimen 2371		Specimen 2372		Specimen 2373		Specimen 2374		Specimen 2375	
		Code		Code		Code		Code		Code
Bio		1		2		1		1		1

Codes: 1 = Normal activity 2 = Deficiency 3 = Partial deficiency



## Newborn Screening Quality Assurance Program

### Overall Statistics

Year: 2003      Quarter: 2

Specimen 2311	T4	TSH	Phe	Gal	17-OHP	Leu	Met
N*	61	175	161	70	75	40	34
Outliers	6	12	4	0	4	0	2
Mean	9.2	13.5	4.2	6.9	19.0	7.7	3.5
UL (95%)	11.9	19.0	5.8	11.3	24.0	10.9	5.1
LL (95%)	6.5	8.0	2.5	2.5	14.0	4.6	1.9

Specimen 2312	T4	TSH	Phe	Gal	17-OHP	Leu	Met
N*	63	177	157	68	73	40	32
Outliers	4	10	6	2	3	0	3
Mean	8.5	10.0	1.4	24.6	3.0	2.5	0.6
UL (95%)	10.7	14.4	2.2	35.7	5.1	4.1	1.0
LL (95%)	6.2	5.7	0.7	13.5	0.8	0.9	0.2

Specimen 2313	T4	TSH	Phe	Gal	17-OHP	Leu	Met
N*	64	175	151	69	76	37	29
Outliers	3	12	7	1	2	3	5
Mean	4.8	70.8	0.7	2.7	10.0	1.4	0.2
UL (95%)	6.5	93.8	1.4	6.1	13.9	2.2	0.3
LL (95%)	3.1	47.9	0.0	0.0	6.1	0.7	0.1



## Newborn Screening Quality Assurance Program Specimen Certification Report

Year: 2003    Quarter: 2

### ENRICHMENT LEVELS\*

Analyte	Specimen 2311	Specimen 2312	Specimen 2313	Specimen 2314	Specimen 2315
T4 (ug/dL serum) **	10	10.3	4.7	4.8	14.5
TSH (uIU/mL serum)	10	9	65	70	9
Phe (mg/dL blood)	2.5	0	0	6	0
Gal (mg/dL blood)	5	21	0	0	0
17-OHP (ng/mL serum)	5	0	5	5	70
Leu (mg/dL blood)	5	0	0	0	0
Met (mg/dL blood)	3	0	0	0	0

\*Endogenous levels not included

\*\*CDC assayed values

### EXPECTED CLINICAL ASSESSMENTS

	Specimen 2311	Specimen 2312	Specimen 2313	Specimen 2314	Specimen 2315
Hypothyroidism	1	1	2	2	1
Phenylketonuria	NE	1	1	2	1
Galactosemia	NE	2	1	1	1



## Newborn Screening Quality Assurance Program Frequency Distribution of Participants' Clinical Assessments

Year: 2003 Quarter: 2

### Qualitative Data

	Specimen 2311		Specimen 2312		Specimen 2313		Specimen 2314		Specimen 2315	
	WNL	ONL	WNL	ONL	WNL	ONL	WNL	ONL	WNL	ONL
Hypothyroidism	180	7	184	3	0	187	0	187	186	1
Phenylketonuria	17	150	165	2	167	0	2	165	166	1
Galactosemia	59	12	1	70	71	0	71	0	71	0
Congenital Adrenal Hyperplasia	69	10	79	0	77	2	78	1	0	79
Maple Syrup Urine Disease	0	43	42	1	43	0	42	1	43	0
Homocystinuria	0	39	36	3	39	0	38	1	39	0
	2204		2202		2202		2204		2205	



