

Newborn Screening 2006

Get ready for some changes
In your state
And at your MTF

Agenda

- Review
 - NBS history, principles
 - Military issues
- Update
 - National Policy development
 - Military Policy development



History

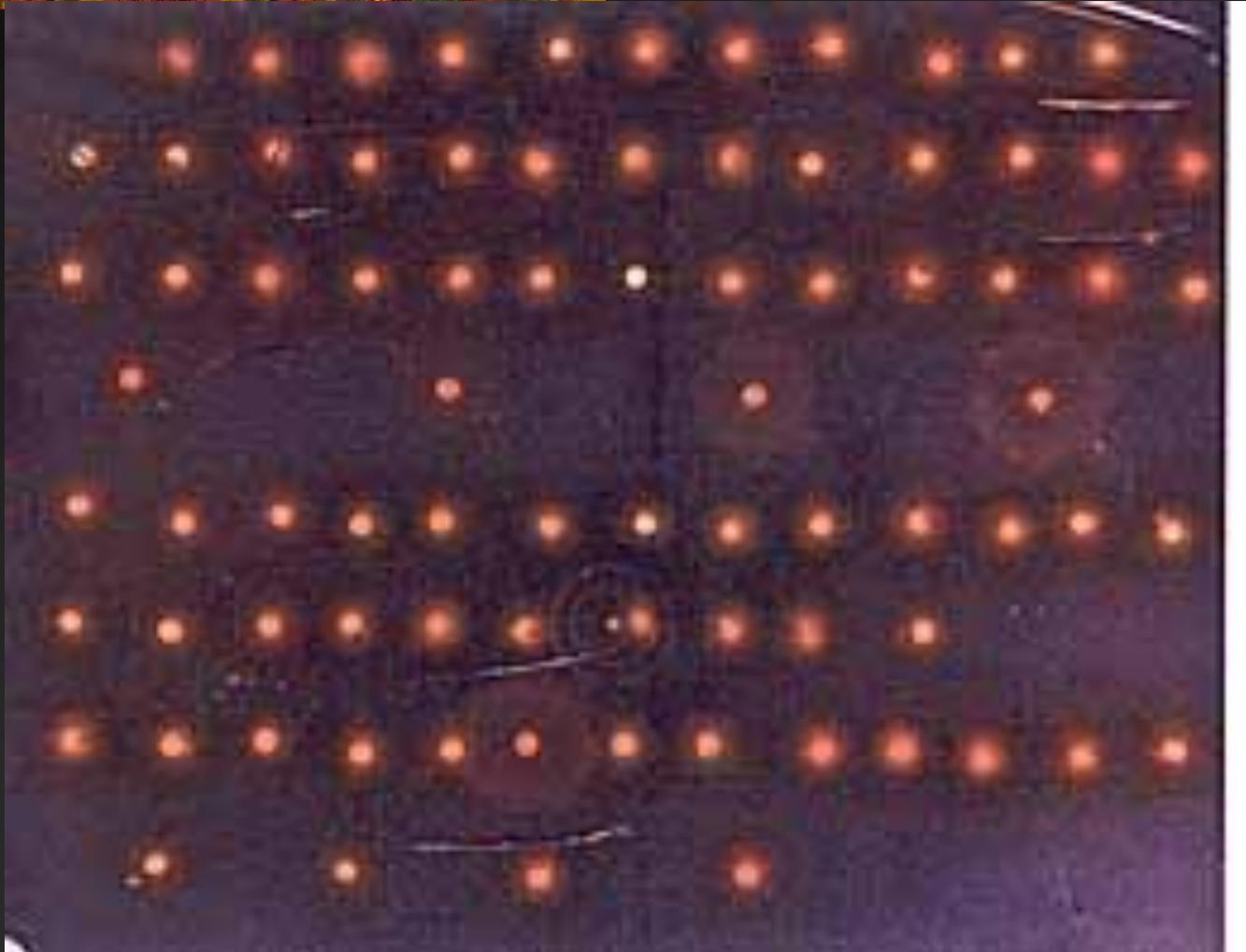
- 1960s PKU
- 1970s Congenital Hypothyroidism
- 1980s Sickle Cell Disease
- 1990s Galactosemia, CAH, others
- 2000s MS/MS
- 2010s ?????

