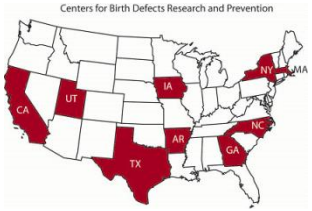

26 Feb 2009 - Washington DC

CENTERS FOR BIRTH DEFECTS RESEARCH & PREVENTION

Monitoring and measuring what counts

Developing a longitudinal, sustainable program to monitor occurrence and outcomes of inherited metabolic conditions

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utah birth defect network

Study funding from
the Centers for Disease Control and Prevention
HRSA (pilot study)

THE UNIVERSITY OF UTAH

Pilot project using the surveillance infrastructure of birth defect (BD) programs

- **Sustainability:** many BD programs have been active for years in the US, with state and federal funding
- **Quality:** High quality BD programs include clinical case review, ongoing evaluation, and active case ascertainment
- **Alignment of targets and resources:** BD programs target babies and children, visit the same hospitals and clinics, have established relations with many providers
- **Effective use of funds:** no need to build a new system, metabolic disease surveillance adds on an existing BD program.

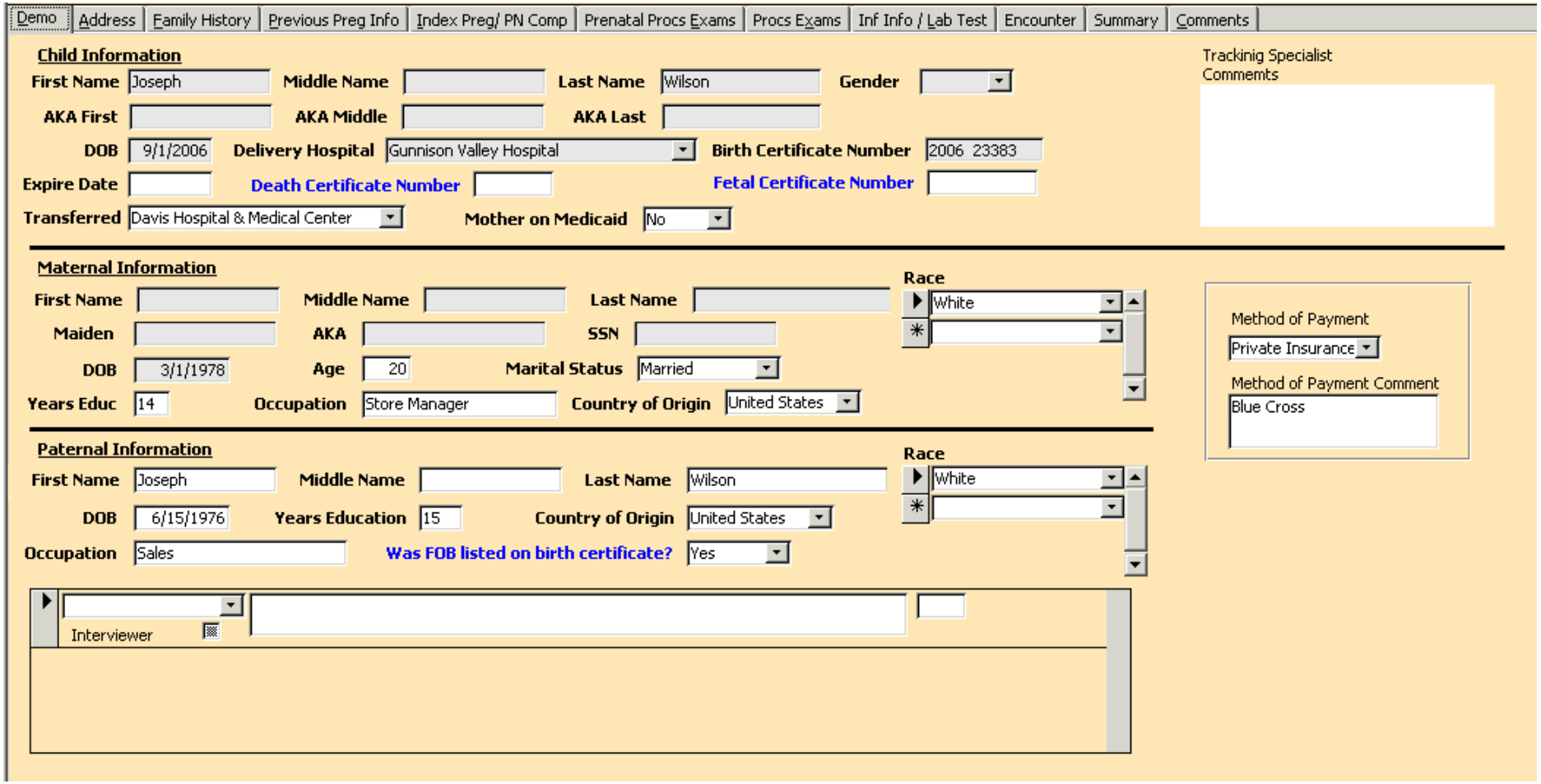
Data needs

- ***high-quality data* on the population-based cohort of children identified by screening**
  - High-quality data are essential, because the required information can be complex. For example, in many cases it will be important to characterize genotype and biochemical phenotype, both as descriptors of occurrence and as stratification variables for outcome assessment. Multiple sources of ascertainment and clinical review will also be needed.
- ***outcome data,* beyond the neonatal period**
  - to assess morbidity (hospitalizations, emergency department visits, disability) and mortality, to better characterize the clinical significance of these conditions and the impact of screening.
- ***utilization of services*.**
  - The goal of public health programs is effective action. Identification needs to be accompanied by sustained, cost-effective interventions. These can be evaluated, for example, by monitoring referral patterns and utilization of health care services, including those such as Medicaid that are state- or federally-funded.
- ***timely dissemination*.**
  - Information for action requires timely and ongoing reports, targeted to specific stakeholders such as policy makers, the public, health care providers, and public health professionals.
- ***effective data sharing***
  - Each metabolic condition is individually rare, so data from multiple states will need to be collected and analyzed. This process will require data standardization, sharing agreements, and programs experienced in preparing and sharing data electronically.

