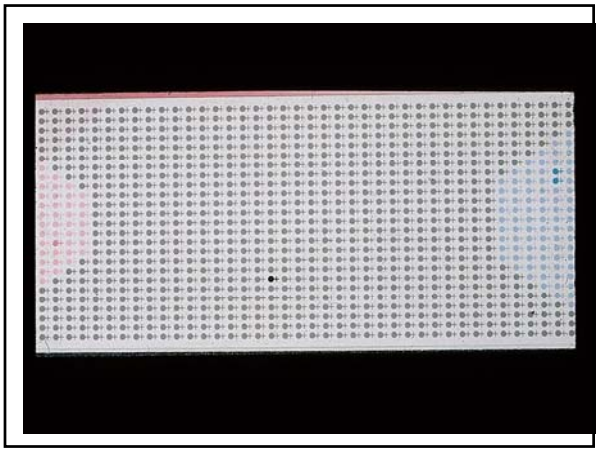


Screening Tests

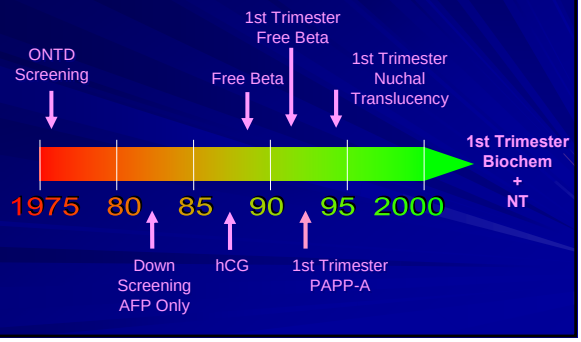
- Healthy patients
- Relatively inexpensive
- Easy to use
- Reliable
- Identify high risk group who may need to consider further testing

CRITERIA FOR SCREENING

- Relatively frequent disease
- Impairing or fatal disease
- Beneficial intervention may be possible
- Sensitive and specific screening test
- Prompt testing and follow up
- Benefits outweigh costs
- Voluntary and educational

Practical Lessons Learned from Genetic Screening

PRENATAL SCREENING
25 YEAR HISTORY



Screening for Down Syndrome

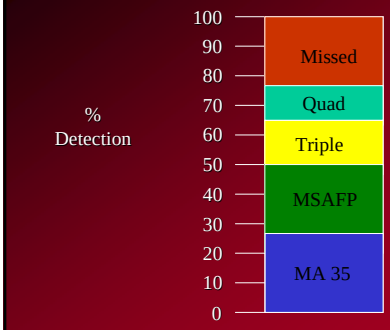
Maternal Age

Cut-Off	Liveborn Risk of Down Syndrome	Second Trimester Risk of Down Syndrome
Age 35	1:380	1:270

"…the age limit is arbitrarily decided by logistical concerns and is not the consequence of a sudden biologic difference between women above and below any given risk".

NICHD, 1979

Screening for Chromosomal Abnormalities



VALUE OF TESTS

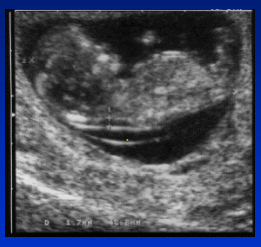
- With a disorder of low prevalence
  - –Even a great test will have a low positive predictive value

First Trimester Screening

First Trimester Serum Markers for Down Syndrome: 1:270 Cut Off

	DS X	DR	FPR
Free ß HCG	1.8 MOM	23%	5%
PAPP A	0.4 MOM	42%	5%
Free ß HCG and PAPP A		62%	5%

Measuring Nuchal Translucency

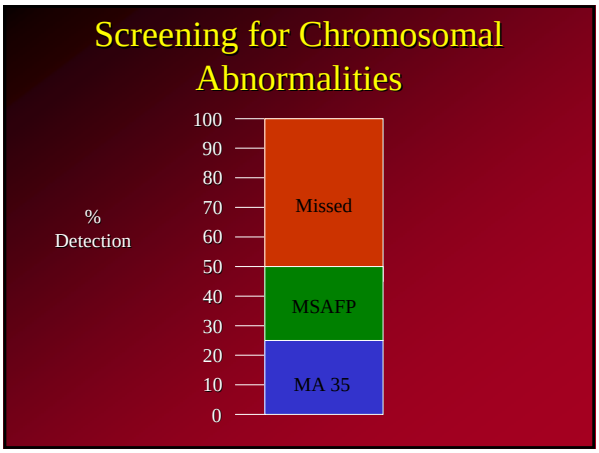


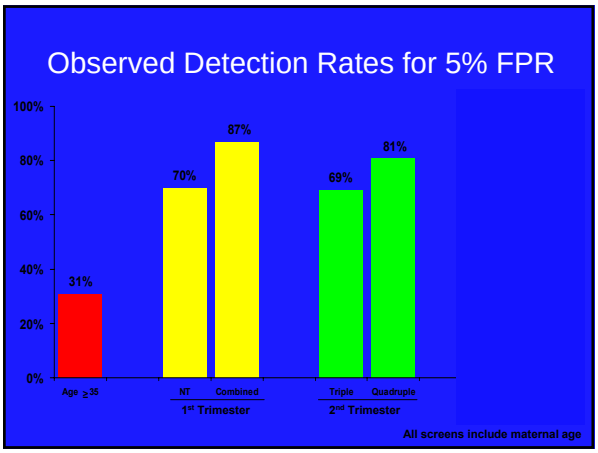
- Gestation 11^{+0} to 13^{+6} wks
- Mid-sagital view
- Image size >75%
- Fetus away from amnion
- Maximum lucency
- Callipers on-to-on

