Research Implications of Defect Classification and Coding Practices

2°ASD as an Illustration

12th Annual
National Birth Defects Prevention Network Meeting
February 24, 2009
Marcia Feldkamp, PhD

utah birth defect network

What do your data look like?

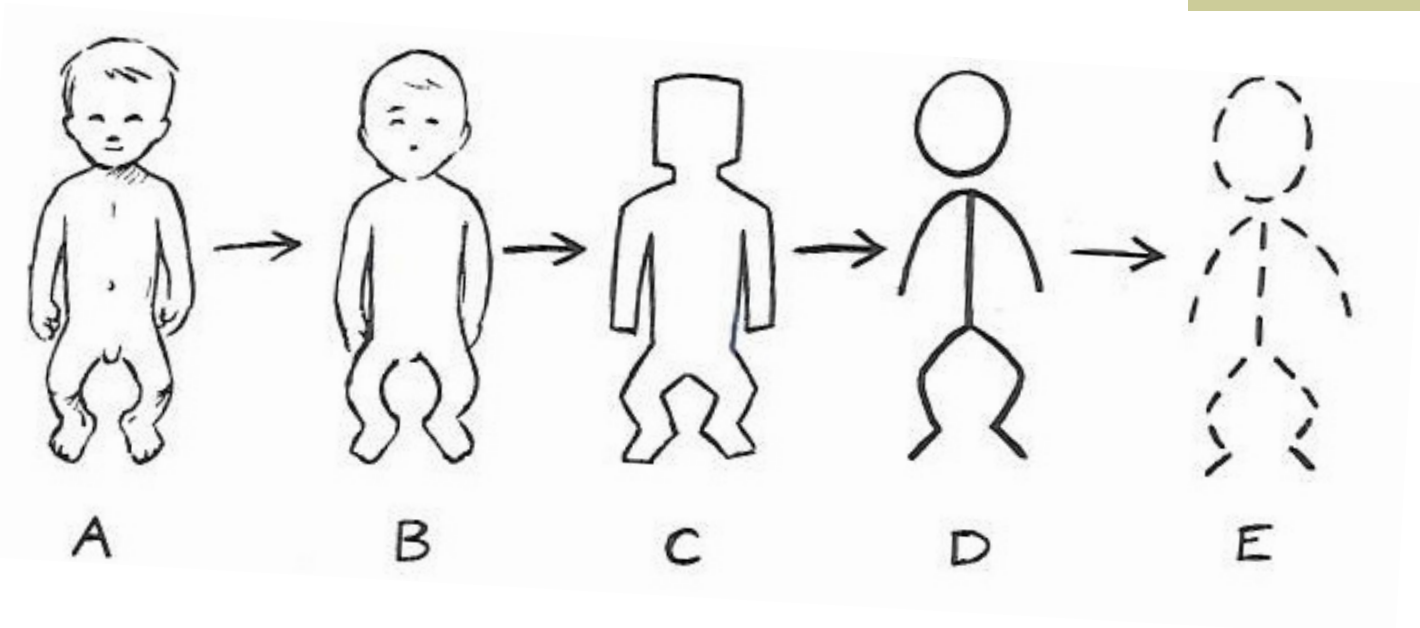


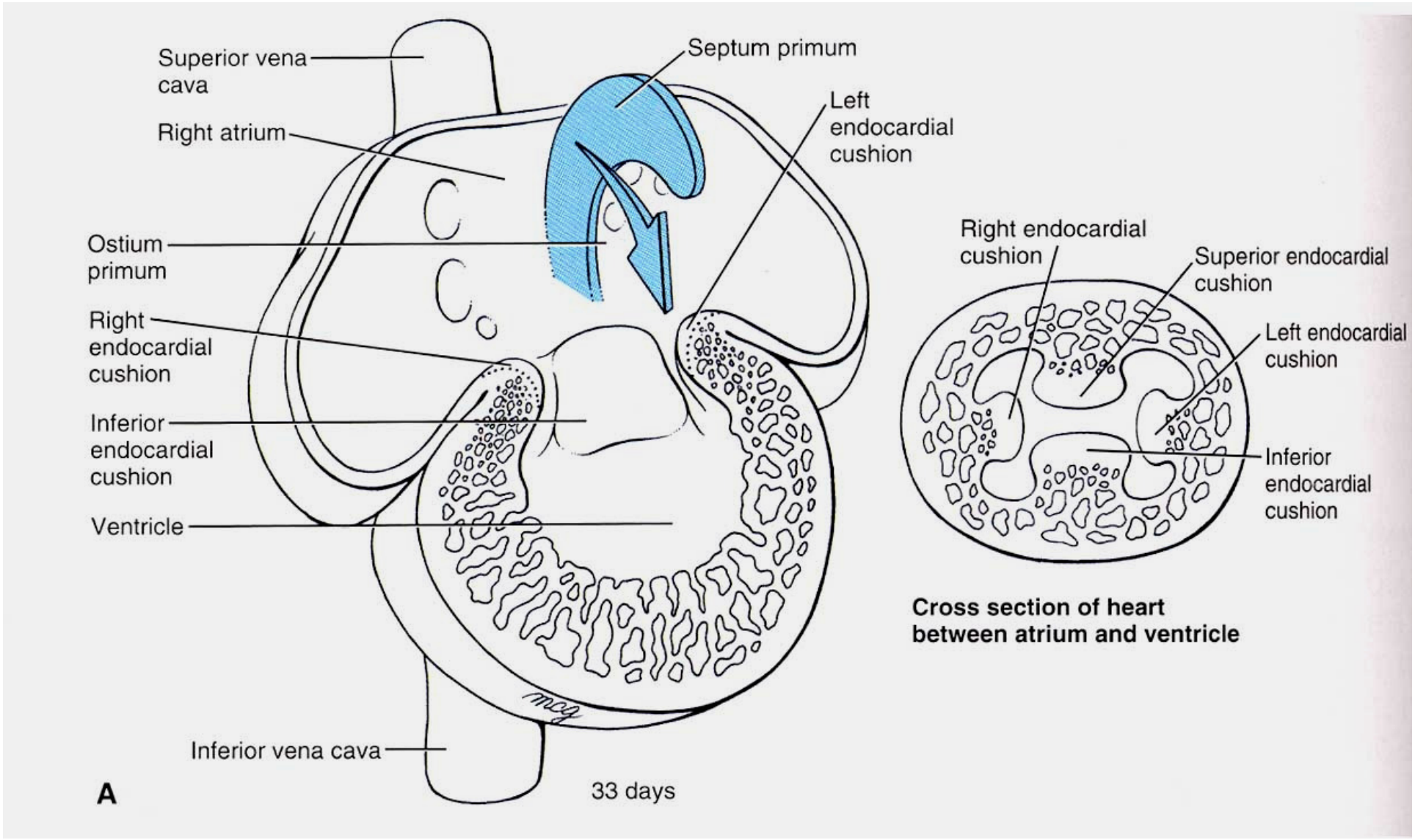
Fig32. Diagram illustrating the distortion of the information in a reporting system, from the infant to the coded data.

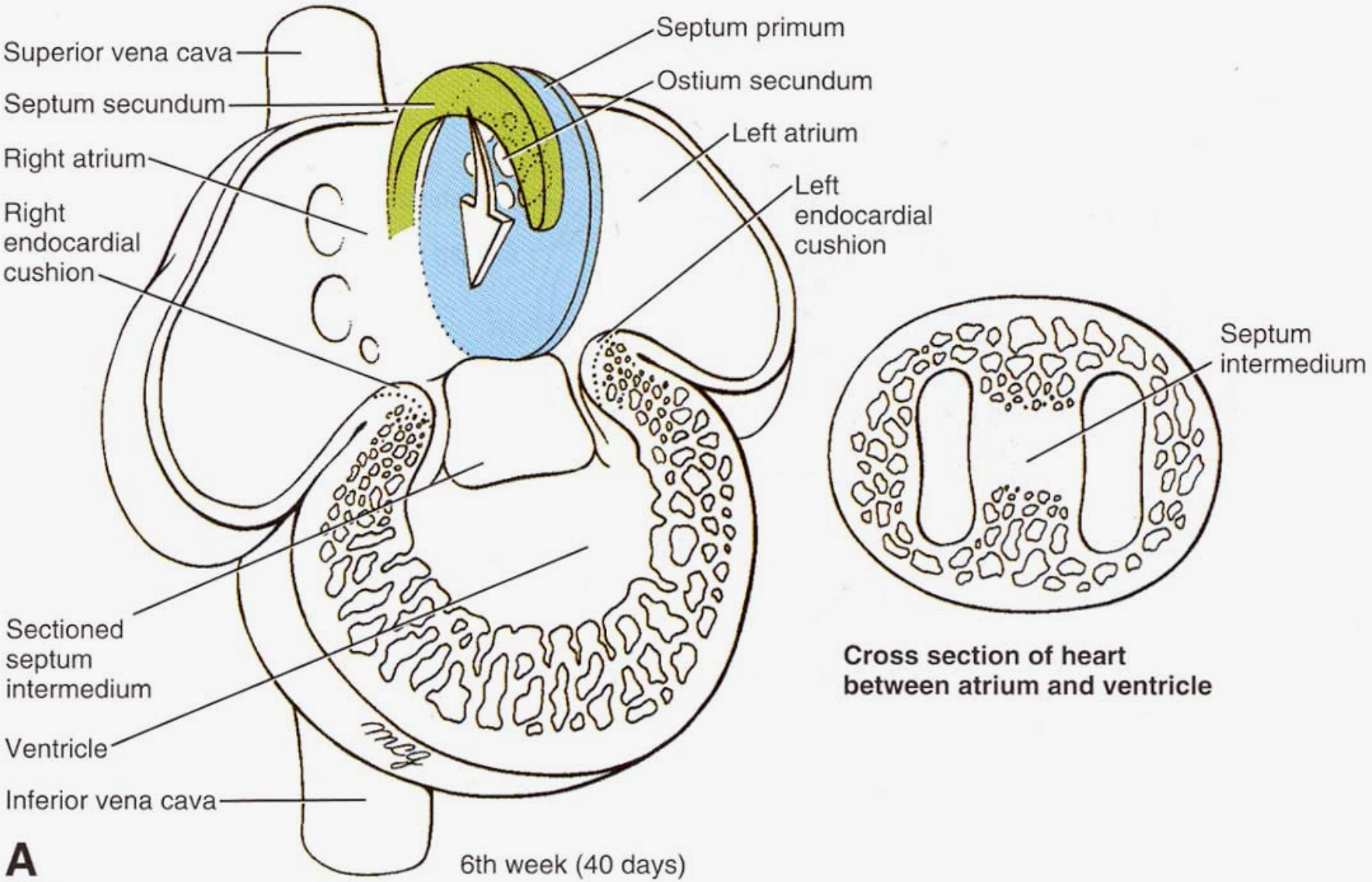
(A) shows the actual infant
(B) is the doctor's picture of it and what is written down in the medical records
(C) is the content of the report form to the surveillance registry
(D) is the interpretation of that form in the registry
(E) is the coded data which is stored in a computer