Long-Term follow up in Utah

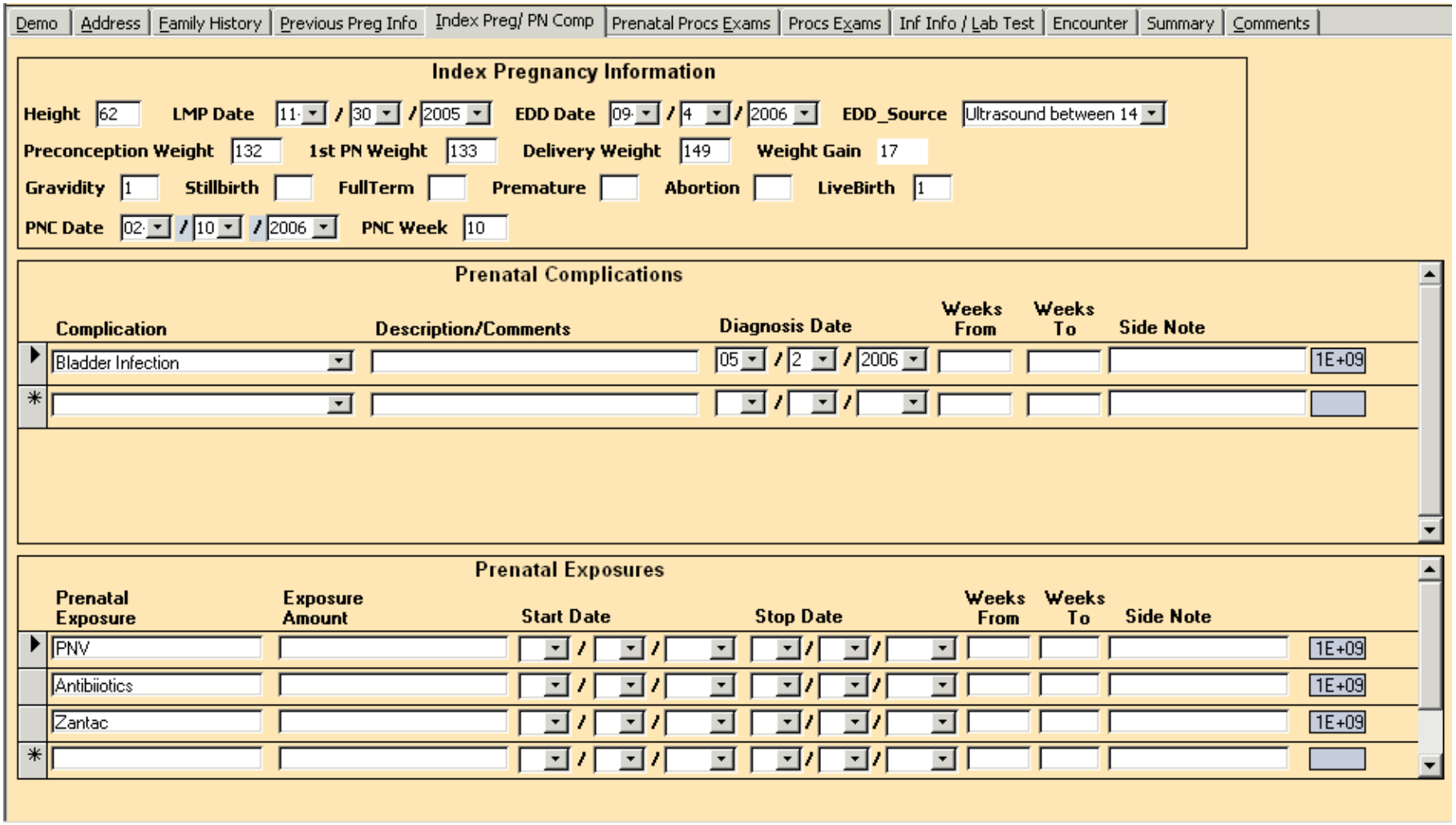
- **Pilot study to define parameters to be collected in long-term follow up (Mountain States Genetics Network/HRSA)**
- **Design of templates to be used in the clinical setting to collect disease-relevant information (Mountain States Genetics Network/HRSA)**
- **Incorporation of LTFU into birth defects registry (CDC/Lorenzo Botto MD): September 2008**
- **Collected data on all diseases since NB screen expansion (2006) by an abstractor using all available data (including those in other hospitals/locations).**

Demographics: identify child, family, contact information, payor at birth



Note: fictitious identifying information

Pregnancy: includes prenatal complications (e.g., HELLP in LCHAD)



Demo | Address | Family History | Previous Preg Info | Index Preg/ PN Comp | Prenatal Procs Exams | Procs Exams | Inf Info / Lab Test | Encounter | Summary | Comments

Index Pregnancy Information

Height 62 LMP Date 11 / 30 / 2005 EDD Date 09 / 4 / 2006 EDD_Source Ultrasound between 14

Preconception Weight 132 1st PN Weight 133 Delivery Weight 149 Weight Gain 17

Gravidity 1 Stillbirth FullTerm Premature Abortion LiveBirth 1

PNC Date 02 / 10 / 2006 PNC Week 10

Prenatal Complications

Complication	Description/Comments	Diagnosis Date	Weeks From	Weeks To	Side Note	
Bladder Infection		05 / 2 / 2006				1E+09
		/ /				