Guthrie's Bacterial Inhibition Assay



Review

Guthrie's Bacterial Inhibition Assay





Newborn Screening is
not just a bunch of tests
but a *public health program*



TEXAS

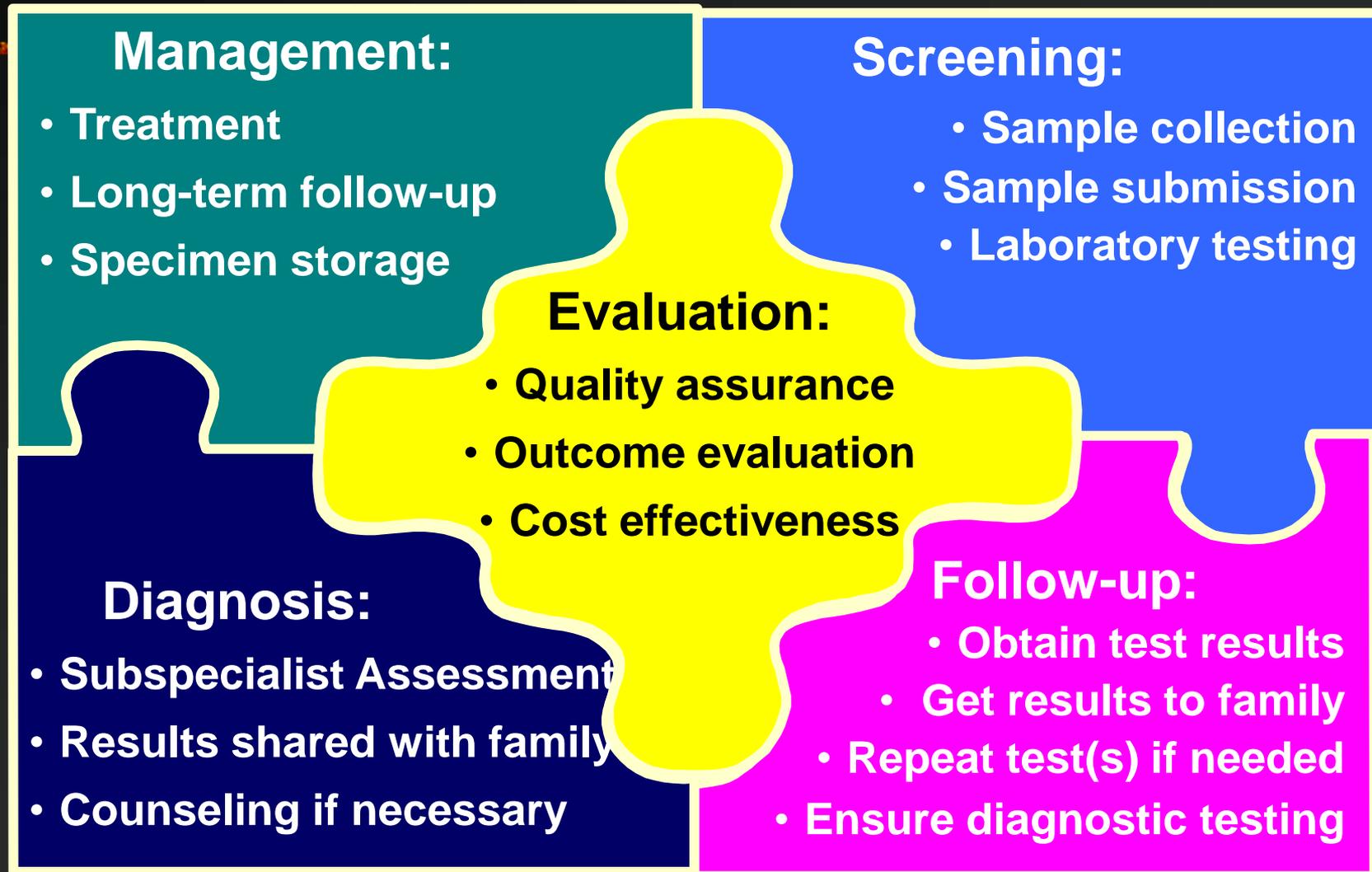