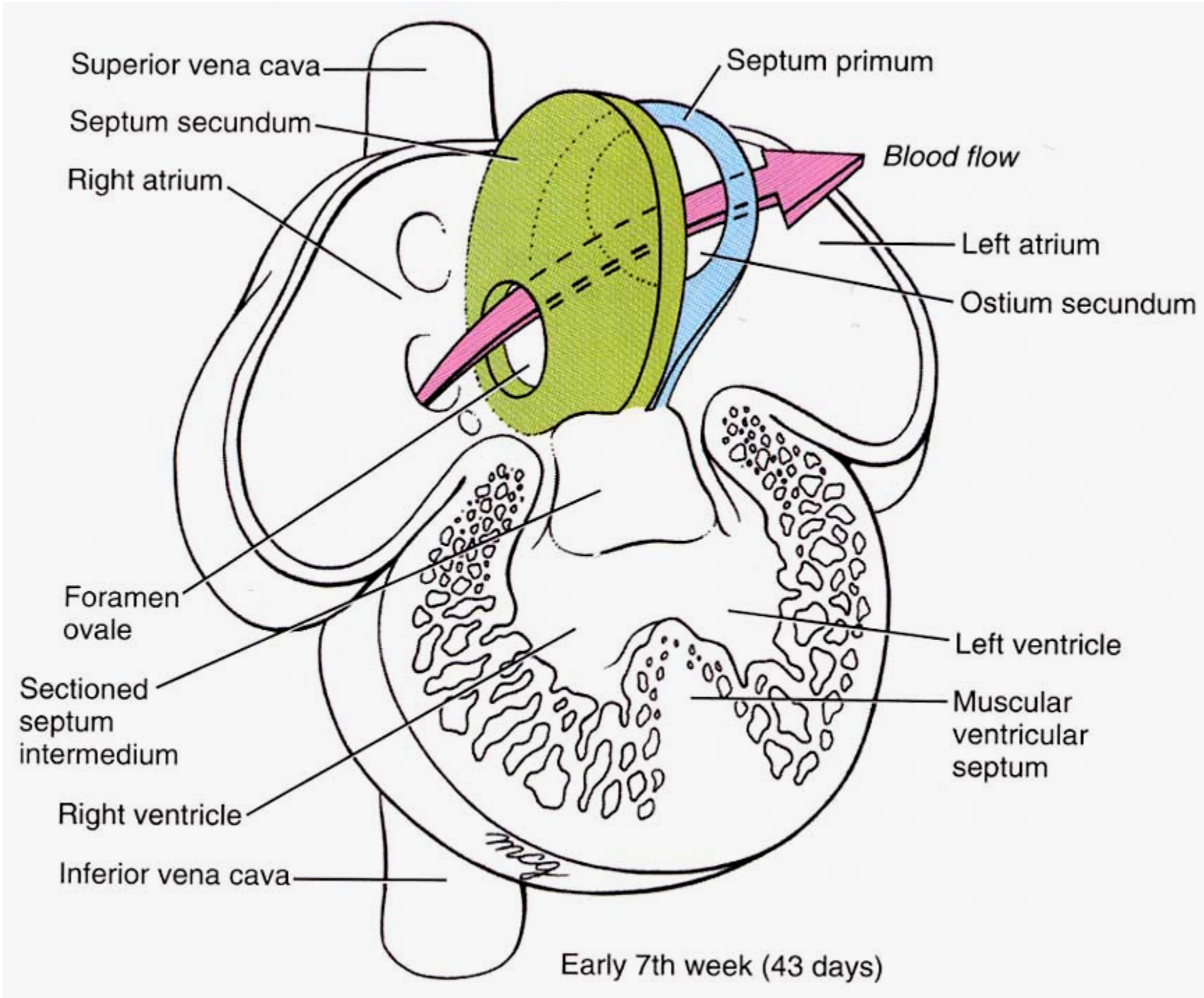
Epidemiology of Human Reproduction, 1988

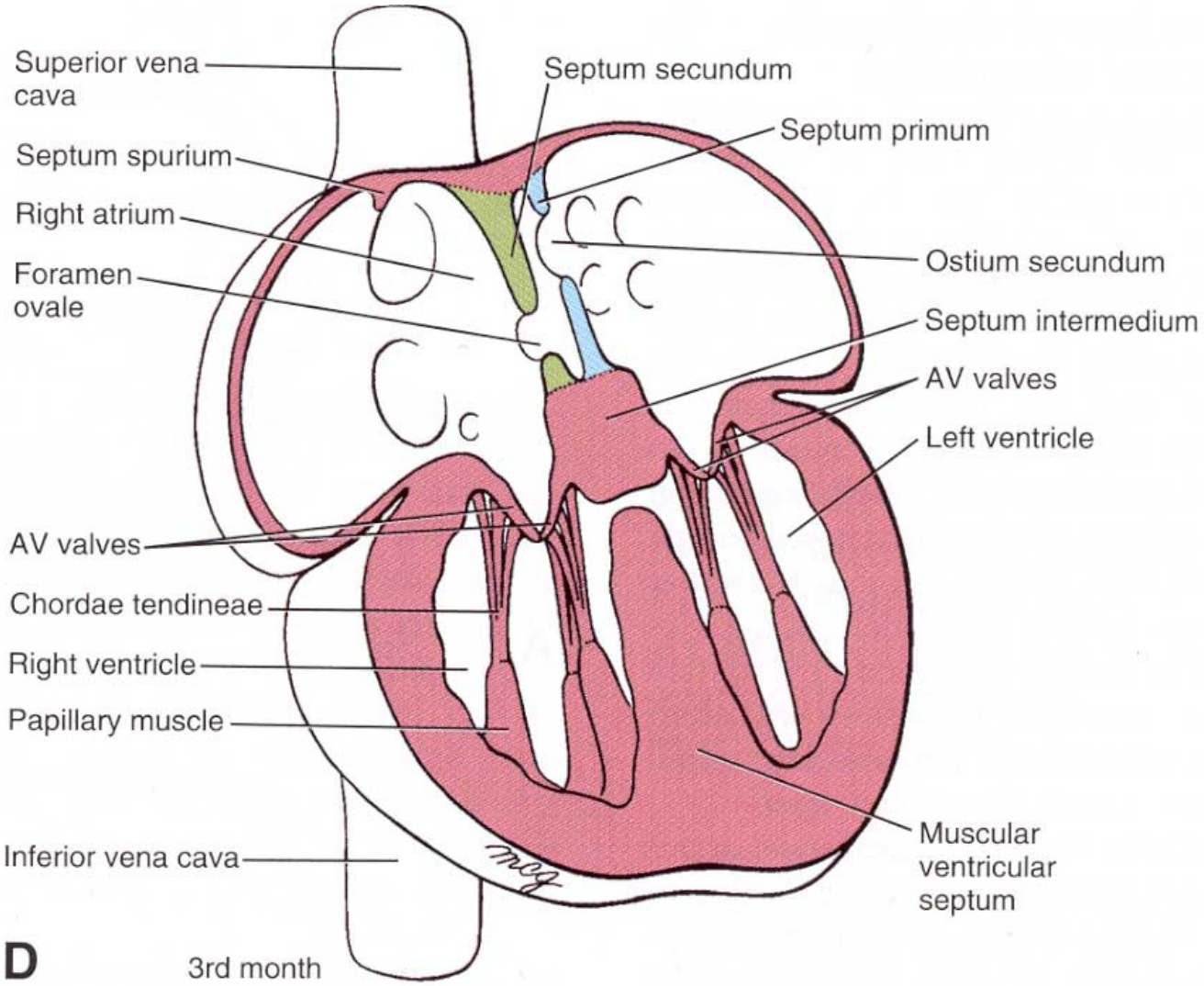
Birth Defect Research

- Important to think in terms of embryology
  - Pathogenesis
    - Normal processes
    - Abnormal processes
  - Timing of structural formation
- Is lumping appropriate?