Sample sent on : July 7, 2003

Report deadline : July 14, 2003

Total screening unit : 11

Total reports returned : 11

Sample No.	A1	A2	A3	B1	B2	C1	C2	C3	C4	C5	D1	G6PD activity*
1	+	0.3(+)	1.3(+)	0.1(+)	+	1.2(+)	+	+	0.6(+)	0.55(+)	0.2(+)	1.8(+)
2	-	1.8(+)	5.7(+)	2.1 (-)	-	1.8 (-)	-	-	1.7(+)	3.16 (-)	1.2 (-)	4.6
3	-	1.9(+)	6.4 (-)	1.7 (-)	-	1.9 (-)	-	-	1.9(+)	2.44 (-)	1.3 (-)	4.6
4	-	2.0(+)	6.3 (-)	1.6 (-)	-	2.5(-)	-	-	1.6(+)	3.07 (-)	1.4 (-)	4.6
5	+	0.4(+)	0.7(+)	0.1(+)	+	0.6(+)	+	+	0.5(+)	0.67 (+)	0.2(+)	1.8(+)
6	-	1.8(+)	5.4(+)	2.0 (-)	-	1.9 (-)	-	-	2.6(-)	3.37 (-)	1.4 (-)	4.6
7	-	1.8(+)	6.7 (-)	1.9 (-)	-	1.7 (-)	-	-	2.6(-)	3.18 (-)	1.3 (-)	4.6
8	+	0.4(+)	1.6(+)	0.1(+)	+	0.2(+)	+	+	0.7(+)	0.63(+)	0.2(+)	1.8(+)
9	-	1.9(+)	6.1(-)	1.7 (-)	-	1.7 (-)	-	-	1.7(+)	3.48 (-)	1.3 (-)	4.6
10	-	1.9(+)	6.1(-)	1.7(-)	-	2.4(-)	-	-	4.8(-)	2.13(-)	1.2(-)	4.6

\* G6PD : U/g Hb, determined at Clin. Biochem. Res. Lab, VGH-Taipei

\*\* The positive result assigned by the participants are indicated by red color in the table.

\*\* The positive result assigned by the participants are indicated by red color in the table.

Reagent Kit	Screening Units
Roche	A1, C2
PE (ND-1000)	A2, B1, C1, D1
Sigma Diagnostic 345B	A3
Gamma (G6PD-2000)	C4
R & D Diagnostics (OSMMR2000-D)	C5
Laboratory prepared	B2, C3

[Clinical Biochemistry Research Laboratory](#)  
[Dept. of Medical Research and Education](#)  
[Veterans General Hospital - Taipei](#)



Address : Peitou P.O. Box 2-207 Taipei, Taiwan, 11216

TEL : 886-2-2875-7401 ; 886-2-2875-7597 ; Fax : 886-2-2873-3517; 886-2-2873-5529

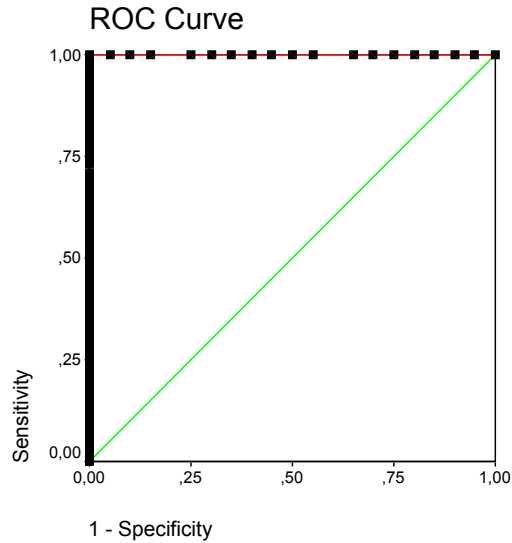
e-mail : [hsiao@mail.pmf.org.tw](mailto:hsiao@mail.pmf.org.tw) ; [joy@mail.pmf.org.tw](mailto:joy@mail.pmf.org.tw)