Department of State Health Services

Review

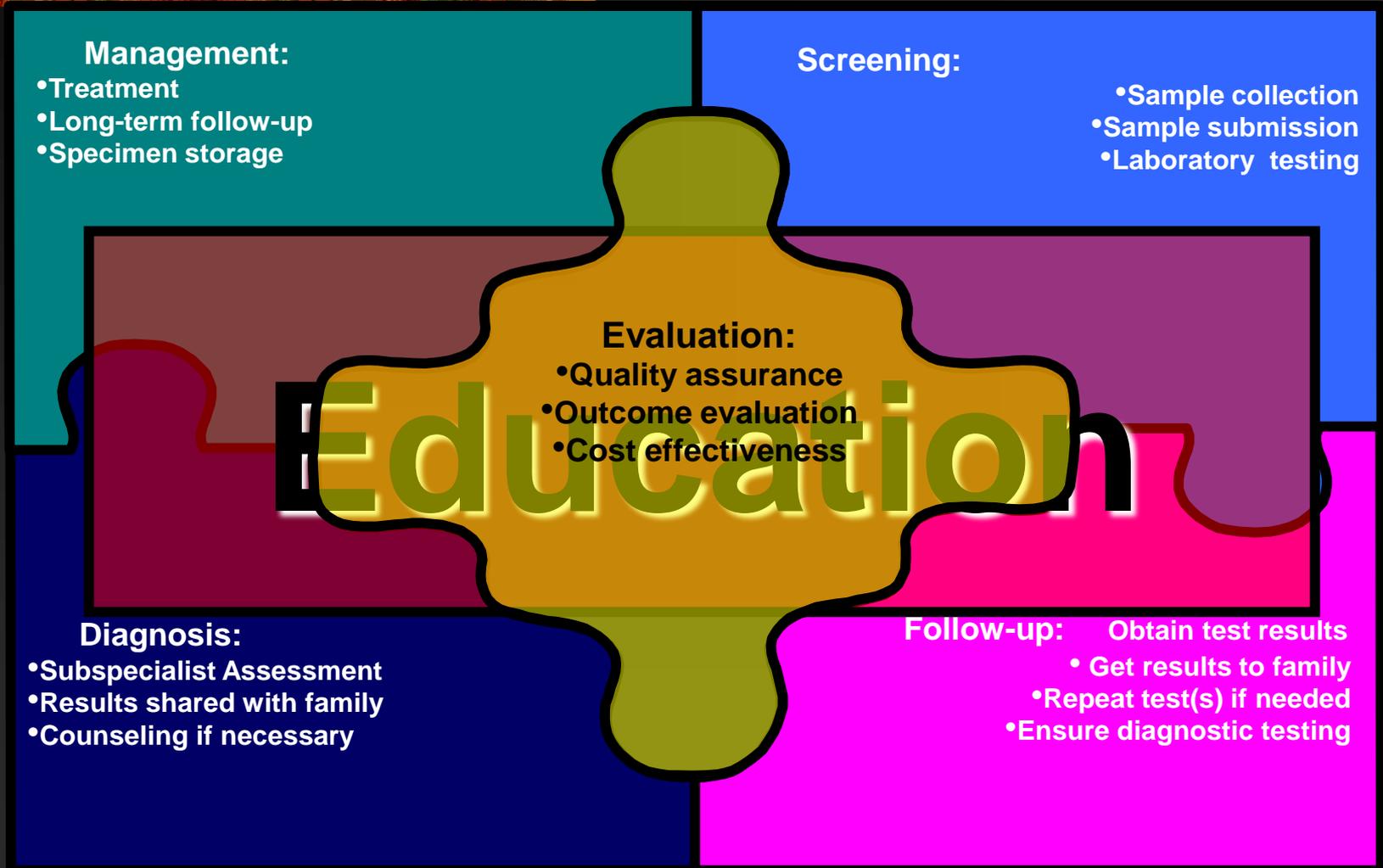
The Components of the Newborn Screening System must fit together to form a seamless system.



