

# Will Diagnostic Systems in FAS Work in Adolescents and Adults

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# Five Methods for Clinical Diagnosis of FASD

1. Emory FAS Clinic (2000) Coles et al. 1997, Blackstone et al. 2005.
2. 4-Digit System (2000) Astley and Clarren, 2000, Astley, 2013.
3. Centers for Disease Control and Prevention (CDC) Fetal Alcohol Syndrome Task Force, (2004)
4. Canadian System (2005) Chudley et al 2005, Loock et al., 2005, Cook JL et al 2016
5. The Collaboration on FASD Prevalence (CoFASP) Criteria; Hoyme et al 2005, Hoyme et al 2016

# Fetal Alcohol Syndrome (FAS)

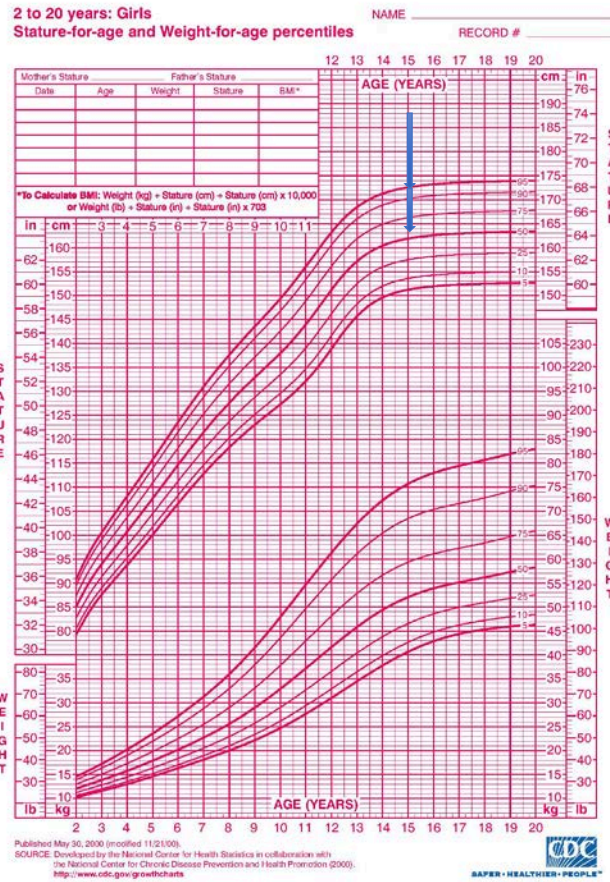
(Based on the criteria established by Hoyme et al 2016)

- 2 or more facial anomalies:
  - Short palpebral fissures ( $\leq 10\%$ ), smooth philtrum (rated 4 or 5 on the Astley-Clarren Lip - Philtrum guide), thin vermilion border (rated 4 or 5 on the Astley-Clarren Lip-Philtrum guide).
- Growth deficiency  $\leq 10^{\text{th}}$  centile
- Head circumference  $\leq 10^{\text{th}}$  centile
- Cognitive and/or behavioral impairment
  - Global impairment  $\geq 1.5$  SD below mean **or**
  - Cognitive deficit in  $\geq 1$  neurobehavioral domain  $\geq 1.5$  SD below mean **or**
  - Behavioral deficit in  $\geq 1$  behavioral domain of self-regulation  $\geq 1.5$  SD below mean

# Parameters To Be Discussed

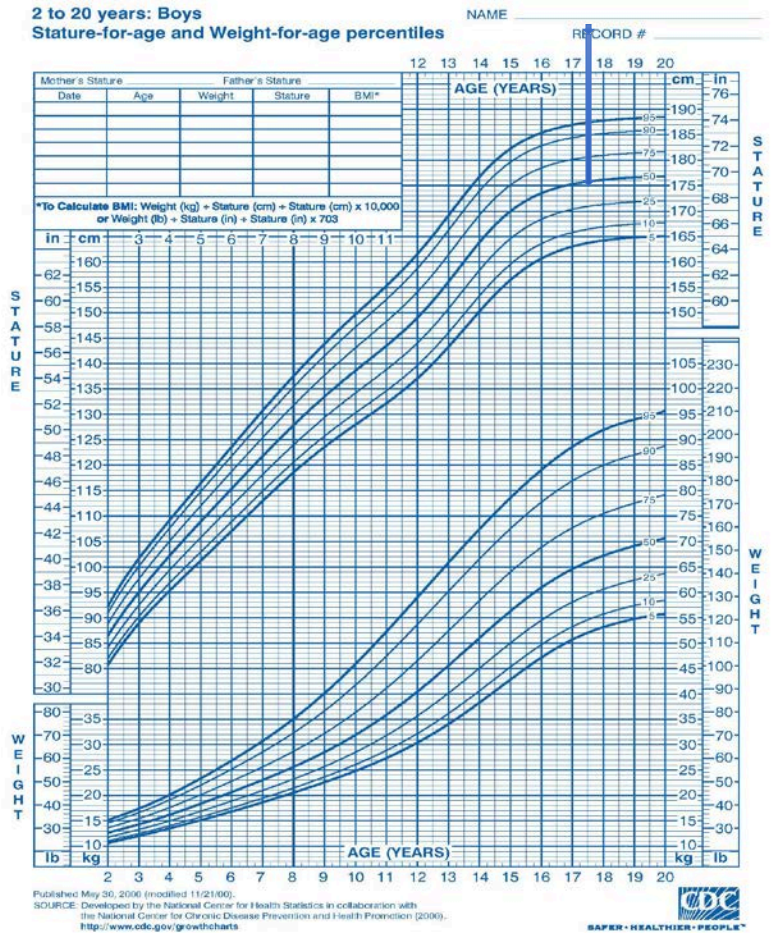
- Growth
- Occipital Frontal Circumference
- Palpebral Fissure Length
- Philtrum
- Vermilion Border

# Adolescent and Adult Growth



In normal children, there is very little growth after 15 years in girls and 17 and 6/12 In boys

This strongly suggests that growth for adolescent girls beyond 15 years and boys beyond 17 and 6/12 with FAS would plateau as well.





## ADOLESCENTS AND ADULTS WITH FAS

43 Adolescents and 18  
Adults

Ages 12 to 40

Mean height 2 SD below  
population mean – Weight  
less affected

Mean weight for height age  
48% - Varied from 3% (very  
thin) to 90% (very heavy)