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updated : 31 July, 2003

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# G6PD cut - off



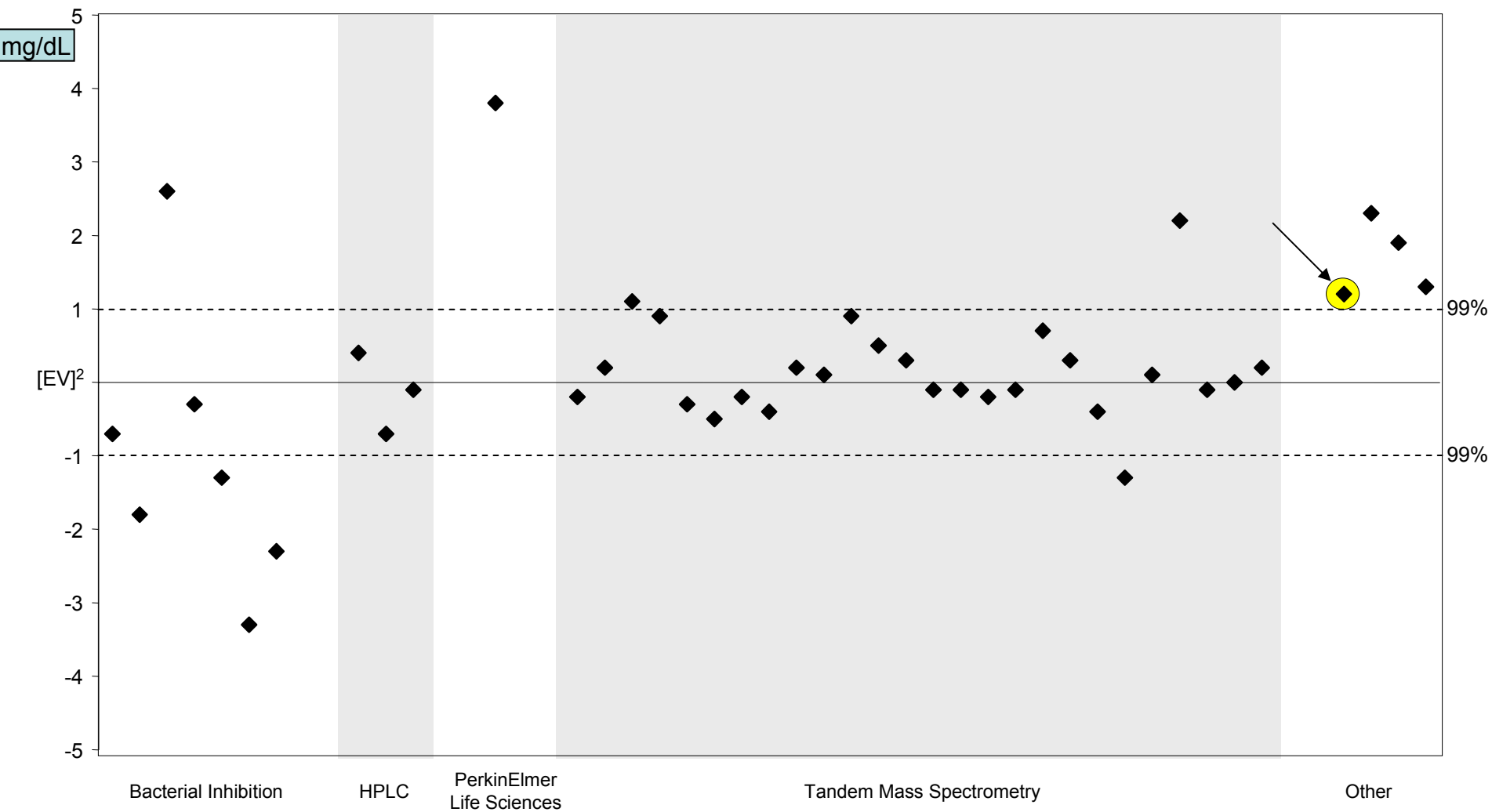
## Coordinates of the Curve

Test Result Variable(s): G6PD

Positive if Greater Than or Equal To <sup>a</sup>	Sensitivity	1 - Specificity
1,8550	1,000	,550
2,1150	1,000	,500
2,1650	1,000	,450
2,2100	1,000	,400
2,2900	1,000	,350
2,3850	1,000	,300
2,5900	1,000	,250
2,7800	1,000	,150
2,7950	1,000	,100
2,9000	1,000	,050
<b>3,1250</b>	<b>1,000</b>	<b>,000</b>
3,2550	,996	,000
3,2950	,991	,000
3,3750	,987	,000
3,4400	,982	,000
3,5900	,978	,000

- a. The smallest cutoff value is the minimum observed test value minus 1, and the largest cutoff value is the maximum observed test value plus 1. All the other cutoff values are the averages of two consecutive ordered observed test values.