Superior vena cava
Right atrium
Septum primum
Left endocardial cushion
Ostium primum
Right endocardial cushion
Inferior endocardial cushion
Ventricle
Inferior vena cava
A
33 days
Right endocardial cushion
Superior endocardial cushion
Left endocardial cushion
Inferior endocardial cushion
Cross section of heart between atrium and ventricle


Superior vena cava
Septum secundum
Right atrium
Right endocardial cushion
Sectioned septum intermedium
Ventricle
Inferior vena cava
Septum primum
Ostium secundum
Left atrium
Left endocardial cushion
Septum intermedium
A
6th week (40 days)
Cross section of heart between atrium and ventricle


Superior vena cava
Septum secundum
Right atrium
Septum primum
Blood flow
Left atrium
Ostium secundum
Foramen ovale
Sectioned septum intermedium
Right ventricle
Inferior vena cava
Left ventricle
Muscular ventricular septum
Early 7th week (43 days)


Superior vena cava
Septum spurium
Right atrium
Foramen ovale
AV valves
Chordae tendineae
Right ventricle
Papillary muscle
Inferior vena cava
Septum secundum
Septum primum
Ostium secundum
Septum intermedium
AV valves
Left ventricle
Muscular ventricular septum
D
3rd month

Atrial Septal Defects

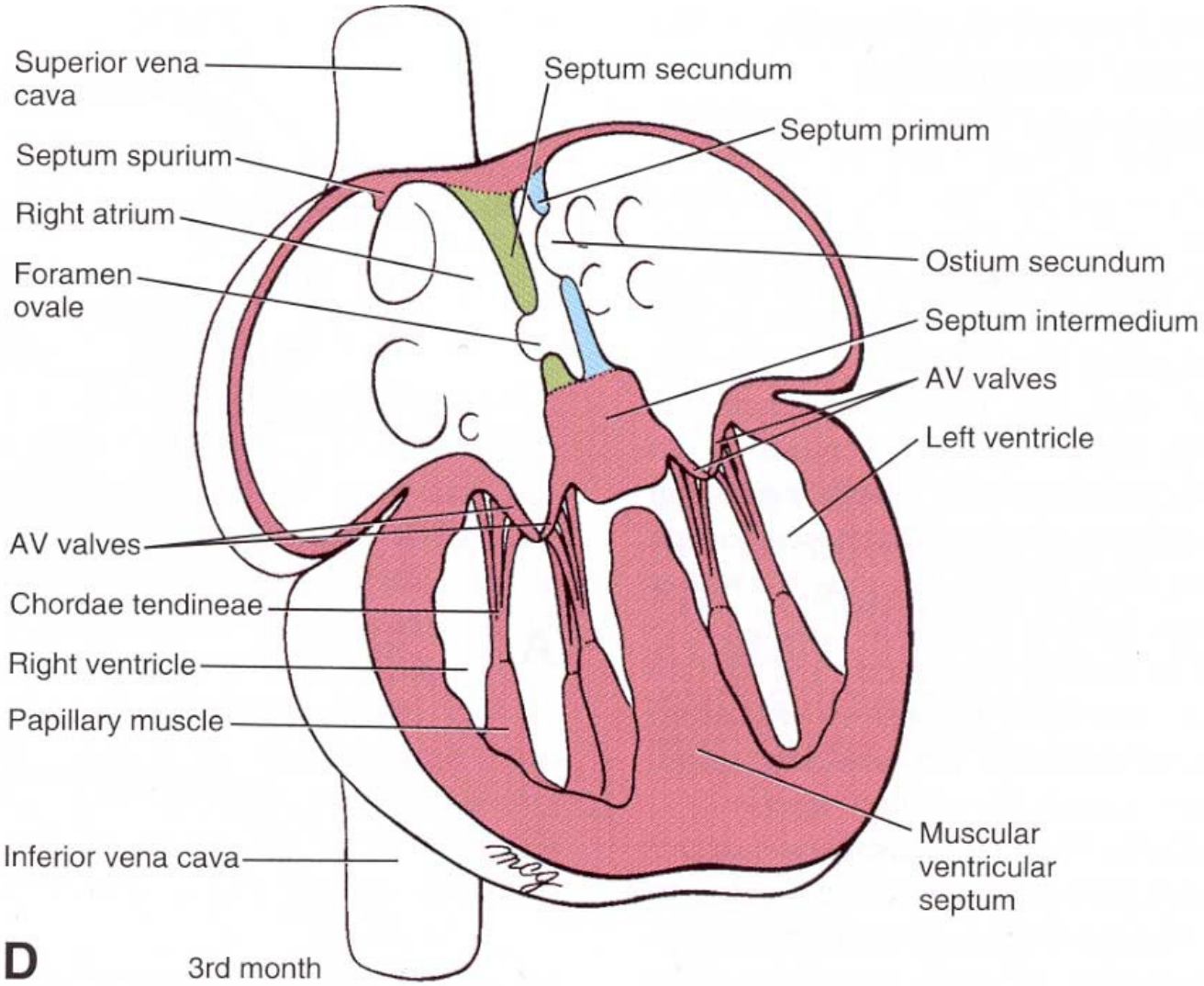
- An opening in the atrial septum, other than a competent foramen ovale
  - Secundum ASDs
  - Sinus venosus ASDs
  - Coronary sinus ASDs
- Classified by location relative to the fossa ovalis

(Moss and Adams, 2008)

Atrial Septal Defects

- Classified by location relative to the fossa ovalis
  - Inadequate formation of septum secundum
  - Ostium secundum too large

(Moss and Adams, 2008)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Right atrium
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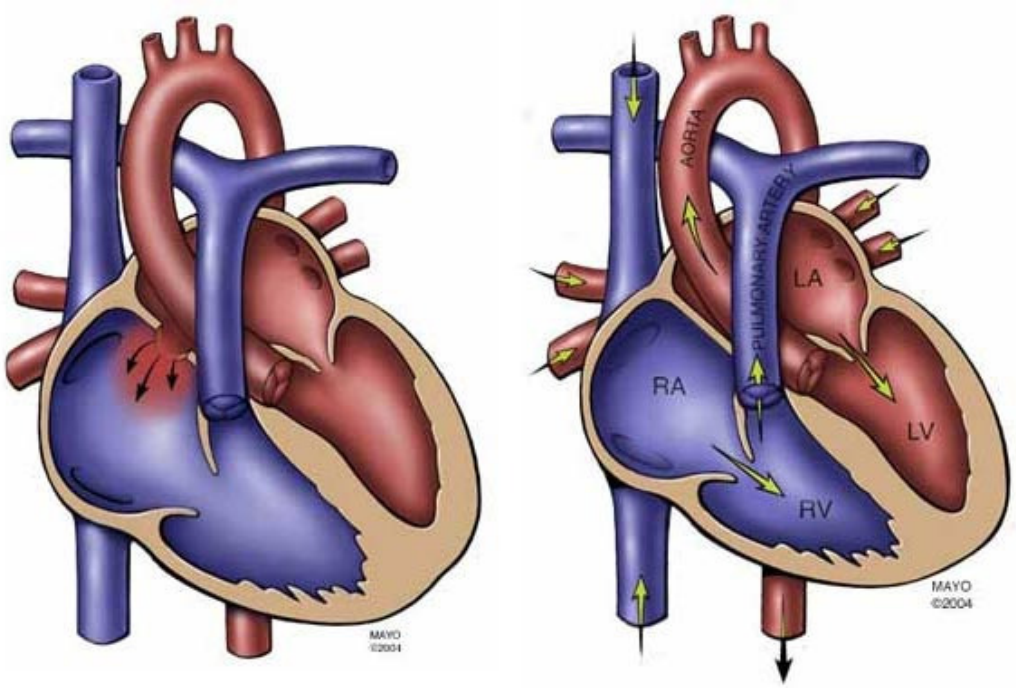
AV valves
Chordae tendineae
Right ventricle
Papillary muscle
Inferior vena cava
Septum secundum
Septum primum
Ostium secundum
Septum intermedium
AV valves
Left ventricle
Muscular ventricular septum
D
3rd month