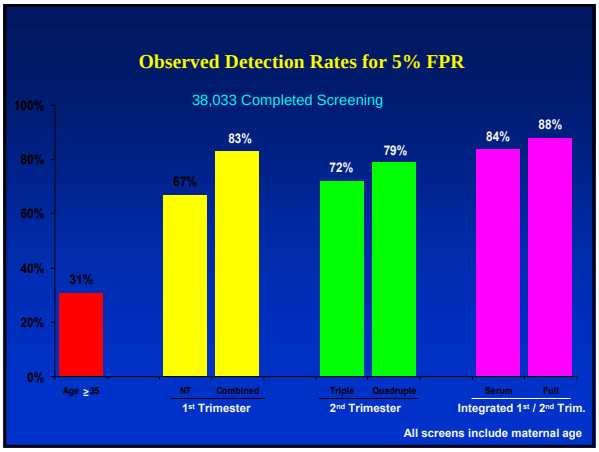
•99.5% of NTs are measurable
•95% of NTs can be measured by transabdominal scanning

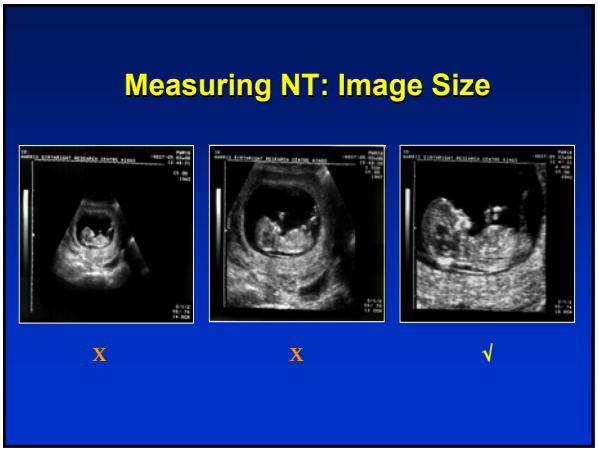
Lessons Learned from Aneuploid Screening Adaptable to Breast Screening

- Individual Risk Assessment (Screening) is now a routine part of OB/GYN care
- Patients and physicians understand screening parameters
  - –DR, FPR, PPV, NPV
- Physcians can integrate new screening techniques into their practice









VALUE OF TESTS

- A test is useful if the odds of having the disease after the test are increased compared to general population
  - (does not by itself mean cost effective)
- A test is useless if the odds of having the disease after the test are unchanged
- A test is worse than useless if the odds of having the disease after the test are lower

Diagnostic Tests

- Definitive answer
- Identify illness / condition
- Usually expensive
- May carry risks

Screening Tests vs Diagnostic Tests

Principles of Screening

AFP - DS

	+	–
+	A: 5	B: 400
–	C: 5	D: 7590

Sensitivity = 5 / 10 = 50%

Positive Predictive Value = 5 / 405 = 1.2%

FOUR QUESTIONS

- WHY DO WE DO TESTS?
- WHAT DO WE EXPECT THEM TO DO?
- WHAT ARE THEIR LIMITATIONS?
- CAN WE APPLY THE SAME MODEL TO EVERYONE?

ADVANCED MATERNAL AGE 1960's

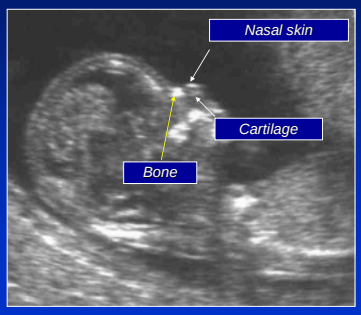
- Association with aneuploidy understood for decades
- Once upon a time was all we had
- Very few pregnancies in AMA group, but risk for them documented to be higher

Nasal Bone Hypoplasia in Trisomy 21

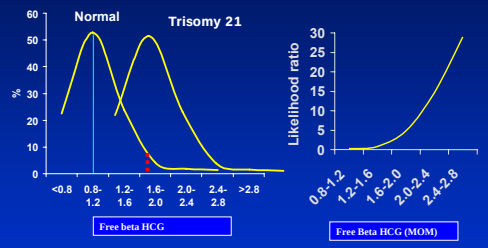
Langdon Down, 1866
Poor skin elasticity
Flat face
Small Nose

Smith's Recognizable Patterns of Human Malformation

Nasal bone at 11-14 wks



Calculation of Likelihood Ratio



A priori age risk 1 in 200

Likelihood ratio = 0.5	Adjusted risk 0.5 in 200 or ~ 1 in 400
Likelihood ratio = 2.0	Adjusted risk 2.0 in 200 or ~ 1 in 100

Screening for Down's Syndrome

maternal age