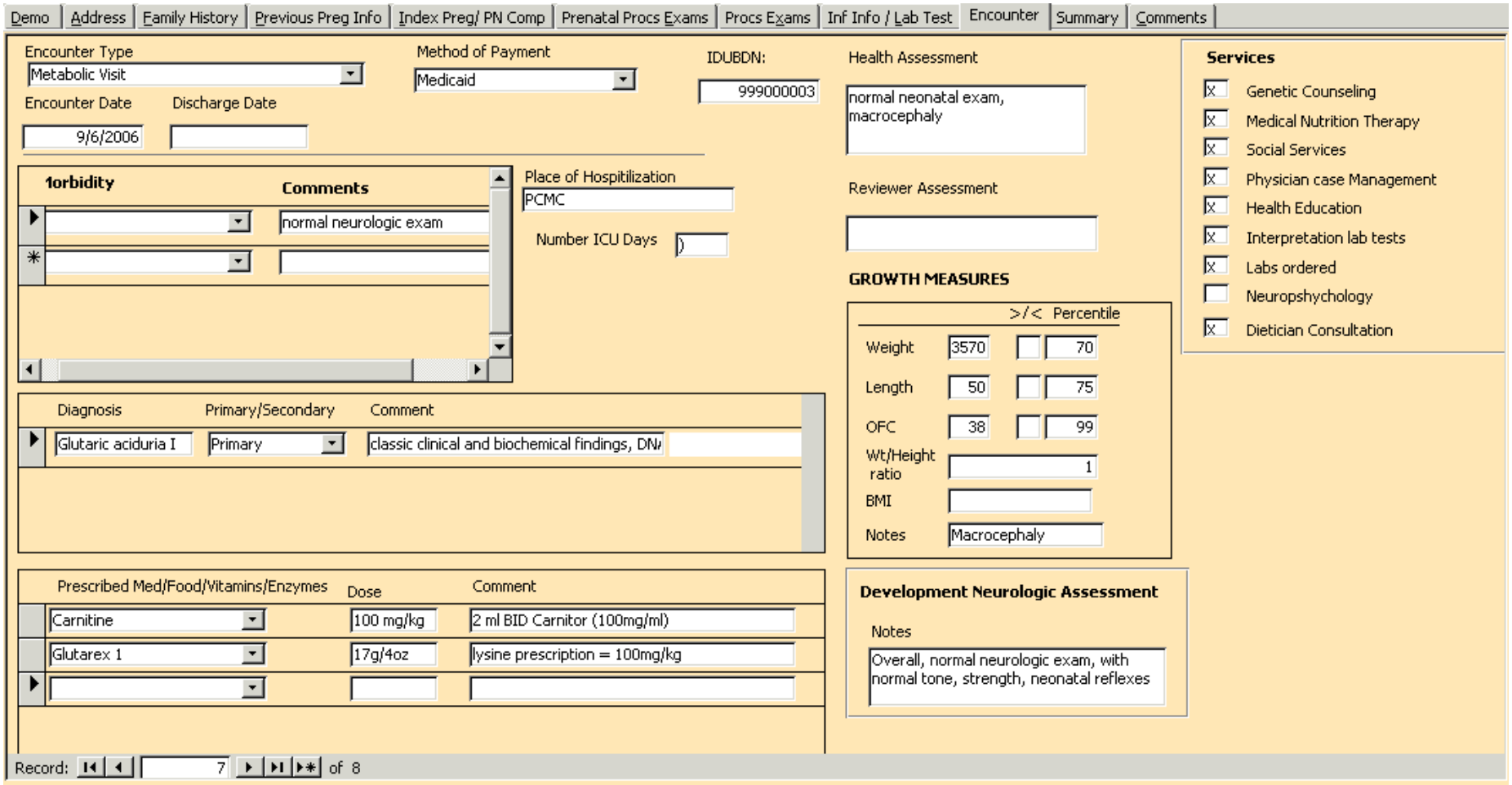
Prenatal Exposures

Prenatal Exposure	Exposure Amount	Start Date	Stop Date	Weeks From	Weeks To	Side Note	
PNV		/ /	/ /				1E+09
Antibiiotics		/ /	/ /				1E+09
Zantac		/ /	/ /				1E+09
		/ /	/ /				