Atrial Septal Defect - Secundum

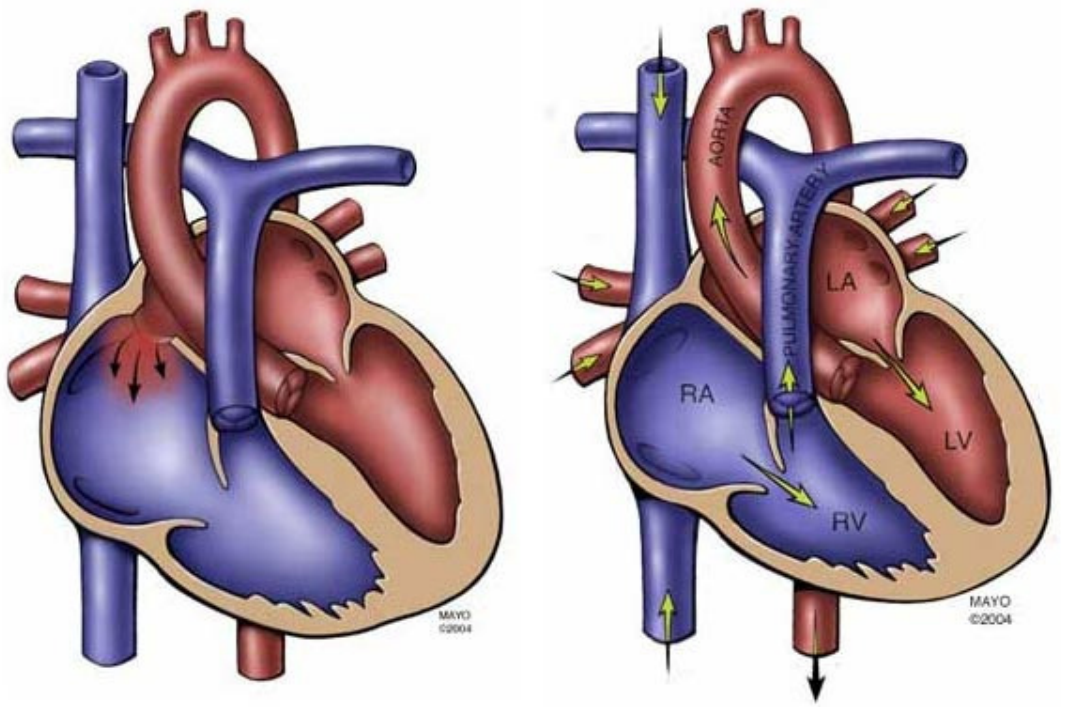
- Most common: 6-10% of all CHDs
- 1 in 1,500 live births
- Most are considered sporadic



(Moss and Adams, 2008; www.mayoclinic.org)

Atrial Septal Defect – Sinus Venosus

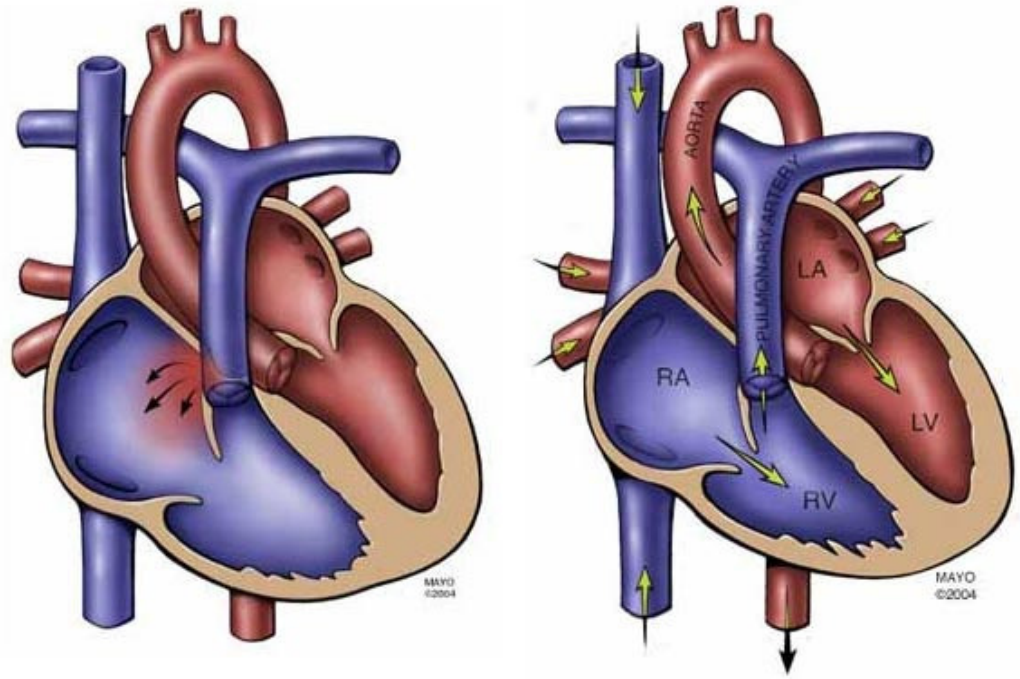
- 5-10% of all ASDs
- Commonly associated with an anomalous pulmonary vein connection



(Moss and Adams, 2008; www.mayoclinic.org)

Atrial Septal Defect – Coronary Sinus

- Rare
- May be associated with complete AV septal defect or heterotaxy



(Moss and Adams, 2008; www.mayoclinic.org)

ASD Codes

- Secundum ASDs - prone to misclassification
  - Distinguishing a PFO vs ASD2 can be difficult for the echocardiographer/interpreter
  - Many atrial level shunts are small
    - Echo obtained during first few weeks of life
    - ASDs may close spontaneously

ASD Codes

- Misclassification of secundum ASDs
  - Differential
    - Bias exposure-disease relationship
    - Unpredictable direction
  - Nondifferential
    - Bias toward the null
- Aggregating heterogeneous phenotypes that pathogenetically are likely not similar lead to missed opportunities to improve our understanding
- Homogeneous groupings important but decrease your sample size

ASD Codes

- International Classification of Diseases 9th
  - 745.5
- British Pediatric Association Classification of Diseases ICD9 Modified
  - 745.500 PDA or PFO; nonclosure of PFO, NOS (exclusions based on gestation)
  - 745.510 atrial septal defect, secundum type (ASD2)
  - 745.520 Lutembacher syndrome → out of date
  - 745.580 other specified atrial septal defect
    - Usually includes the sinus venosus, coronary sinus or vena cava atrial septal defects
  - 745.599 atrial septal defect, NOS; auricular septal defect, NOS; partial foramen ovale; PFO vs ASD

ICD9 ASD Codes

- 745.5 Ostium Secundum Type ASD
  - A combination of atrial septal defect and mitral stenosis
  - 745.5 is a specific code that can be used to specify a diagnosis
  - 745.5 contains 50 index entries
  - Also known as:
    - Defect:
      - atrium secundum
      - fossa ovalis
    - Lutembacher's syndrome (mitral stenosis w/ ASD usually 2°)
    - Patent or persistent:
      - foramen ovale
      - ostium secundum