**Bias Plot**  
**Reported Values<sup>1</sup> By Method**  
**Leucine Specimen 3313 — Quarter 3, 2003**  
**[Expected Value (EV) 3.3 mg/dL]<sup>2</sup>**



<sup>1</sup>Each observation is the mean of values reported by a laboratory.

<sup>2</sup>EV is the sum of the endogenous and enrichment levels.

**Deutsche Vereinte  
Gesellschaft für  
Klinische Chemie und  
Laboratoriumsmedizin  
e.V.**



**DGKL**

**Präsidium**

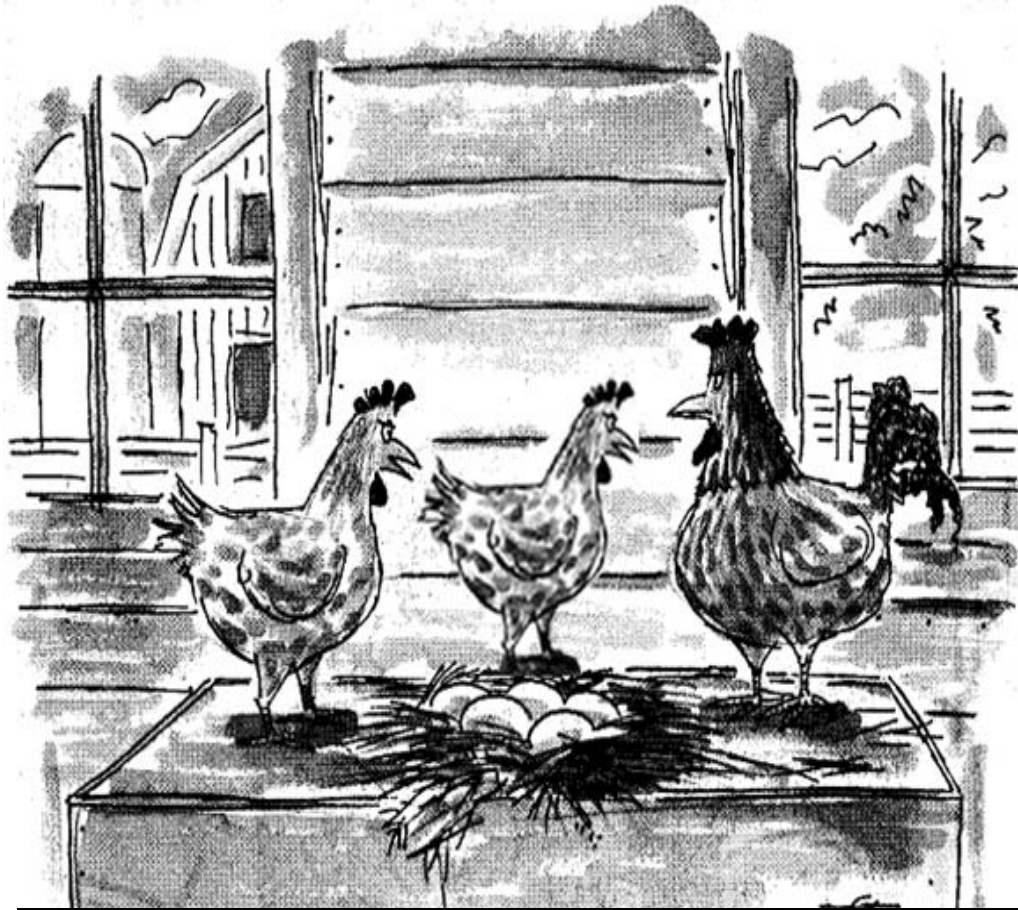
**Satzung**

**Jahrestagung 2003: Euregio Kongress für Klinische Chemie und Laboratoriumsmedizin, Aachen**

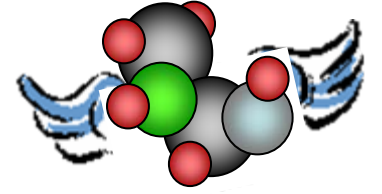
**Repetitorium "Klinische Chemie 2003"**

**Referenzinstitut für Bioanalytik**

# The Quality Alliance Working Together



**They're not just our eggs,  
they're your eggs too!**



# TEŞEKKÜRLER