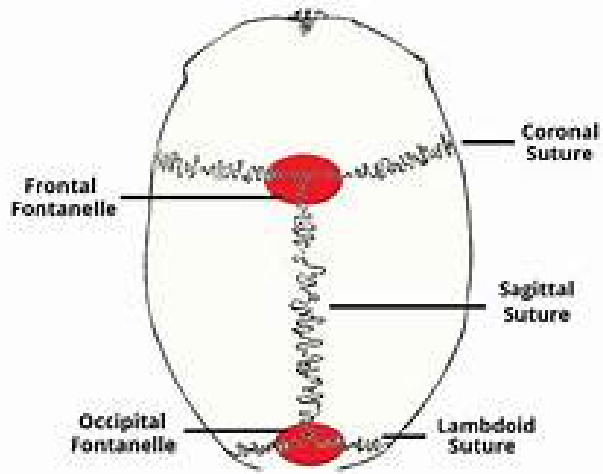
Onset of Puberty - WNL



# The Value of Growth in Diagnosis of Adolescents and Adults with FAS

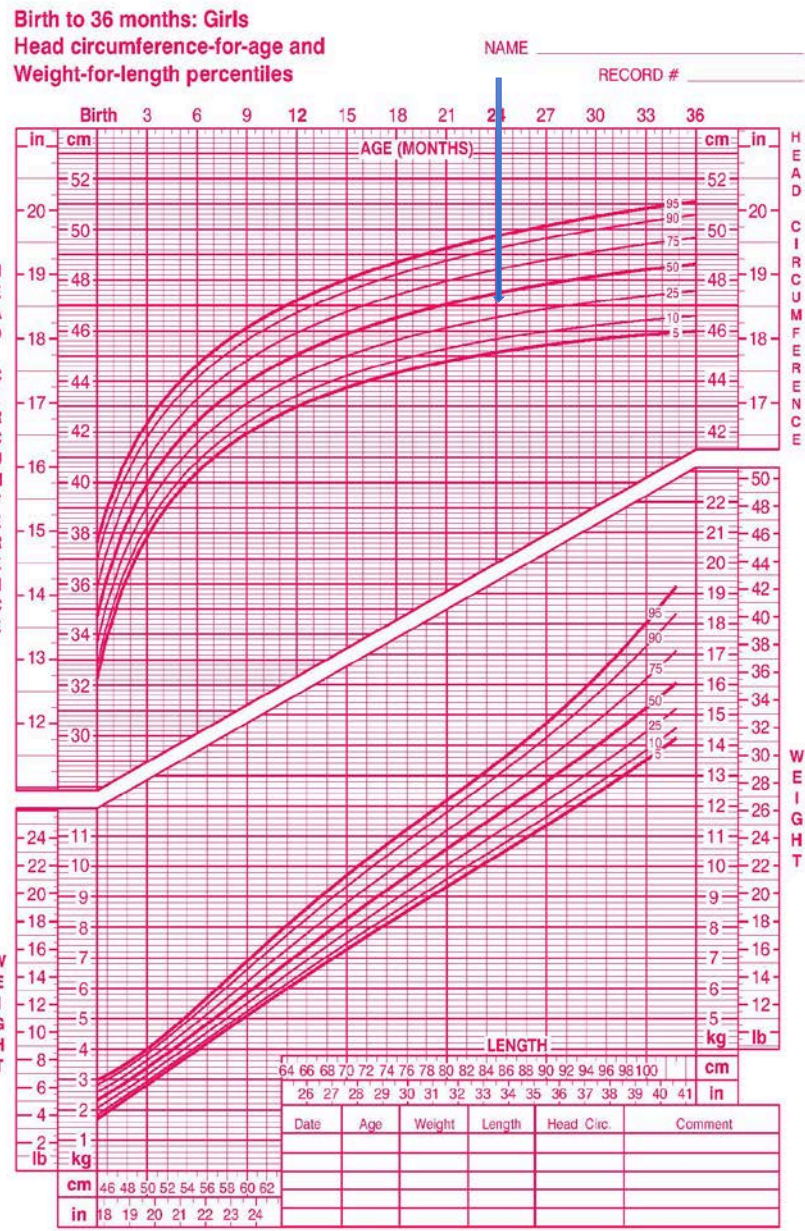
- Height can be helpful in diagnosis of FAS in Adolescents and Adults – Weight is Less Helpful
- Based on a publication by Carter et al (confirmed in a recent report by Chambers et al), prenatal growth restriction is perhaps the most important predictor of intellectual performance in children with FAS, particularly when it occurs in the absence of postnatal catch-up growth.

# NORMAL HEAD CIRCUMFERENCE



The fontanels and sutures allow the brain to grow

In humans, 38% of fontanels close by the 1st year and 96% by the 2<sup>nd</sup>. They close because the brain no longer pushes them apart. Therefore, most of brain growth occurs by the 2<sup>nd</sup> yr of life



OFC at Birth – 35cm  
12 months – 45 cm  
24 months – 47.5 cm  
16 years - 54.5 cm

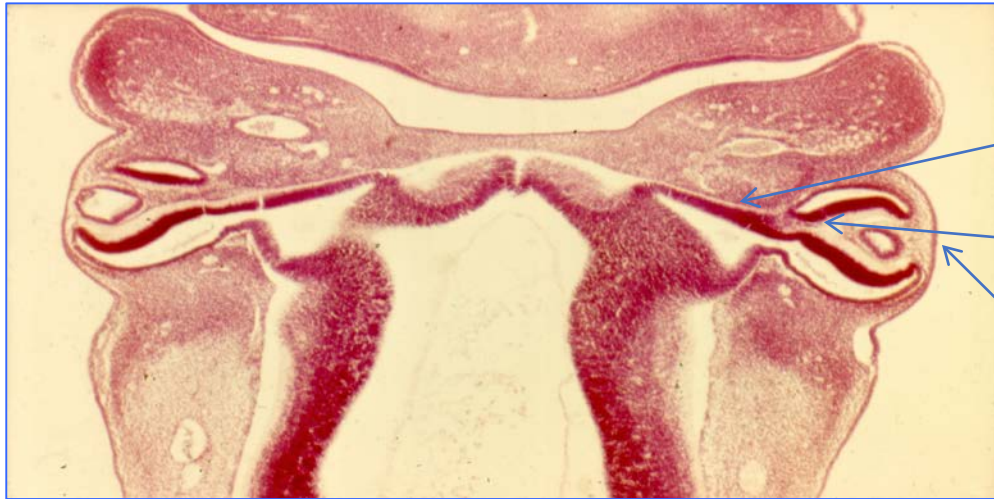
Therefore it would be expected that the head circumference in an adolescent or adult would continue to be a good diagnostic sign of FAS

In a study of 43 adolescents and 18 adults mean OFC > 2SD below mean but 28% had normal OFC  
Stressguth et al. 1991

Published May 30, 2000 (modified 10/16/00).  
SOURCE: Developed by the National Center for Health Statistics in collaboration with the National Center for Chronic Disease Prevention and Health Promotion (2000).  
<http://www.cdc.gov/growthcharts>