http://www.icd9data.com/2009/Volume1/740-759/745/745.5.htm

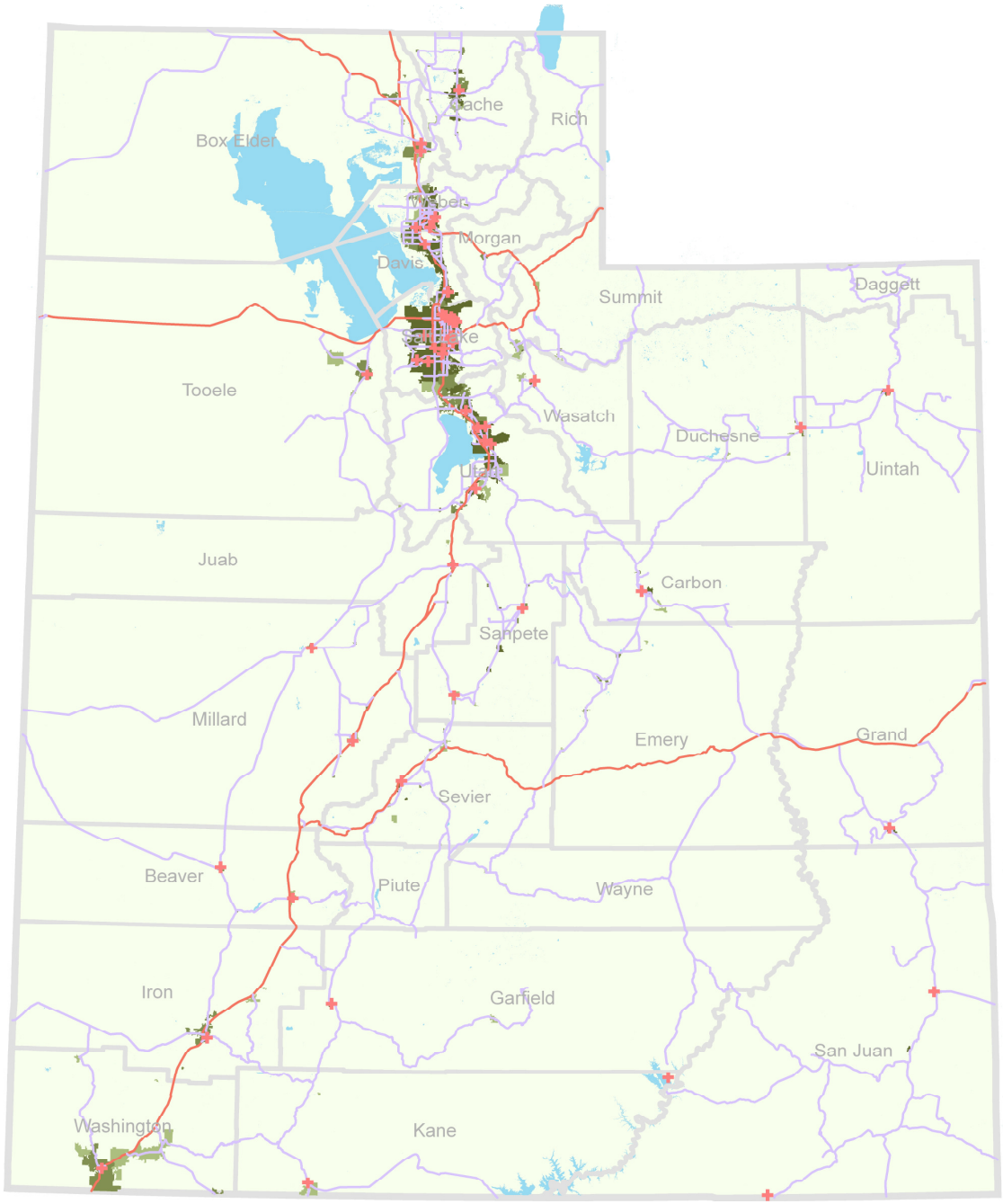
ICD10 ASD Codes

- Q21.1 Atrial septal defect Coronary sinus defect
  Patent or persistent:
  · foramen ovale
  · ostium secundum defect (type II)
  Sinus venosus defect

http://www.who.int/classifications/apps/icd/icd10online/?gq20.htm+q211

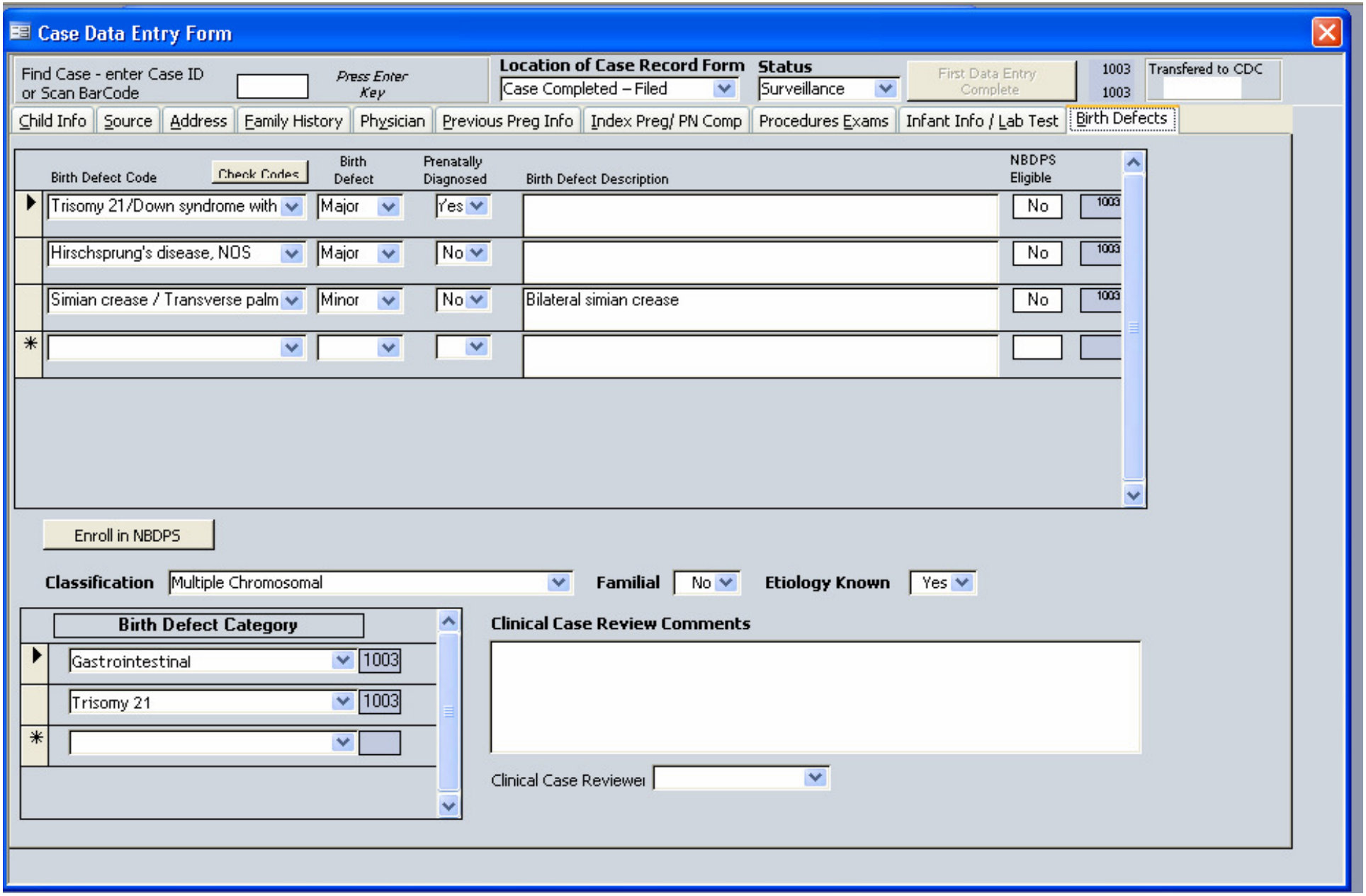
Utah Birth Defect Network

ASDs 2003-2006

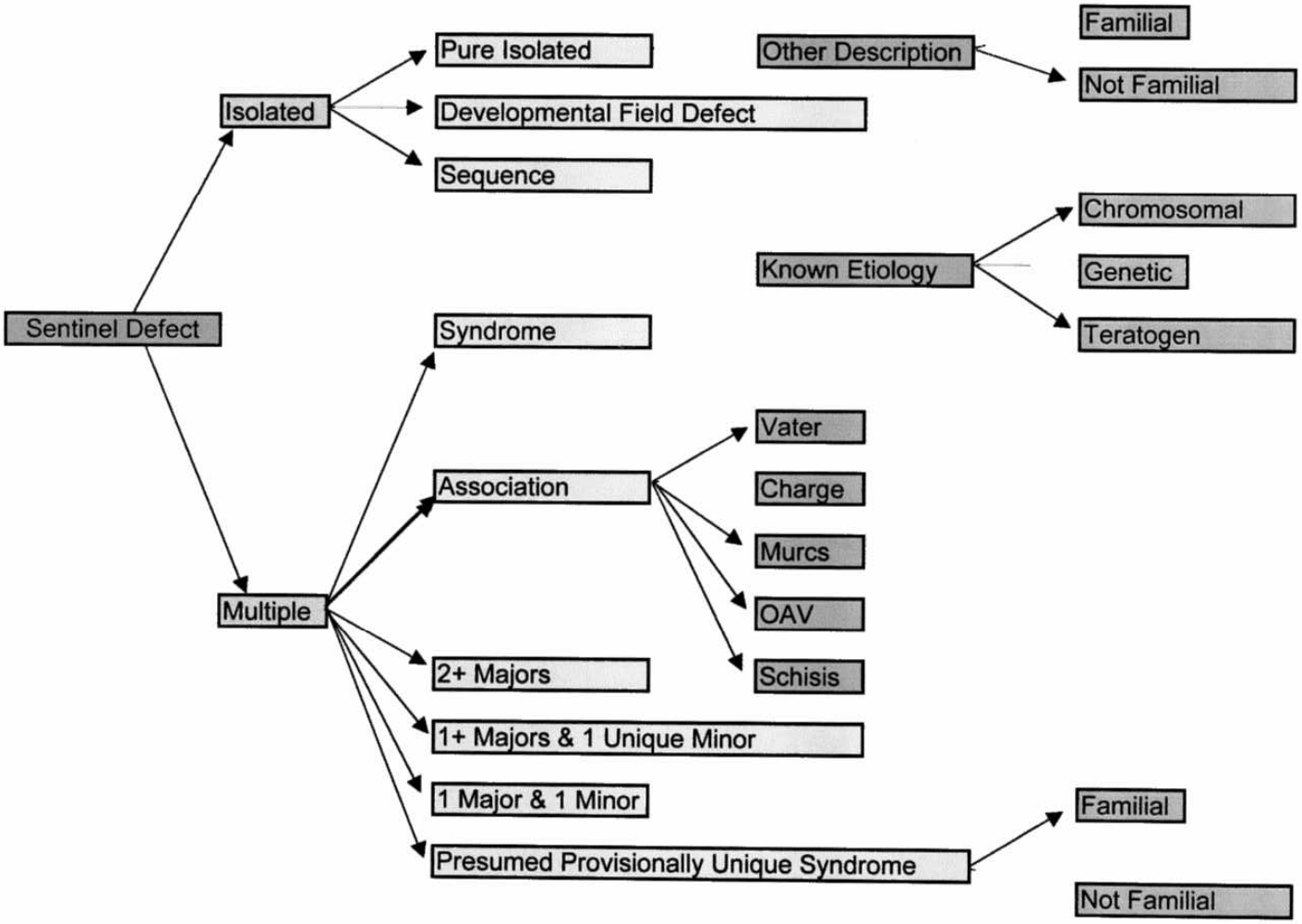

Box Elder
Rich
Morgan
Davis
Summit
Daggett
Tooele
Wasatch
Duchesne
Uintah
Juab
Carbon
Sanpete
Millard
Emery
Grand
Sevier
Beaver
Piute
Wayne
Iron
Garfield
San Juan
Washington
Kane