Components of the Newborn Screening System

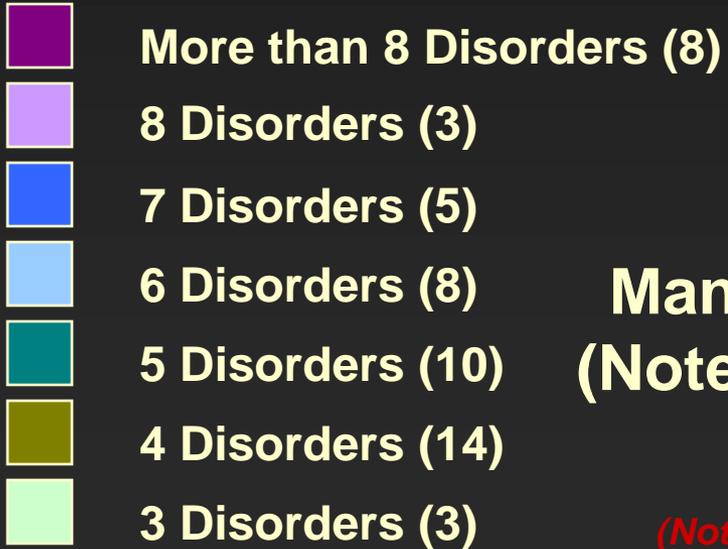
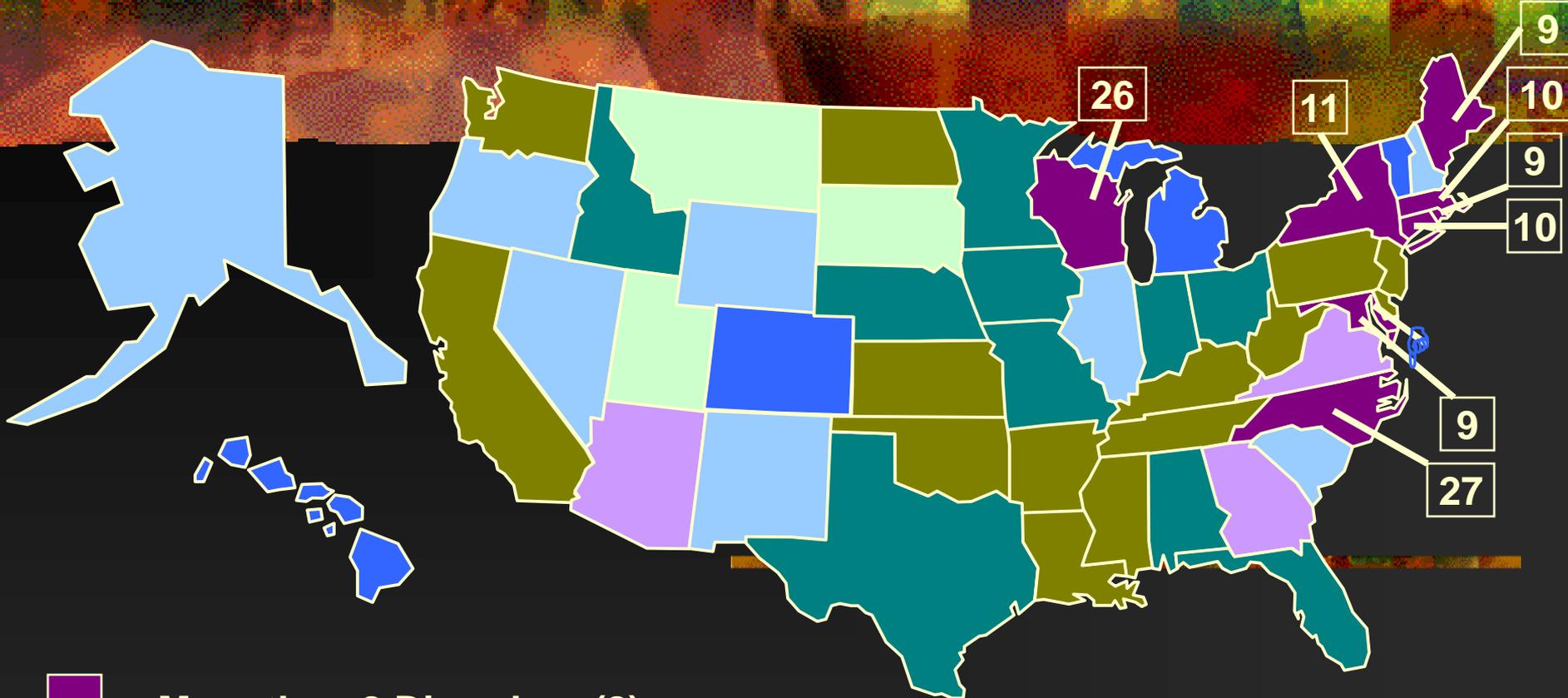