# PALPEBRAL FISSURE LENGTH



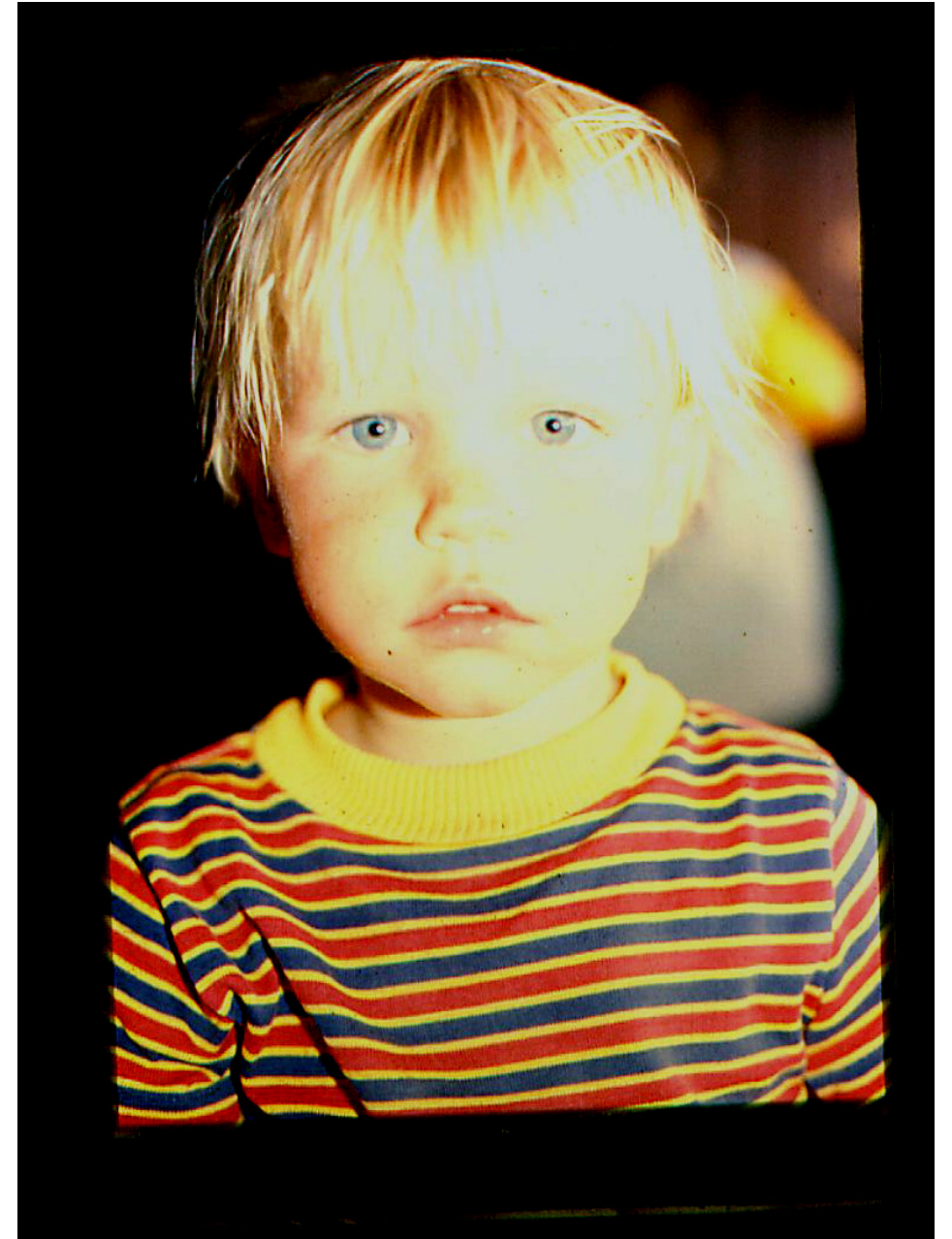
Optic Stalk

Optic Vesicle

Overlying  
Ectoderm

32 – 34 day Human Embryo

- The palpebral fissure is a dependent structure which depends on the optic vesicle which is an out-pouching from the frontal brain.
- Shortness of the palpebral fissure is a function of decreased volume of the optic vesicle.



# Palpebral Fissures in Newborns with FAS

% deviation relative to controls

Case #1 +3.4	Case #7 -2.1	Case #13 -15.4
Case #2 +2.1	Case #8 -7.9	Case #14 -16.3
Case #3 -0.9	Case #9 -9.9	Case #15 -17.0
Case #4 -1.2	Case #10 -10.3	Case #16 -20.0
Case #5 -1.3	Case #11 -13.6	Case #17 -23.1
Case #6 -1.6	Case #12 -14.8	Case #18 -32

# Ocular Volume in Newborns with FAS

% deviation relative to controls

Case #1 +9.4	Case #7 -16.9	Case #13 -28.6
Case #2 +3.8	Case #8 -20.8	Case #14 -29.0
Case #3 -1.7	Case #9 -21.4	Case #15 -31.7
Case #4 -3.8	Case #10 -21.5	Case #16 -37.5
Case #5 -5.0	Case #11 -24.1	
Case #6 -10.9	Case 12 -26.4	