Classification of Birth Defects

- Clinical geneticists consider:
  - Mechanism
    - pure defects, sequences, developmental field defects
  - Cause
    - chromosome abnormalities, genetic conditions, teratogens, in-utero events
  - Family history
    - Considered familial if 1 or more parents or sibs with same defect


Case Data Entry Form
Find Case - enter Case ID or Scan BarCode
Press Enter Key
Location of Case Record Form
Case Completed – Filed
Status
Surveillance
First Data Entry Complete
1003
1003
Transfered to CDC
Child Info
Source
Address
Family History
Physician
Previous Preg Info
Index Preg/ PN Comp
Procedures Exams
Infant Info / Lab Test
Birth Defects
Birth Defect Code
Check Codes
Birth Defect
Prenatally Diagnosed
Birth Defect Description
NBDPS Eligible
Trisomy 21/Down syndrome with
Major
Yes
No
1003
Hirschsprung's disease, NOS
Major
No
No
1003
Simian crease / Transverse palm
Minor
No
Bilateral simian crease
No
1003
Enroll in NBDPS
Classification
Multiple Chromosomal
Familial
No
Etiology Known
Yes
Birth Defect Category
Gastrointestinal
1003
Trisomy 21
1003
Clinical Case Review Comments
Clinical Case Reviewer

Utah Birth Defect Network
Classification Structure

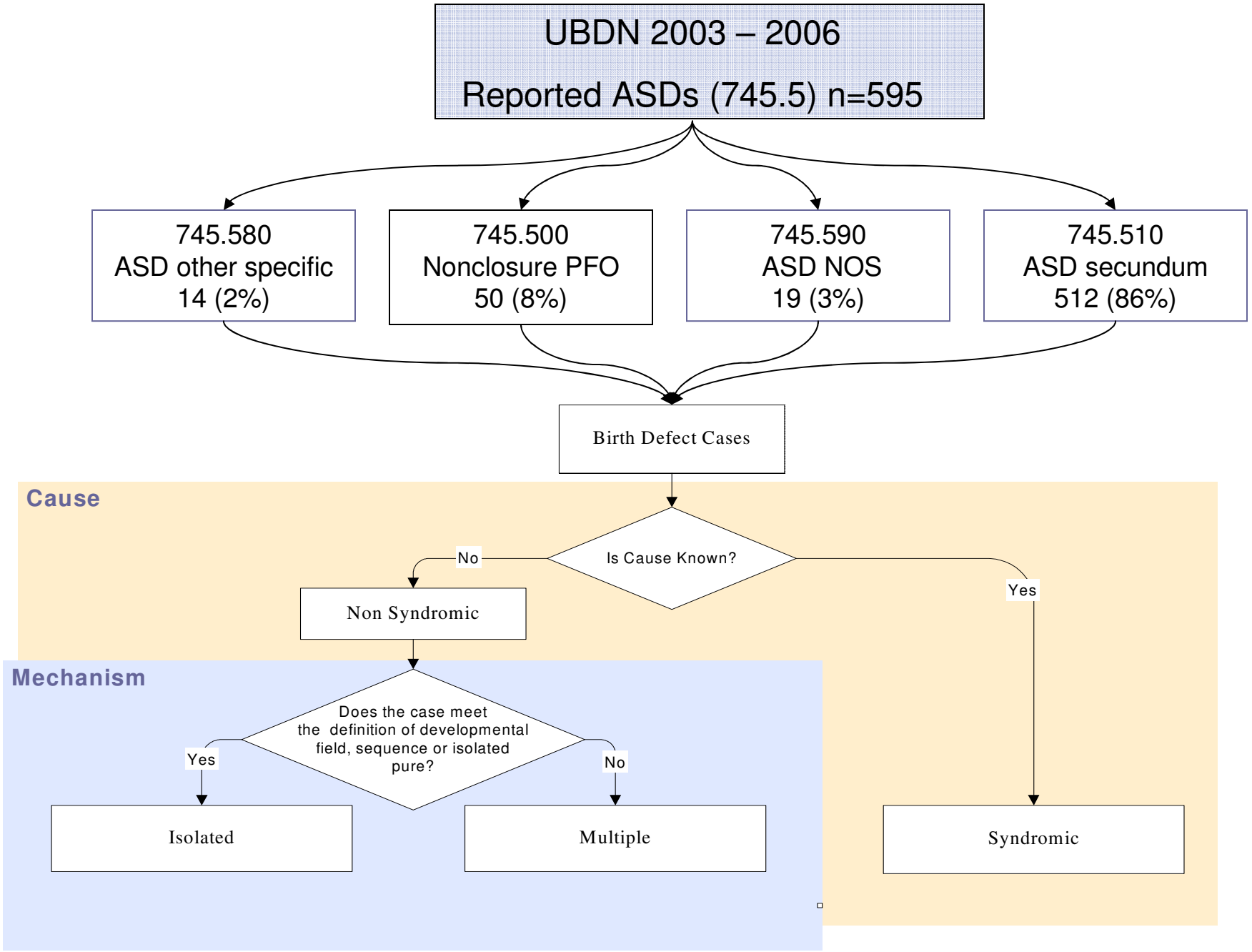


Created by Dr. John Carey

UBDN Reported Potential ASDs

	Number Reported 2003-2006	Percent
Birth Certificates	7	<1
NonIHC Hosp D/C	40	2
IHC Hosp D/C	1142	62
PCMC Hosp D/C	[illegible]	8
UofU Hosp D/C	163	9
Ped Cardiology	354	19
Total	**1855**	

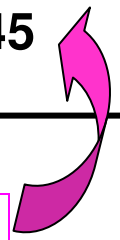
Determined to be NOT A CASE


UBDN 2003 – 2006
Reported ASDs (745.5) n=595
745.580
ASD other specific
14 (2%)
745.500
Nonclosure PFO
50 (8%)
745.590
ASD NOS
19 (3%)
745.510
ASD secundum
512 (86%)
Birth Defect Cases
Cause
Is Cause Known?
No
Yes
Non Syndromic
Mechanism
Does the case meet the definition of developmental field, sequence or isolated pure?
Yes
No
Isolated
Multiple
Syndromic

Classification Tool in Action

Overall Frequency and Prevalence by Classification

ASDs	2003-2006		
Classification	**Frequency (%)**	**Prevalence (per 10,000 births)**	
Isolated	321 (58.9)	15.5	1 in 645
Multiple	87 (16.0)	4.2	1 in 2381
Syndromic	137 (25.1)	6.6	1 in 1515
Total	**545**	**26.4**	**1 in 379**