Confirmation of diagnosis

- **Metabolic results**
- **Enzyme assay**
- **Molecular studies**

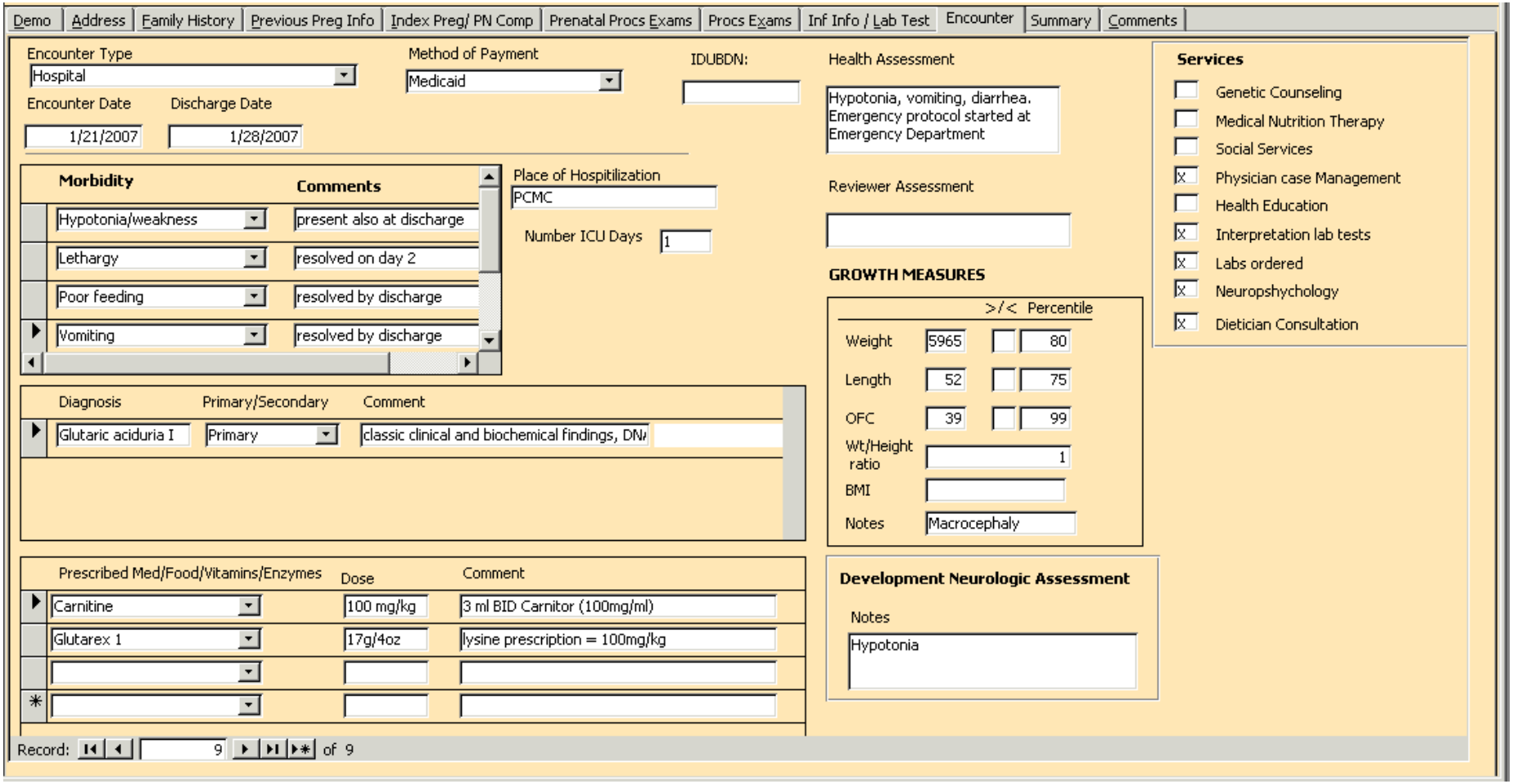
Encounters: information on clinical findings, morbidity, use of services