**Mean : -16.6%**

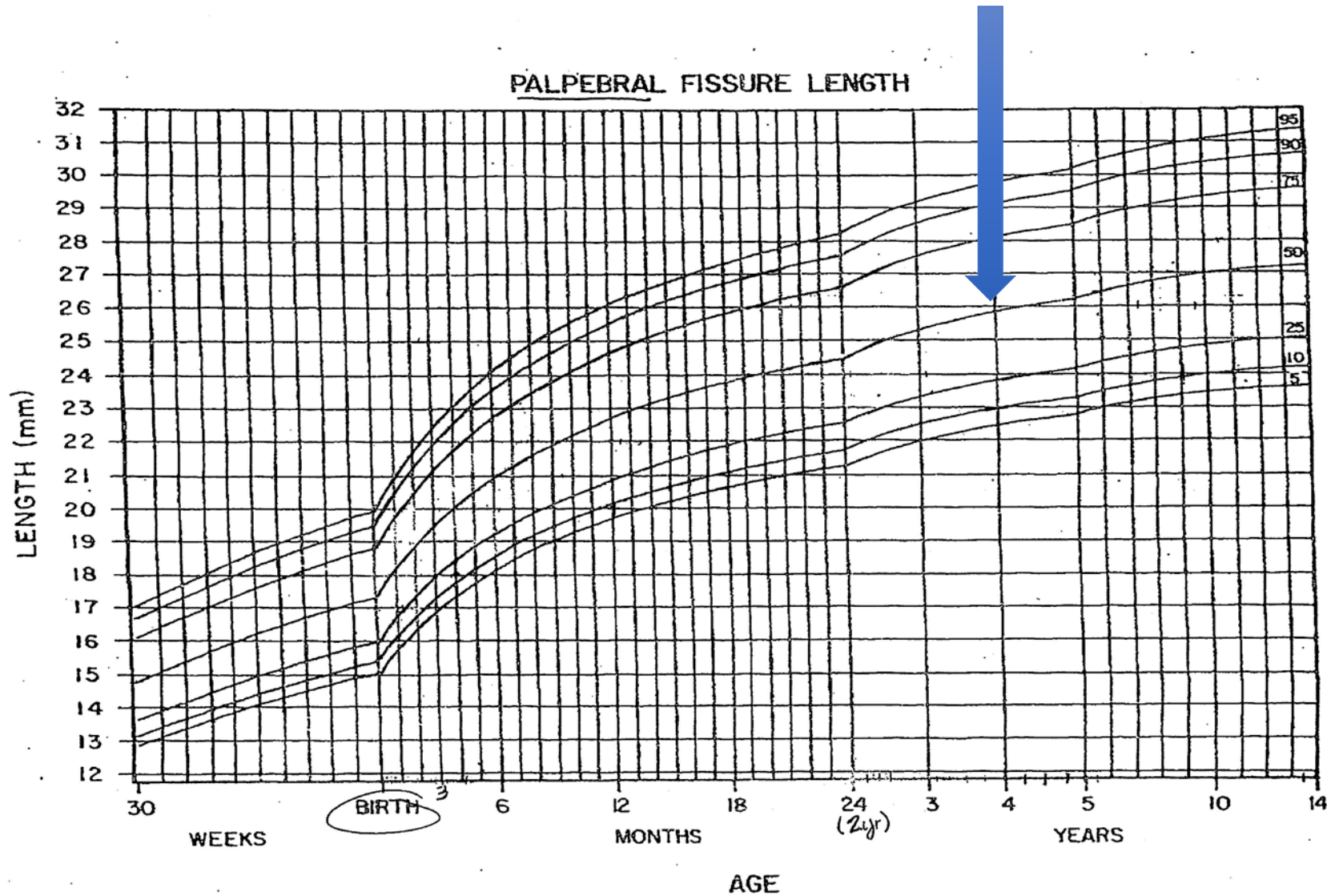








# Palpebral Fissure Length in Normal Males and Females

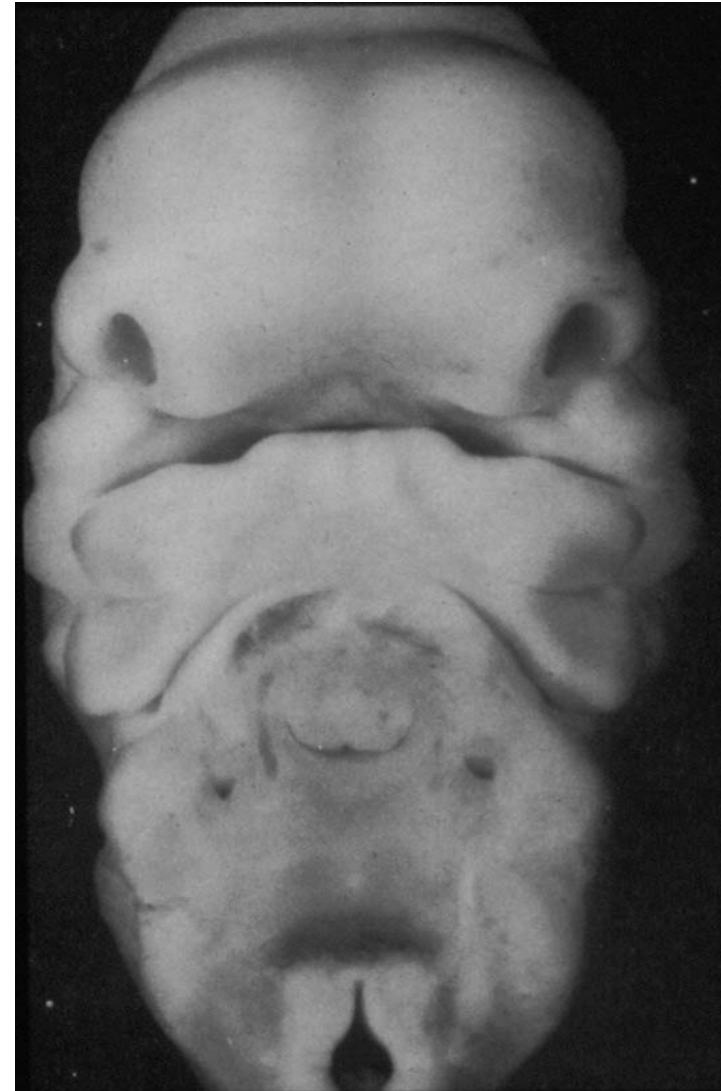


After 4 years of Age the palpebral fissure increases by 1 mm in normal children

The in utero insult to optic vesicle volume which determines PFL in FAS remains constant following birth resulting in a PFL that does not continue to grow past 4 years

Therefore it would be expected that the PFL in an adolescent or adult would continue to be a good diagnostic sign of FAS

## NORMAL DEVELOPMENT OF THE PHLTRUM AND VERMILION BORDER



# STRUCTURAL BASIS OF PHILTRUM

- Normal philtral anatomy:  
32 fetuses from 8 to 21 fetal weeks
- Specimens lacking lateral philtral ridges:  
Holoprosencephaly  
Prolabium of bilateral cleft lip  
Heavy Prenatal Alcohol Exposure

Martin RA, Jones KL, Benirschke K. Absence of the lateral philtral ridges: A clue to the structural basis of the philtrum. *Amer J Med Genetics* 65: 117-123, 1996.

## Normal Development of the Philtrum

Medial Nasal Processes

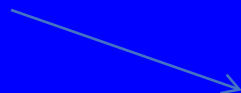


Secondary Structures  
(Frenulum Associated Connective Tissue)

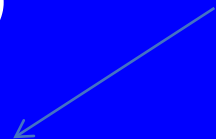
Maxillary Processes



Secondary Structures  
(Orbicularis Oris Muscle  
Fibers)