11.2% of all UBDN cases

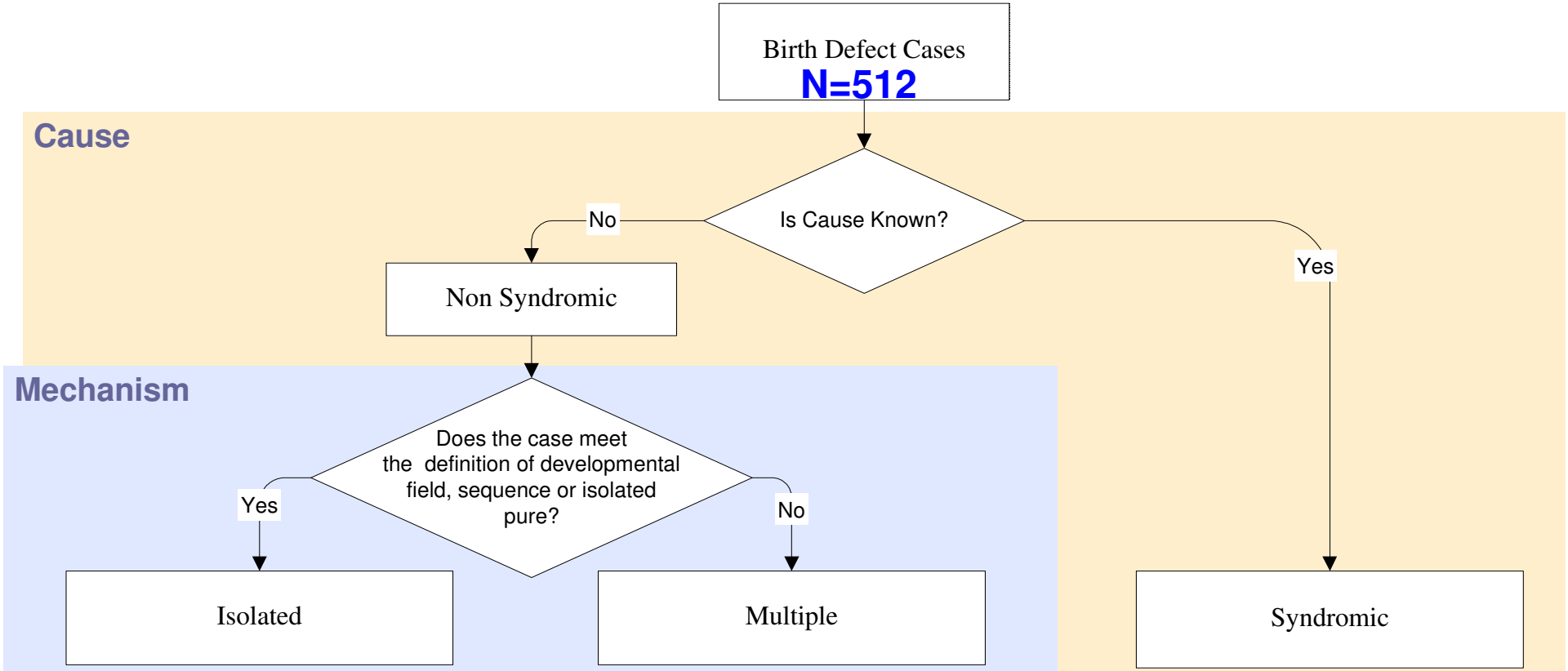
Classification Tool in Action

Overall Frequency and Prevalence by Classification

ASD2°	2003-2006		
Classification	**Frequency (%)**	**Prevalence (per 10,000 births)**	
Isolated	297 (58.9)	14.4	1 in 694
Multiple	84(16.0)	4.1	1 in 2439
Syndromic	133 (25.1)	6.4	1 in 1562
Total	**512**	**24.7**	**1 in 404**

10.5% of all UBDN cases

6.4% change

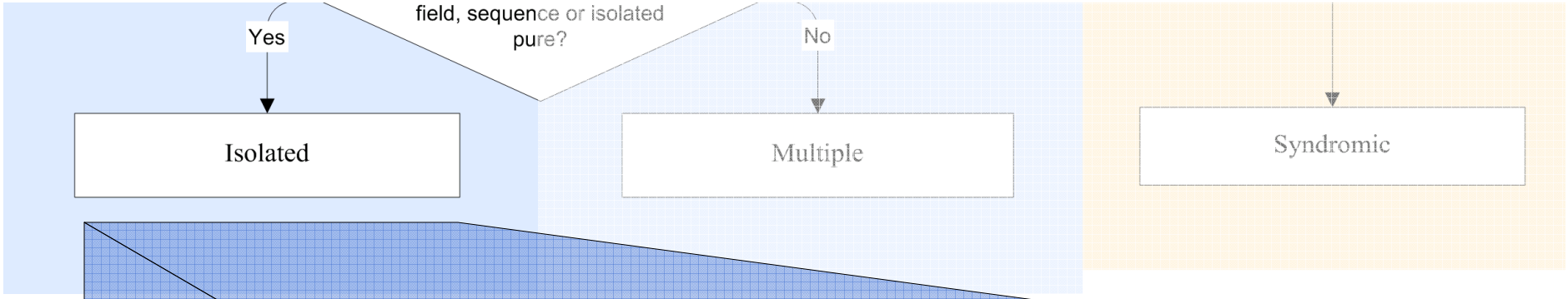


Classification n=297	Cases # (%)		Familial (%)	
Pure				
Pure	293	(99)	6	(2)
Sequences				
Pierre Robin				
Amniotic Band				
Amn.Band & Limb-Body Wall				
Limb-Body Wall				
Frontonasal Dysplasia				
Oligohydramnios				
Urethral Obstruction				
Twinning Abnormality				
Developmental Field				
Sirenomelia				
Holoprosencephaly				
Cloaca				
Cantrell Pentology				
Heterotaxia	4	(1)	0	(0)

Classification n=84	Cases # (%)		Familial (%)	
Multiple				
2+ Majors	70	(83)	0	(0)
1Major/Minors	11	(13)	0	(0)
Association	1	(1)	0	(0)
Additive	1	(1)	0	(0)
Recognizable Pattern	1	(1)	0	(0)

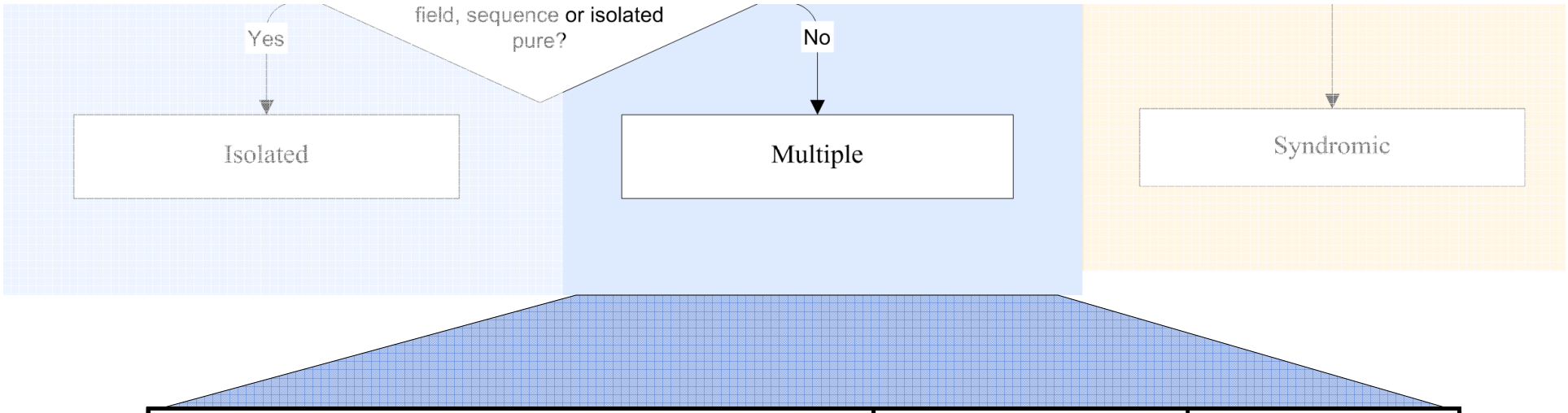
Classification n=133	Cases # (%)		Familial (%)	
Syndromic				
Chromosomal	125	(94)	1	(1)
Genetic	8	(6)	1	(1)
Teratogen	0	(0)	0	(0)

ASD Secundum only (n=512)



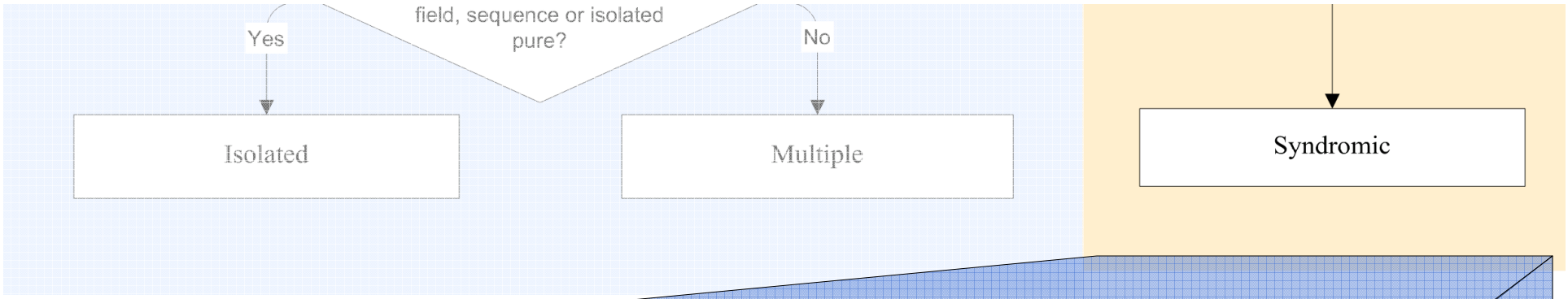
Classification n=297	*Cases # (%)*	*Familial (%)*
Pure		
Pure	293 *(99)*	6 *(2)*
Sequences		
Pierre Robin		
ABS		
ABS/LBWC		
LBWC		
Frontonasal Dysplasia		
Oligohydramnios		
Urethral Obstruction		
Twinning Abnormality		
Developmental Field		
Sirenomelia		
Holoprosencephaly		
Cloaca		
Cantrell Pentology		
Heterotaxia	4 *(1)*	0 *(0)*

ASD Secundum only (n=512)



Classification n=84	*Cases # (%)*		*Familial (%)*	
Multiple				
2+ Majors	70	*(83)*	0	*(0)*
1Major/Minors	11	*(13)*	0	*(0)*
Association	1	*(1)*	0	*(0)*
Additive	1	*(1)*	0	*(0)*
Recognizable Pattern	1	*(1)*	0	*(0)*

ASD Secundum only (n=512)