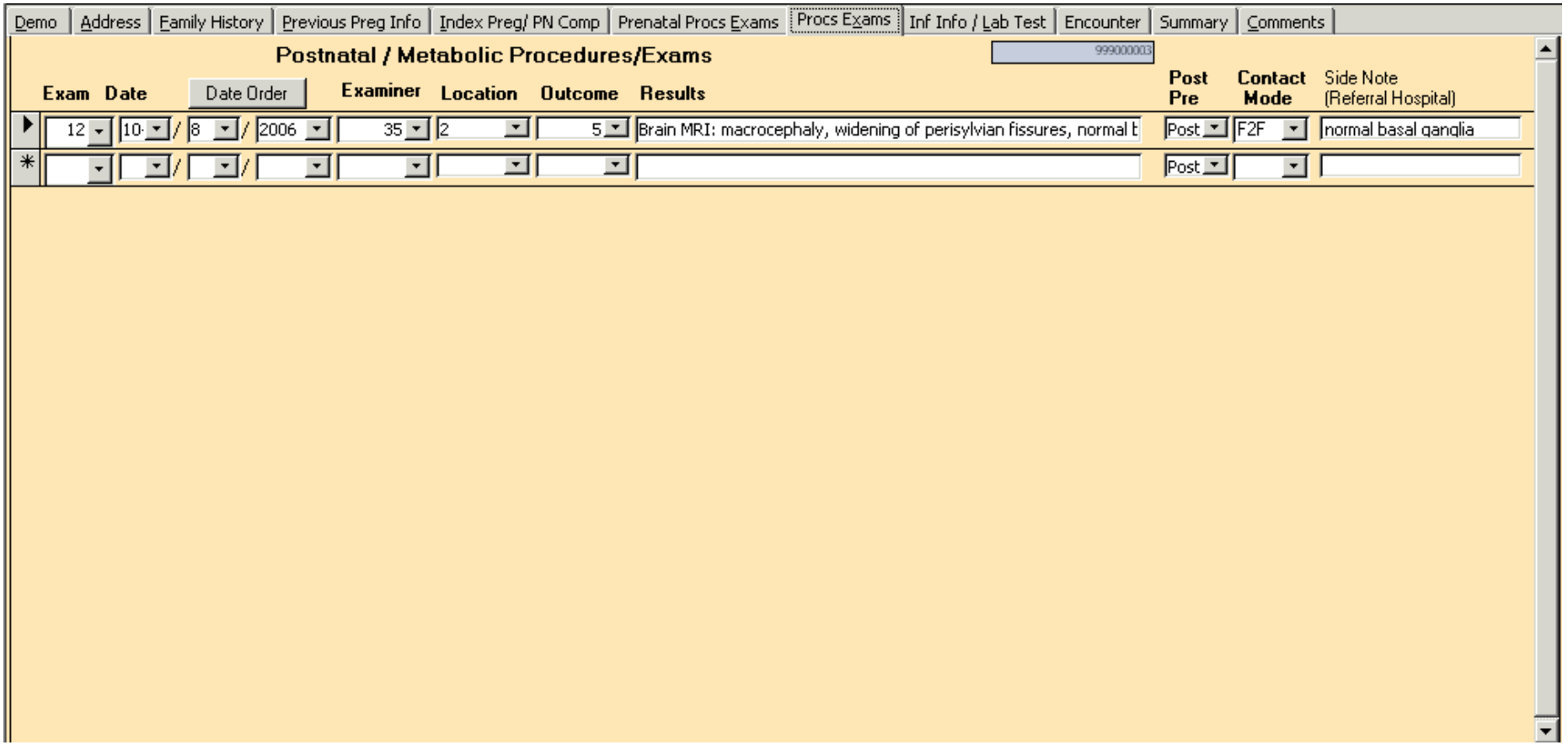
Common and disease-specific elements

- **Medical treatment**
- **Metabolic results reflecting adequacy of treatment and compliance**
- **Functional outcome: growth, development, IQ, occupation**