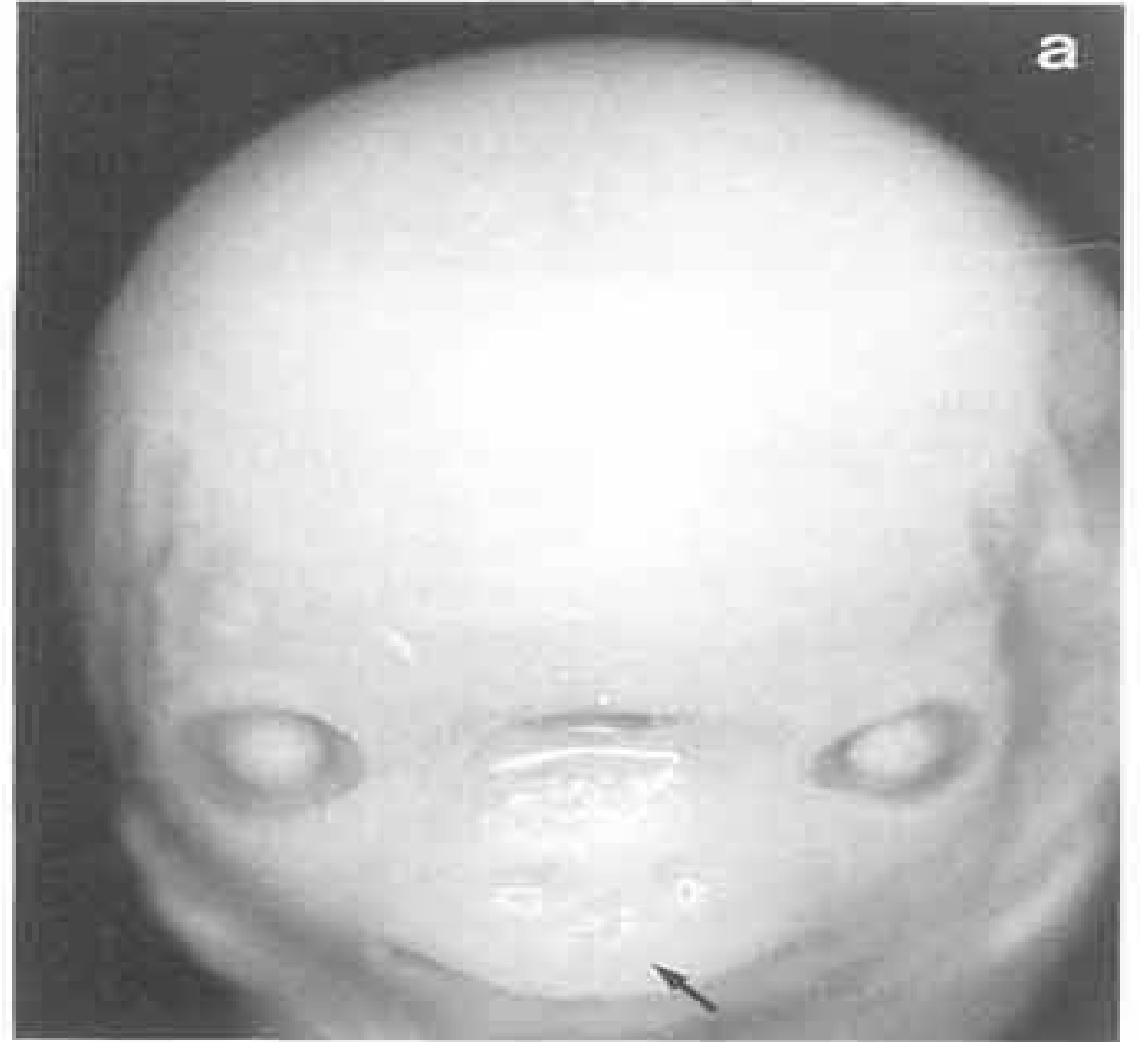
Interaction



Normal Philtrum



# NORMAL 9 WEEK HUMAN FETUS





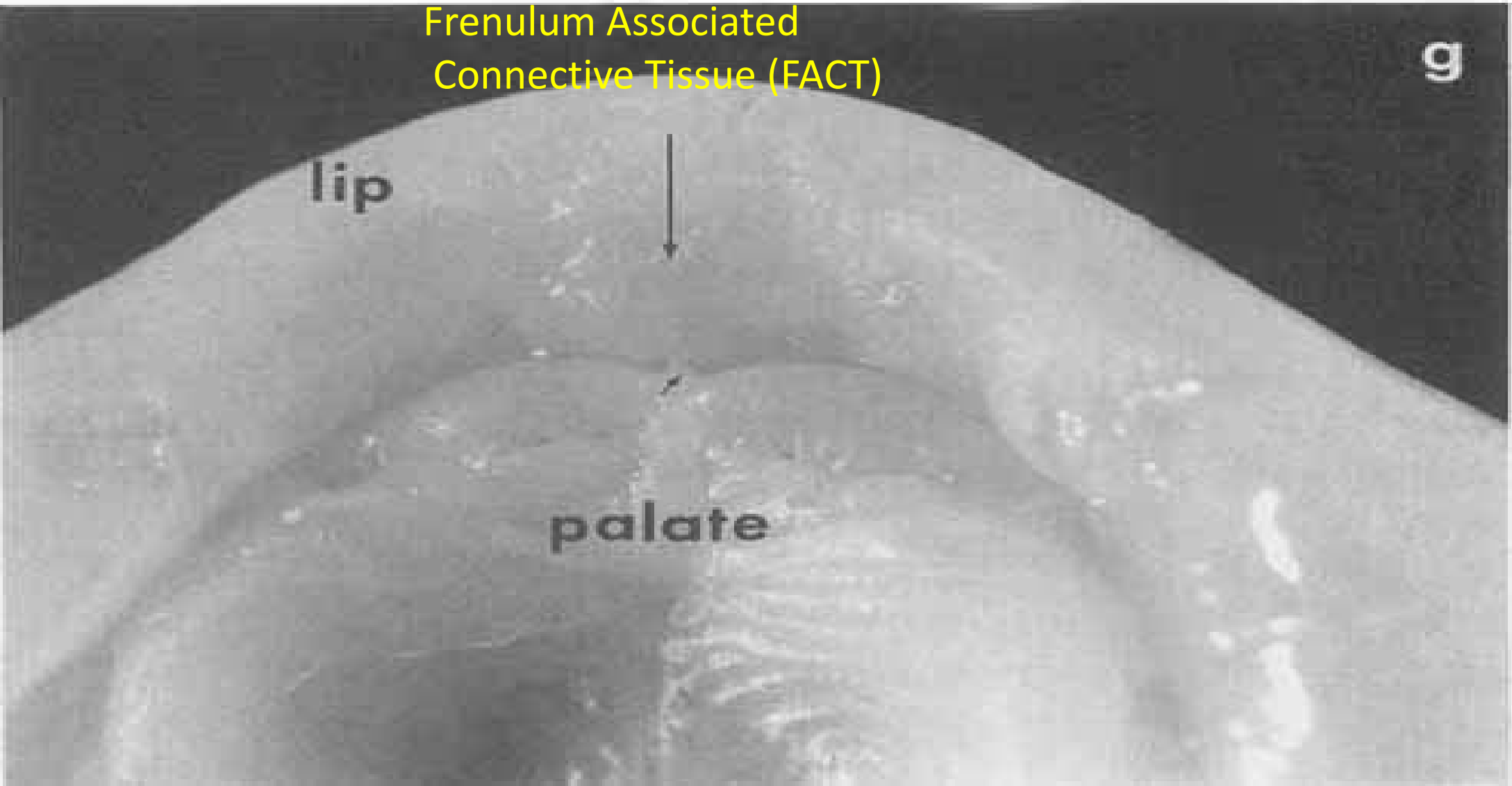
Frenulum Associated  
Connective Tissue (FACT)