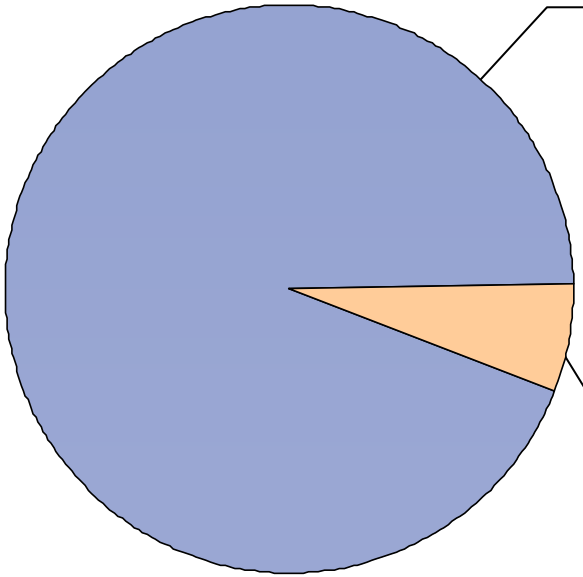


Classification n=137	*Cases # (%)*		*Familial (%)*	
Syndromic				
Chromosomal	125	*(94)*	1	*(1)*
Genetic	8	*(6)*	1	*(1)*
Teratogen	0	*(0)*	0	*(0)*

ASD Secundum only (n=512)

Syndromic cases

(Known cases)



Chromosomal n=125	*Cases # (%)*	
Trisomy21	86	*(69)*
Trisomy18	7	*(6)*
Trisomy13	4	*(3)*
Turner	4	*(3)*
Deletion 22q11	8	*(6)*
Prader-Willi 15q deletion	0	*(0)*
Wolf-Hirschhorn 4p deletion	0	*(0)*
Other conditions	16	*(13)*
Total # of cases	**125**	***(100)***

Genetic n=8	*Cases # (%)*	
Arthrogryposis	1	*(13)*
Apert syndrome	1	*(13)*
CHARGE	1	*(13)*
Noonan syndrome	2	*(25)*
BWS	1	*(13)*
Cornelia de Lange	1	*(13)*
Conradi syndrome	1	*(13)*
Total # of cases	**8**	***(100)***

What if?

Disease Misclassification	Disease			No Disease			OR (95%CI)
	E_1	E_o	Total	E_1	E_o	Total	
15% - E_1	200	375	575	75	425	500	3.0 (2.2, 4.1)
15% - E_1 , E_o	162	413	575	75	425	500	2.2 (1.6, 3.0)
15% - E_o	125	450	575	75	425	500	1.6 (1.2,2.2)
real	125	375	500	75	425	500	1.9 (1.4, 2.6)

Fixed P_o=0.15 and P_1=0.25

Why is this important?

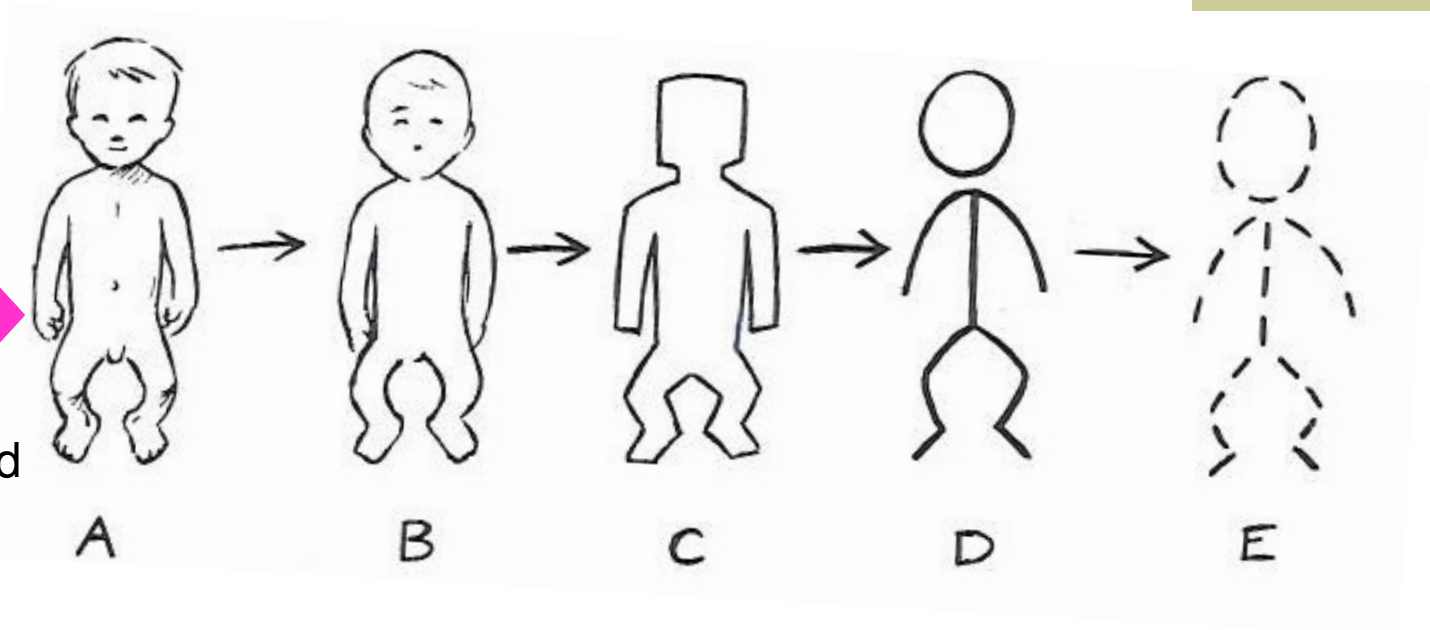
- Effective monitoring and finding causes of birth defects are crucial but not yet achieved goals
- Birth defect coding likely limits our ability to improve our understanding
- Compared to traditional approaches, classification that includes cause and mechanism will hopefully advance our understanding of birth defect etiology
- Such classification requires accurate and detailed information as well as expert clinical review
- Surveillance system databases must be flexible in order to reclassify cases as genes are identified
- Homogeneous case grouping is extremely important

Challenges: Surveillance to Research

- Surveillance systems are limited to what is in the medical records
  - Not all cases ascertained – vary by phenotype
  - Stillbirth and ToP will be missed if phenotype not prenatally diagnosed or autopsy obtained
- Need additional text vs. coding
- Paradigm shift for clinicians describing the defect
- Small sample size when you create very homogeneous case groups
- Pathogenesis
  - Embryologic timing of event
- Etiology

Decisions on data collected are very important!

Gold standard



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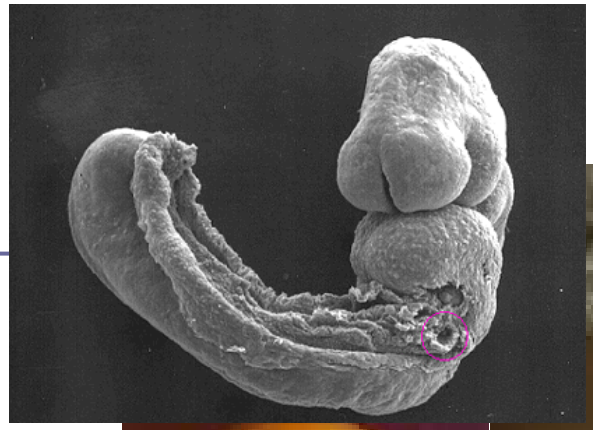
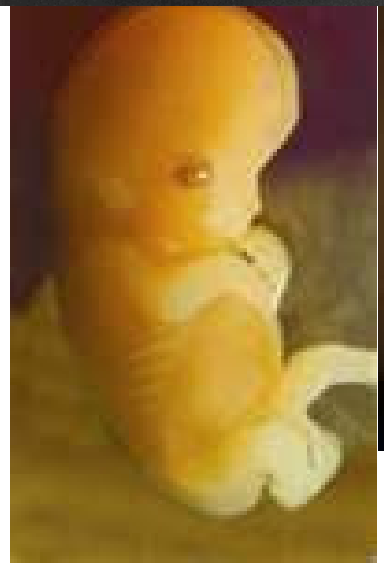
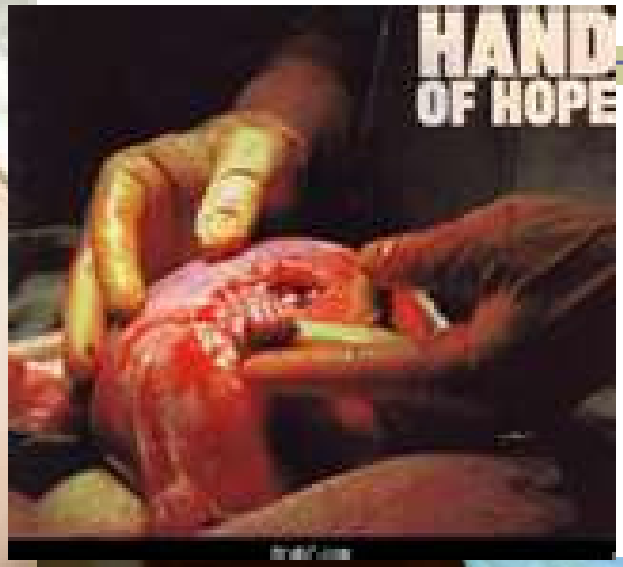
Epidemiology of Human Reproduction, 1988







Thank You!