Components of the Newborn Screening System



Screening Criteria

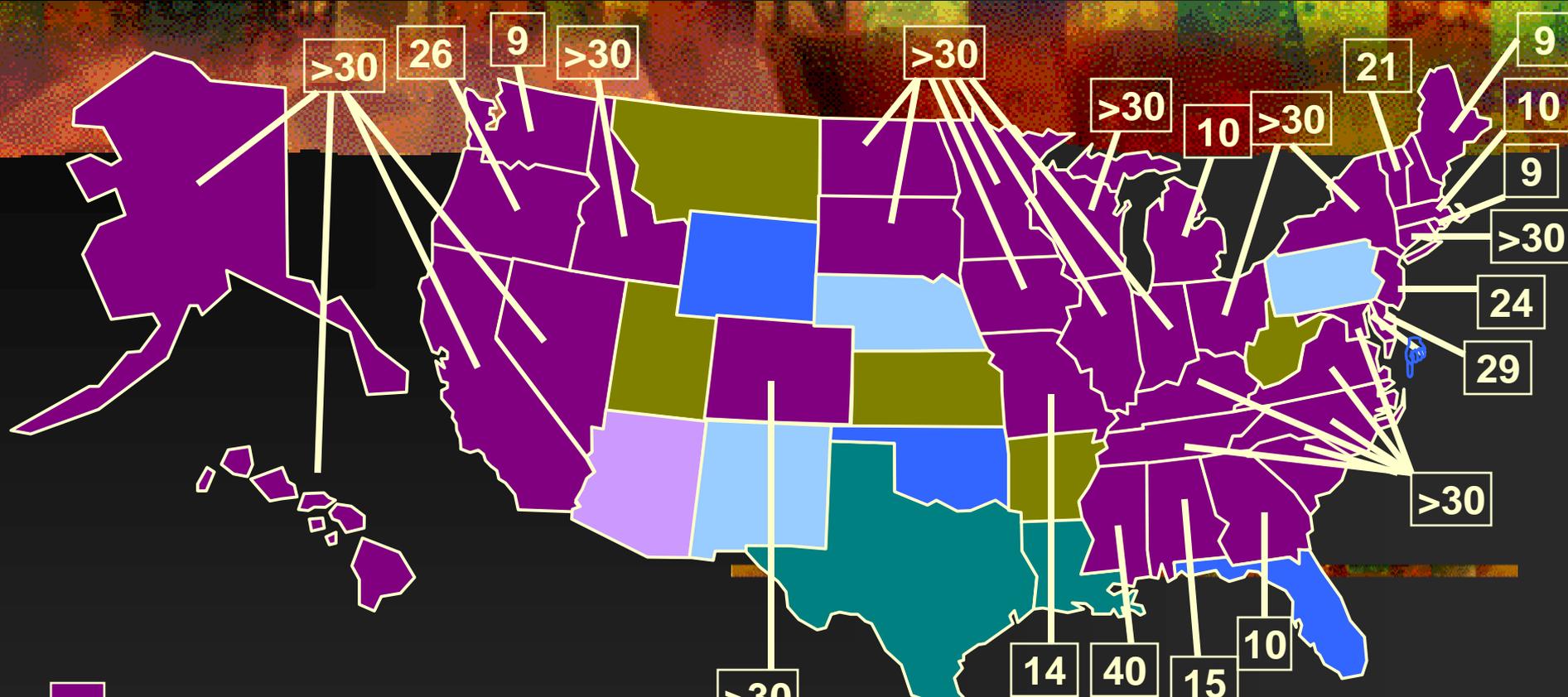
- Disease is serious and the natural history well-understood
- Treatment is effective, available, and accepted
- Test is rapid, cheap, specific, and sensitive
- Follow-up and counseling are available
- Benefits outweigh costs
- Case-finding is continuous



U.S. Newborn Screening

Mandated Disorders – October 2000
(Note: Other disorders may be offered but are not mandated)

(Note: Hemoglobinopathy screening counts as 1 screening disorder.)



- More than 8 Disorders (36)
- 8 Disorders (1)
- 7 Disorders (4)
- 6 Disorders (3)
- 5 Disorders (2)
- 4 Disorders (5)
- 3 Disorders (0)

U.S. Newborn Screening

Mandated Disorders – October 2005
(Note: Other disorders may be offered but are not mandated)

(Note: Hemoglobinopathy screening counts as 1 screening disorder.)