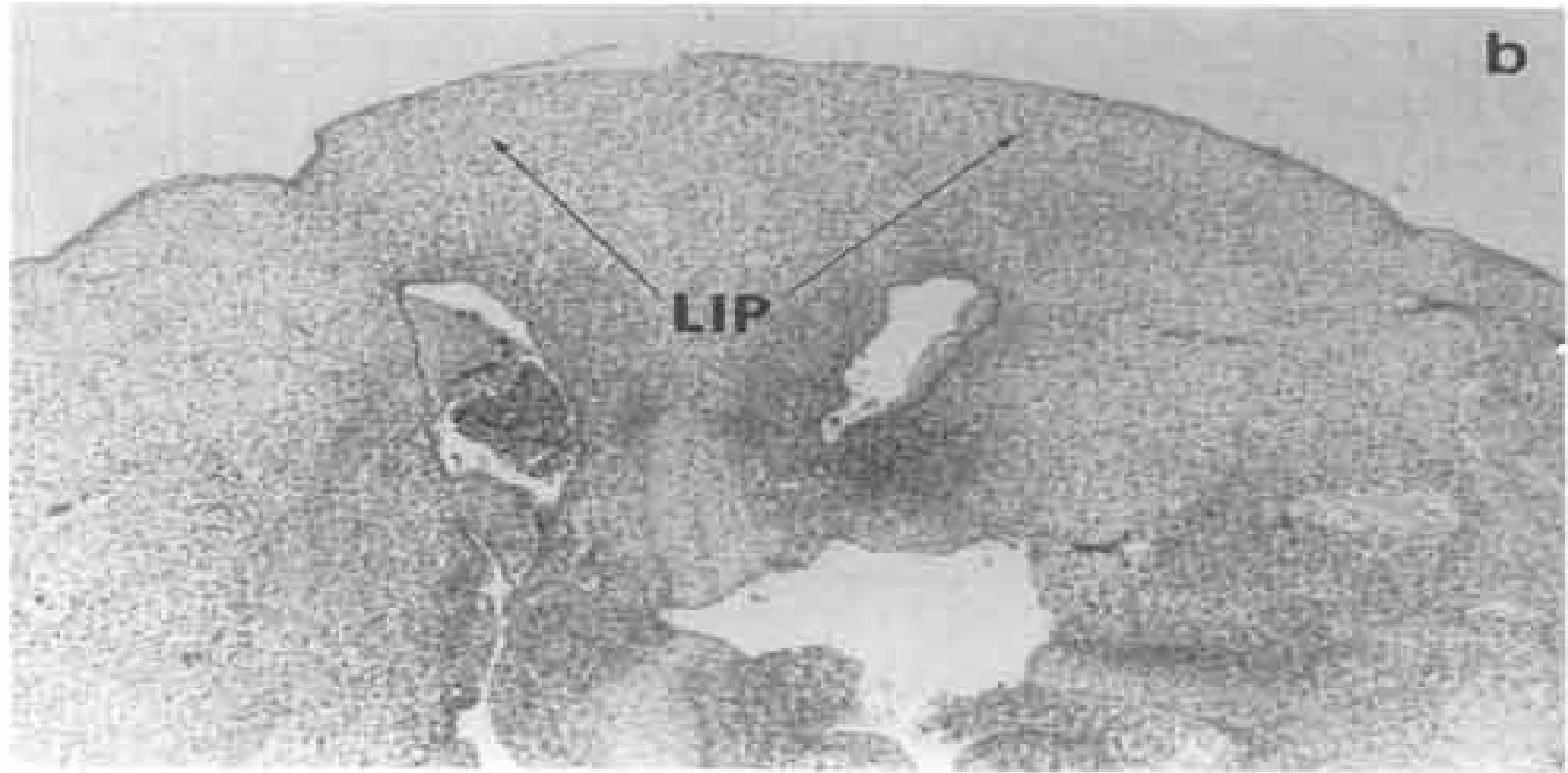
g

lip

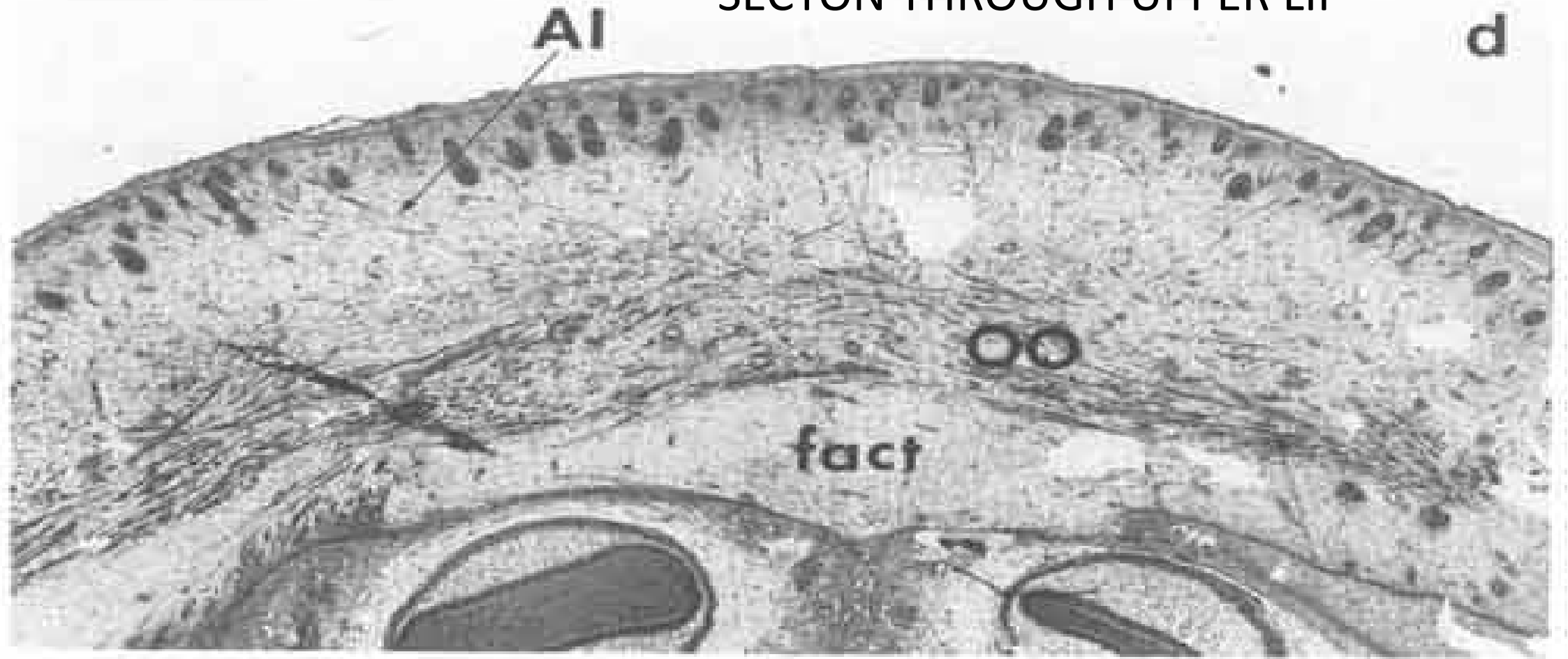


palate

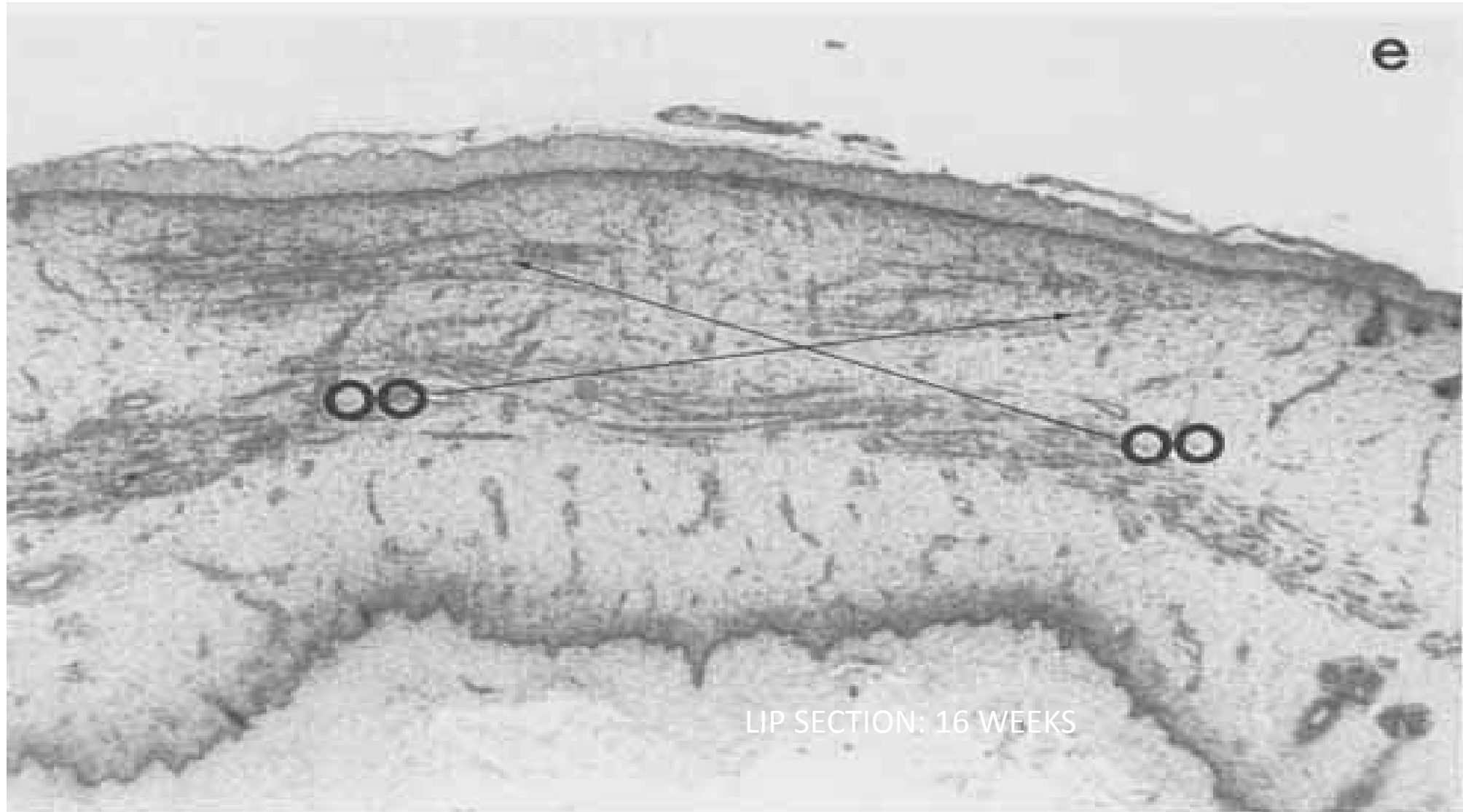




NORMAL 12 WEEK HUMAN FETUS:  
SECTION THROUGH UPPER LIP



NORMAL 13 WEEK HUMAN FETUS:  
SECTION THROUGH UPPER LIP



# Normal Development of the Philtrum

Medial Nasal Processes

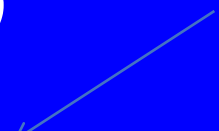
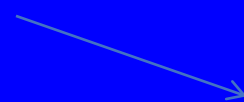


Secondary Structures  
(Frenulum Associated Connective Tissue)

Maxillary Processes



Secondary Structures  
(Orbicularis Oris Muscle Fibers)