Encounters (2): hospitalizations, metabolic visits, consultations



Procedures: evaluating management and use of services (GA-1 = MRI, G-tube, etc)

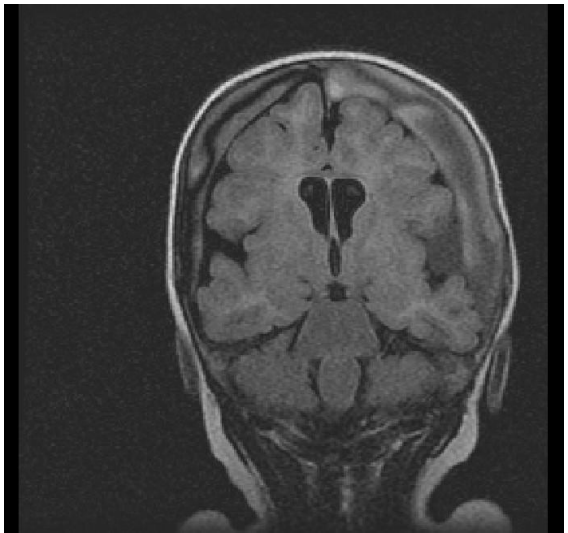


GLUTARIC ACIDEMIA TYPE 1 (GA-1)

Outcome?

Patients with GA-1 can appear normal at birth. Many have or develop macrocephaly, can be mildly hypotonic. They can develop acute dystonia with the first episode of fever/vomiting/fasting. This is irreversible. Patients without decompensation can have normal mentality. About 90% of patients will become spastic and wheel-chair bound without treatment.

Patients identified by newborn screening can develop dystonia even without decompensation.

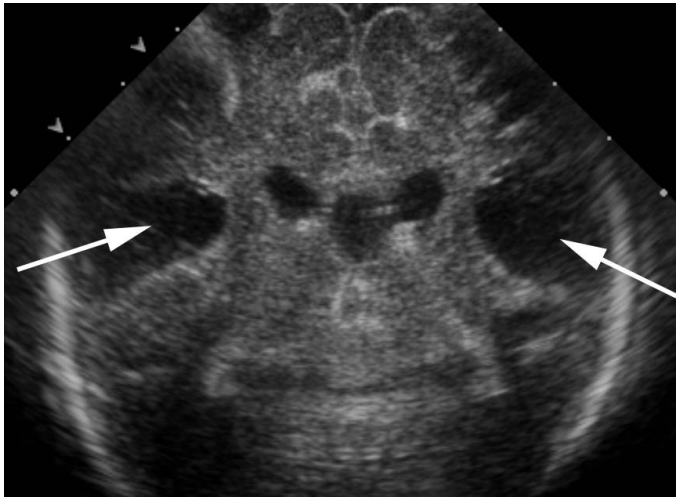


GA-1 IN UTAH

12 Patients 5 Males 7 Females
Diagnosis confirmed in all by DNA testing/enzyme assay.
All with different mutations (Genetic heterogeneity)
4 NB Screen / 7 Symptomatic / 1 affected sibling

Among other data, we are entering data on brain imaging in our patients to determine whether brain atrophy and caudatum or putamen degeneration are present.

Our hypothesis is that patients who develop dystonia without decompensation have damage of caudatum and putamen at birth or shortly after.



CONCLUSIONS

Long-term follow-up is essential for understanding the natural course of rare diseases and the effects of screening and treatment.

Different models can be used for this activity. Incorporation into birth defect surveillance programs, where present, can build on an ongoing infrastructure with public health and research capabilities.

Data from multiple centers need to be combined to obtain statistically significant results. Longitudinal data (multiple years) are needed to truly define outcome.

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