Military Issues

- Frequent military family PCS travel – true positives lost to follow-up
 - Widely dispersed population – many different screens, lack of uniformity; high-risk newborns may not receive appropriate tests
 - Clinics/labs often have inexperienced supervisors and short institutional memories
 - OCONUS arrangements foster delays in testing and intervention
-

What's new in newborn screening

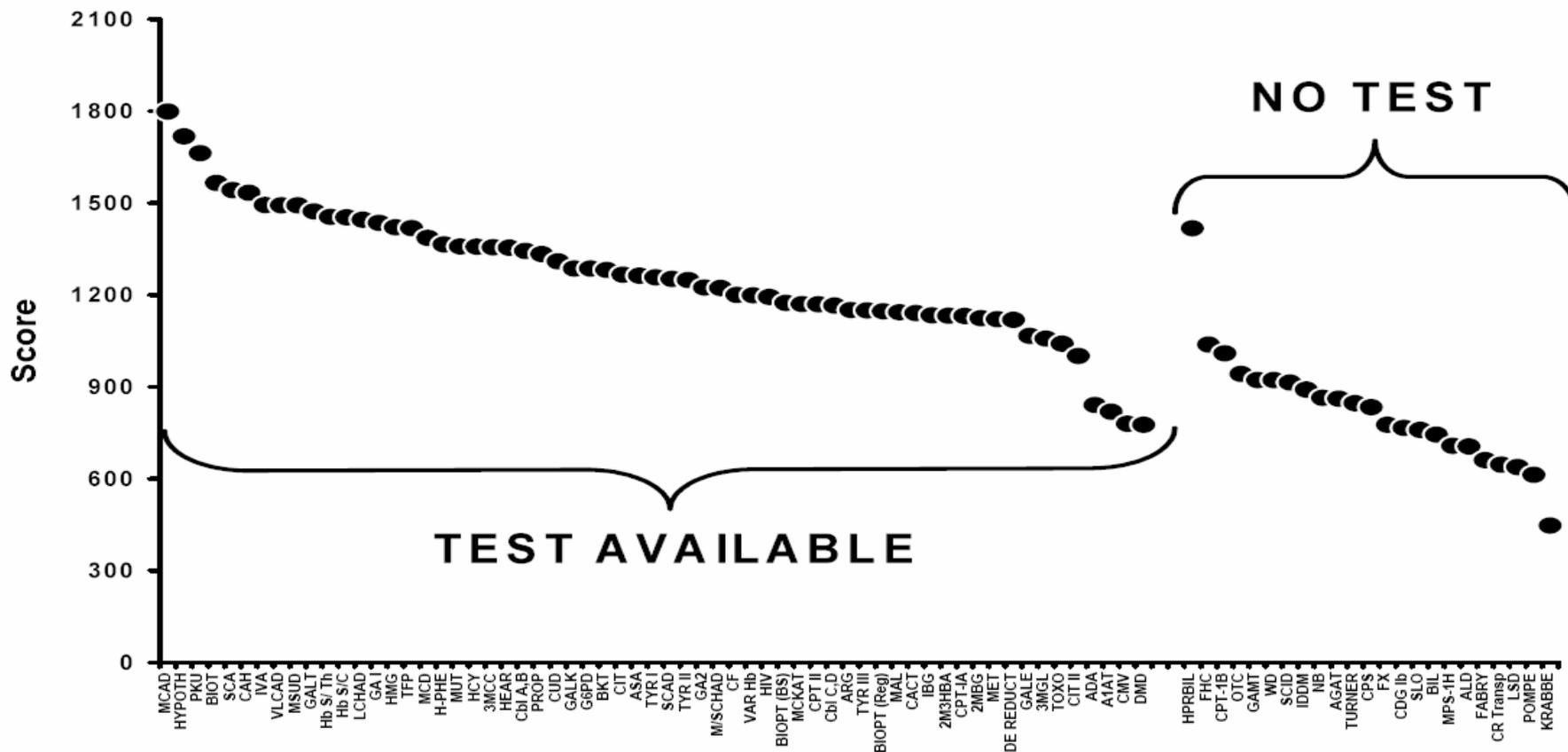
National Policy Development

- **Newborn Screening Task Force.** Serving the family from birth to the medical home: a report from the Newborn Screening Task Force convened in Washington DC, May 10-11, 1999. *Pediatrics*. 2000; 106(suppl):383-427.
- **HRSA/ACMG: Report on Uniform Newborn Screening Panel.** Federal Register March 2005. *Pediatrics*. 2006; 117:296-307. DOI: 10.1542/peds.2005-2633I.

A new paradigm for NBS

Figure 1: Scoring by Test Availability

Separates out those conditions that have an acceptable, validated, population-based screening test from those that do not.