Interaction



Normal Philtrum



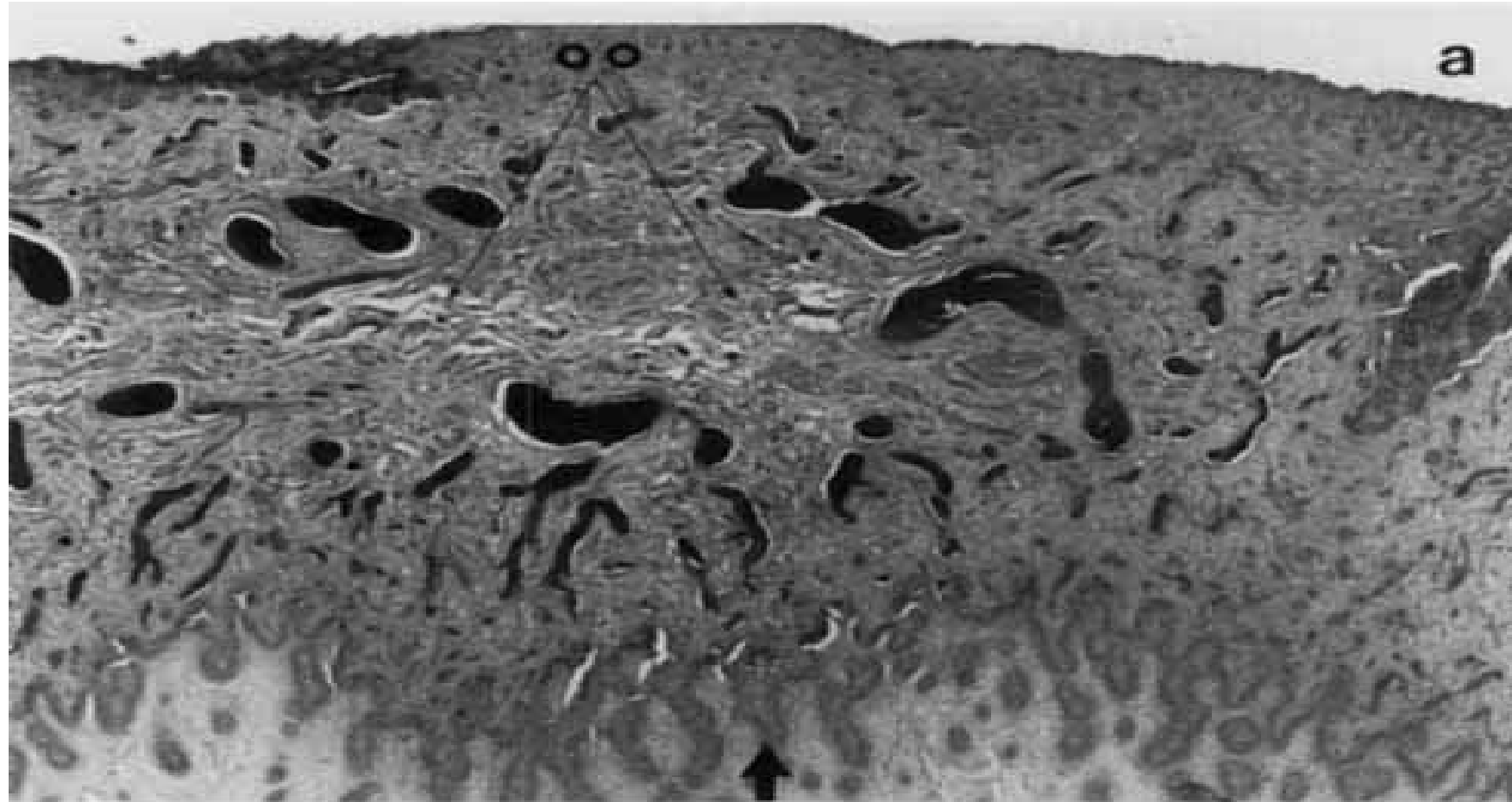


# STRUCTURAL BASIS OF PHILTRUM

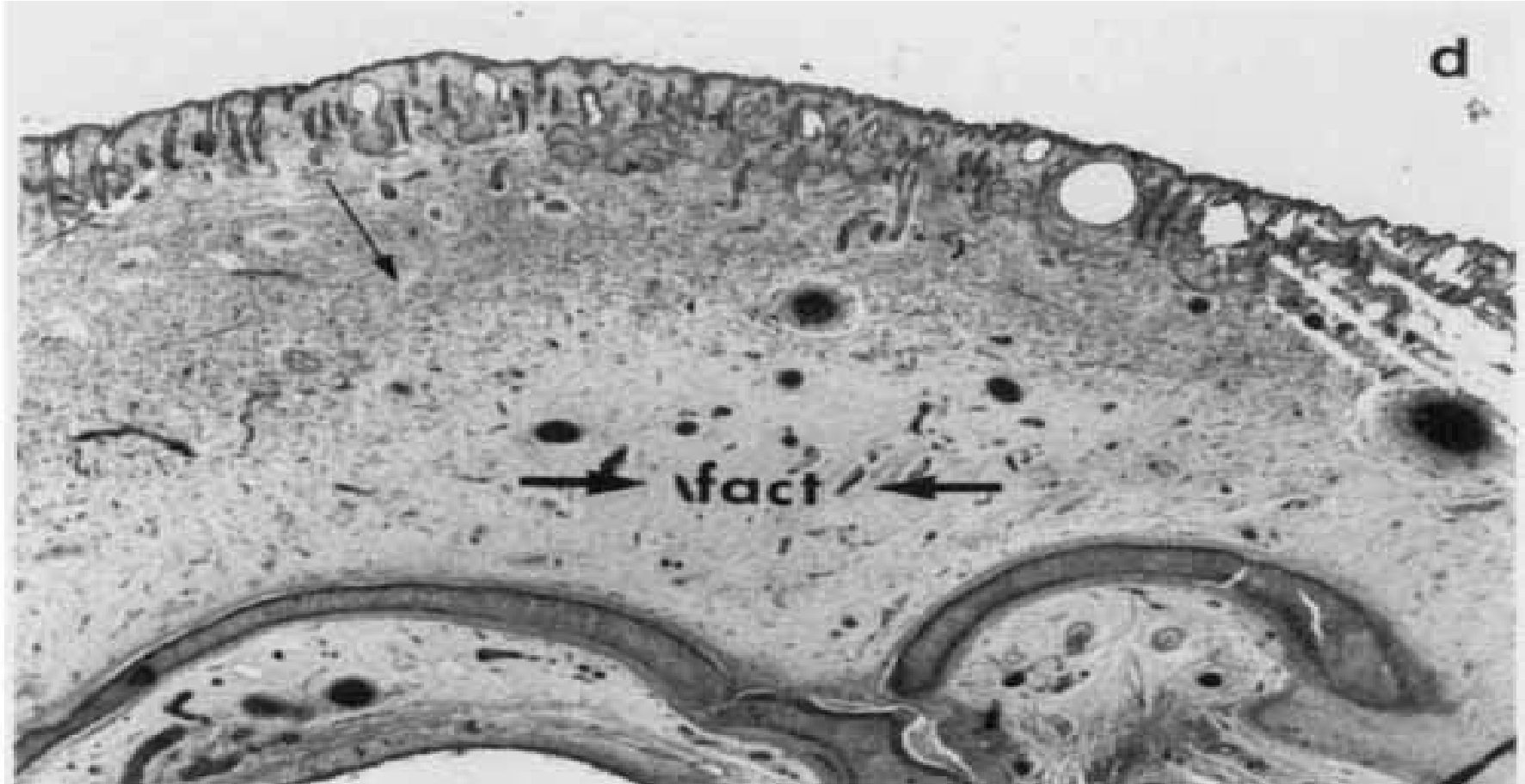
- Normal philtral anatomy:
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  - Heavy Prenatal Alcohol Exposure