Core Panel (29) and Secondary Targets (24)

Table 2: Newborn Screening Panel: Core Panel and Secondary Targets

MS/MS				
Acylcarnitines		Amino acids		
9 OA	5 FAO	6 AA	3 Hb Pathies	6 Others
CORE PANEL				
IVA GA I HMG MCD MUT* 3MCC* Cbl A,B* PROP BKT	MCAD VLCAD LCHAD TFP CUD	PKU MSUD HCY* CIT ASA TYR I*	Hb SS* Hb S/βTh* Hb S/C*	CH BIOT CAH* GALT HEAR CF
SECONDARY TARGETS				
6 OA	8 FAO	8 AA	1 Hb Pathies	2 Others
Cbl C,D* MAL IBG 2M3HBA 2MBG 3MGA	SCAD GA2 M/SCHAD MCKAT CPT II CACT CPT IA DE RED	HYPER-PHE TYR II BIOPT (BS) ARG TYR III BIOPT (REG) MET CIT II	Var Hb*	GALK* GALE

Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children

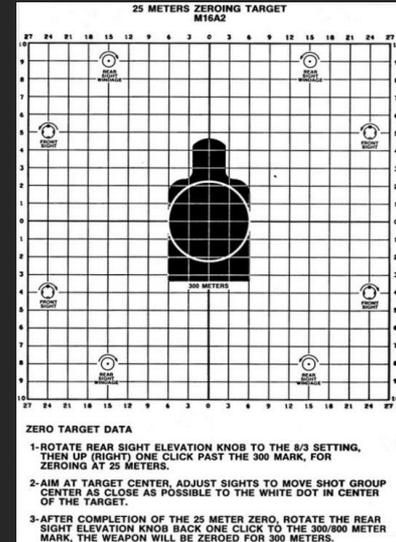
- *End Product: National Guidelines*
 - *29 Core and 24 Secondary Conditions*
 - *Universal Screening*
 - *Uniform Screening*
 - *Education of Physicians and Consumers*
 - *Treatment and Management Systems*
 - *Quality Assurance*

Military Health System Initiative

- Newborn Metabolic Screening Integrated Project Team → comprehensive, uniform NBS Program for all DoD infants (Chartered June 2005)
 - Reports to Tricare Management Activity (TMA)/Health Affairs (HA)
-

What we are aiming for ...

- Single laboratory
- Results within days, not weeks
- Secure, internet-accessible data
- Immediate access to “cookbook” response guidelines if a result is abnormal



Action Sheets



Newborn Screening ACT Sheet [Elevated C16 and/or C18:1 acylcarnitine] Carnitine Palmitoyltransferase 2 (CPT2) Deficiency

Differential Diagnosis: Carnitine palmitoyltransferase (CPT2) deficiency; Carnitine/acylcarnitine transferase (CACT) deficiency;

Condition Description: In both the transferase and CPT2 deficiencies, the acylcarnitines cannot be transported into the mitochondria for fatty acid oxidation. Thus, the need for generation of energy from fatty acids during fasting or increased demand (fever, stress) cannot be met. In addition, the neonatal form of CPT2 deficiency is associated with multiple congenital anomalies.

You Should Take the Following IMMEDIATE Actions:

- Contact family to inform them of the newborn screening result and ascertain clinical status (poor feeding, vomiting, lethargy).
- See and evaluate infant (hepatomegaly, cardiac insufficiency; history of sudden unexpected death in a sibling; dysmorphic facies).
- Consultation/referral to a metabolic specialist to determine appropriate follow-up.
- Emergency treatment if symptomatic and/or hypoglycemia present.
- Report findings to newborn screening program.

Confirmation of Diagnosis: Plasma acylcarnitine analysis reveals increased C16 and/or C18:1. Urine organic acid analysis reveals increased lactic acid and dicarboxylic acids.

Clinical Considerations: In the neonatal form of CPT2 deficiency, the neonate is profoundly ill with marked hypoglycemia, metabolic acidosis, cardiac arrhythmias, and facial dysmorphism. Only rarely will these infants survive. In the later-onset muscular form of CPT2 deficiency, the neonate is asymptomatic but muscle disease develops in the adolescent or adult years. Transferase deficiency presents similarly to the neonatal form of CPT2 deficiency.

Additional Information:

(Click on the name to take you to the website. Complete URLs are listed in the Appendix)

[New England Consortium of Metabolic Programs](#)

[Gene Tests](#)

[Genetics Home Reference](#)

[CPT2](#)

[CACT](#)

Referral (local, state, regional and national):

[Search for Metabolic Specialist](#)

[Testing](#)

[Clinical](#)

Disclaimer: These standards and guidelines are designed primarily as an educational resource for physicians to help them provide quality medical services. Adherence to these standards and guidelines does not necessarily ensure a successful medical outcome. These standards and guidelines should not be considered exclusive of all proper procedures and tests or exclusive of other procedures and tests that are reasonably directed to obtaining the same result. In determining the propriety of any specific procedure or test, the healthcare provider should apply his or her own professional judgment to the specific clinical circumstances presented by the individual patient or specimen. It may be prudent, however, to document in the patient's record the rationale for any significant deviation from these standards and guidelines.

*You Should Take the Following **IMMEDIATE** Actions:*

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What we are aiming for .



- Integrated education and training for providers, laboratory personnel
- Responsive case management support team
- Registry of newborns to track quality and facilitate follow-up

Good Resource

- National Newborn Screening and Genetics Resource Center

<http://genes-r-us.uthscsa.edu/>



Questions and Comments



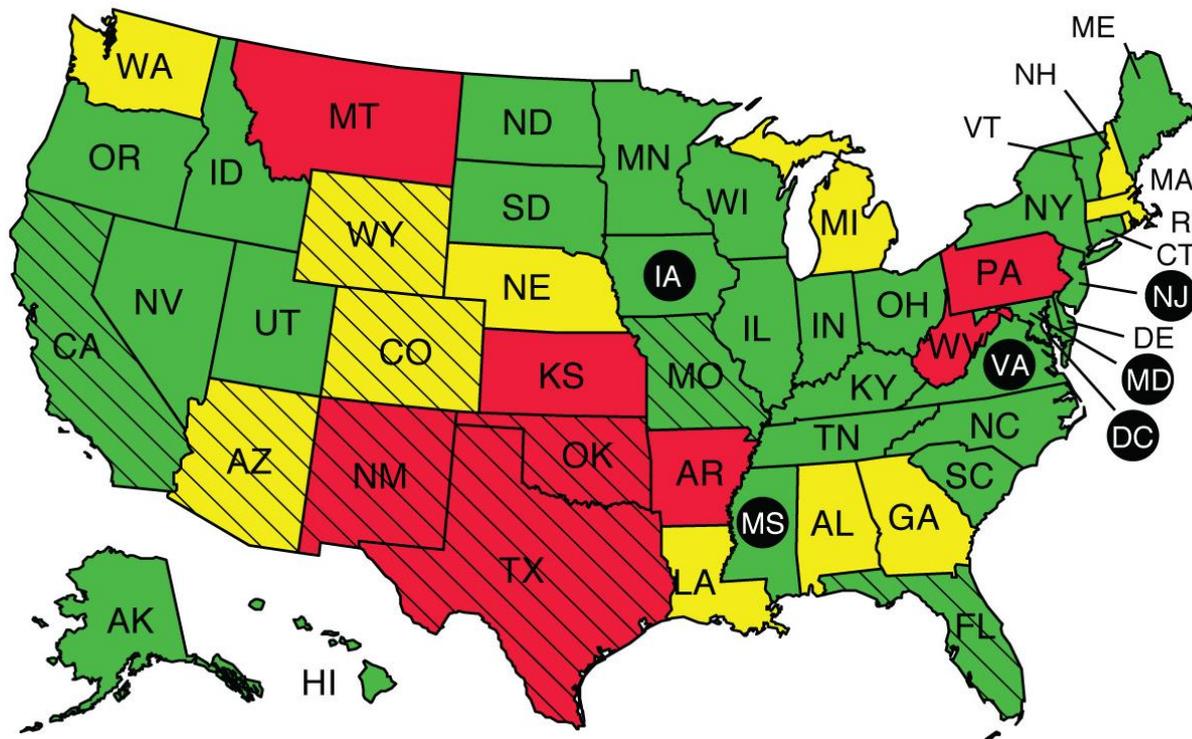
Thank you!

Players

- Public Health Policymakers
 - HRSA, SACHDGDNC → Hon. Michael Leavitt
- Professional Organizations
 - AAP, ACMG
- March of Dimes
- Genetic Alliance
- Government Accounting Office
- Politicians
 - Senator Christopher Dodd, D Conn
 - Senator Mike DeWine, R Ohio



Newborn Screening Tests by U.S. States, 2006



- More than 20 core conditions (31)
- 10–20 core conditions (12)
- Fewer than 10 core conditions (8)
- Hatch marks indicate testing for some conditions required but not yet implemented.

Screening 29 Core Conditions

District of Columbia
Iowa
Maryland
Mississippi
New Jersey
Virginia

Source: March of Dimes. Data reported from NNSGRC as of June 1, 2006.
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