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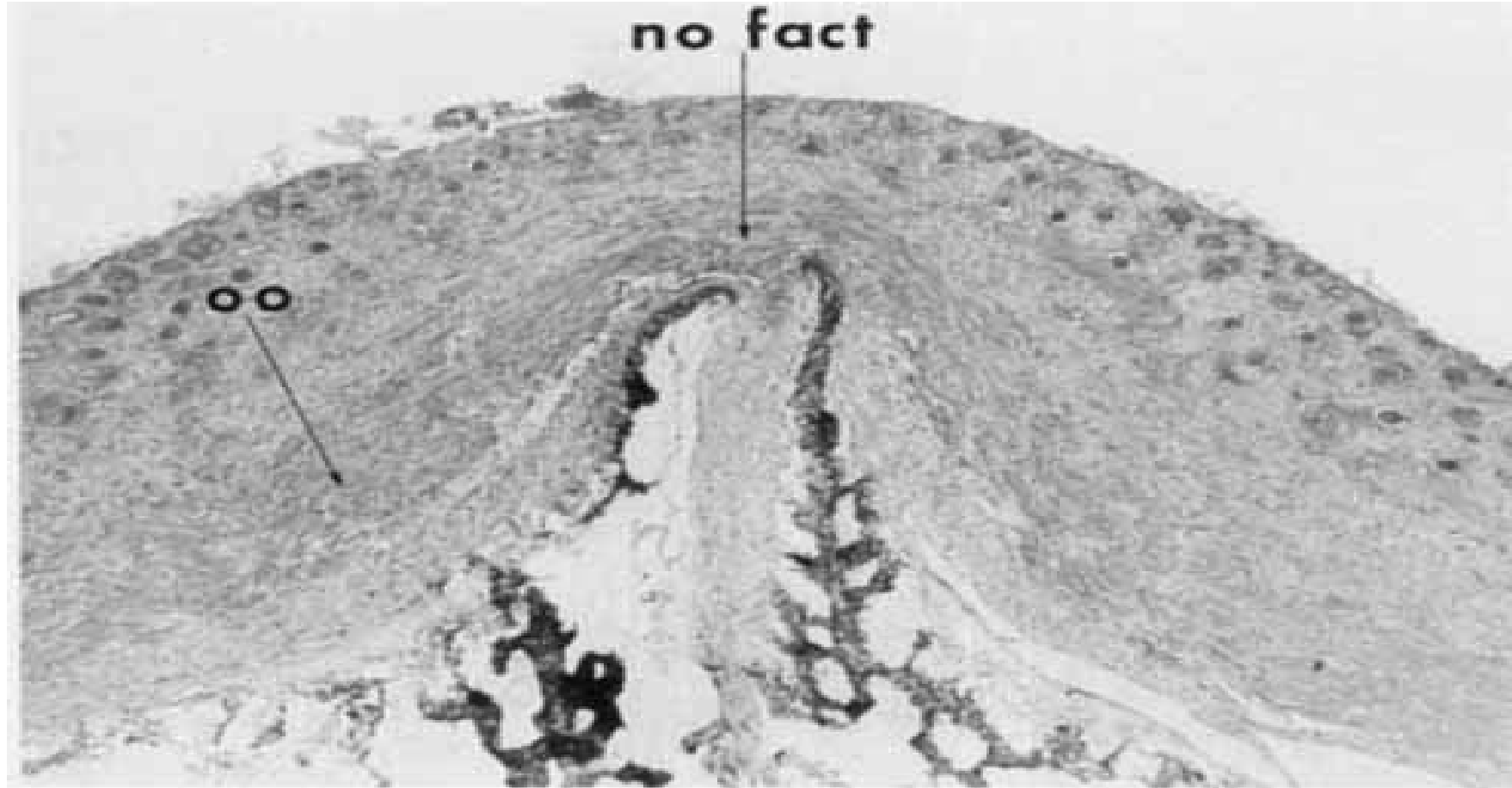








# Heavy Prenatal Alcohol Exposure



# Normal Development of the Philtrum

Medial Nasal Processes

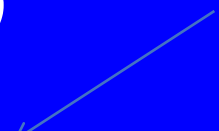
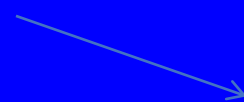


Secondary Structures  
(Frenulum Associated Connective Tissue)

Maxillary Processes



Secondary Structures  
(Orbicularis Oris Muscle Fibers)



Interaction



Normal Philtrum





# Conclusions

- The smooth philtrum and thin vermilion border of the upper lip are helpful for diagnosis of FAS in adolescents and adults up to 60 years of age
- However smoothness of the philtrum in normal adults over 60 years of age is common and results from hypotonia of muscles derived from the maxillary processes associated with older age
- Prior to 60 years of age the philtrum and vermilion border are consistent diagnostic features of FAS

# SMOOTHNESS OF PHILTRUM AND THINNESS OF VERMILION WITH INCREASING AGE IN NORMAL



5 y/o



10 y/o



15 y/o



20 y/o



40 y/o



50 y/o



60 y/o



80 y/o









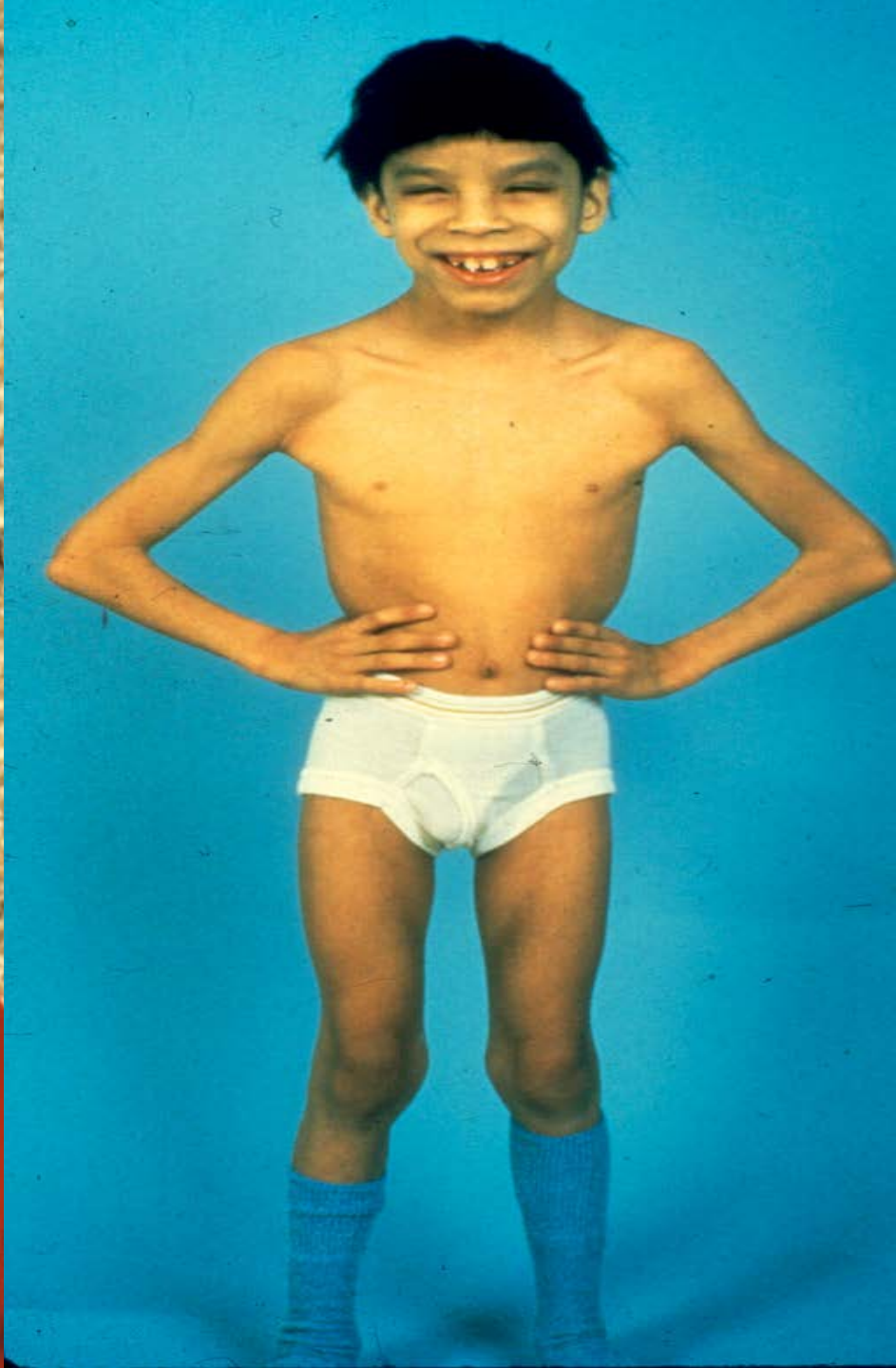














# SUMMARY

- Height can be helpful in diagnosis of FAS in Adolescents and Adults. Weight is less consistent
- Decreased brain growth manifest by a decrease head circumference remains a good diagnostic sign of FAS in the majority of Adolescents and Adults.
- PFL in Adolescents and Adults continue to be a good diagnostic sign of FAS
- The smooth philtrum, and thin vermilion of upper lip remain useful for diagnosis up until 60 years of age when the philtrum and vermilion border become smooth and thin in normal individuals

