Better Safe Than Sorry:

The Biological Basis of Fetal Alcohol Syndrome and other Alcohol-Related Birth Defects

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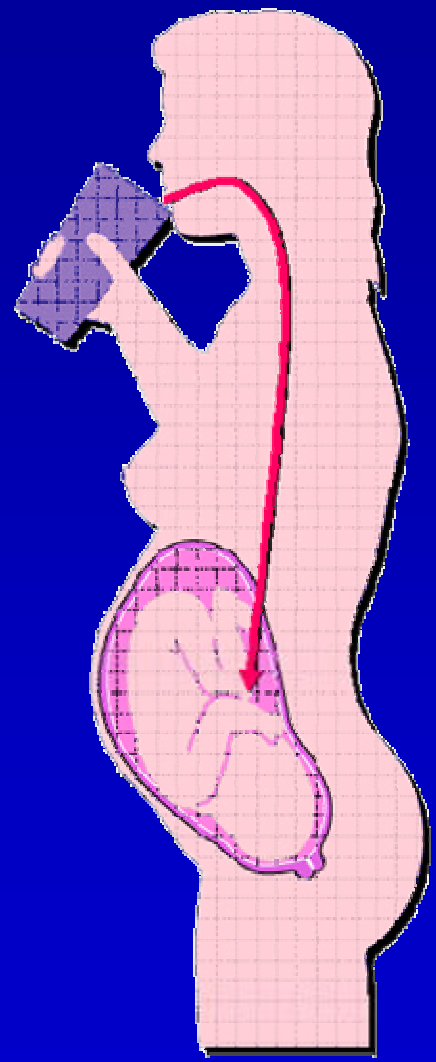
When a mother drinks, her unborn child is exposed to alcohol.



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Alcohol-Related Birth Defects Include:

- **Fetal Alcohol Syndrome (FAS)**

which is characterized by

1. central nervous system problems
2. low birth weight and height
3. typical facial features

- **Fetal Alcohol Effects (FAE)**

which result from maternal alcohol abuse but are found in the absence of the full-blown syndrome

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The facial features of Fetal Alcohol Syndrome are:

- Small eyelid openings (palpebral fissures)
- Short, upturned nose
- Long upper lip (from nose to mouth) with a thin red border and a deficient central groove (philtrum)
  Reduced size of the head (microcephaly)

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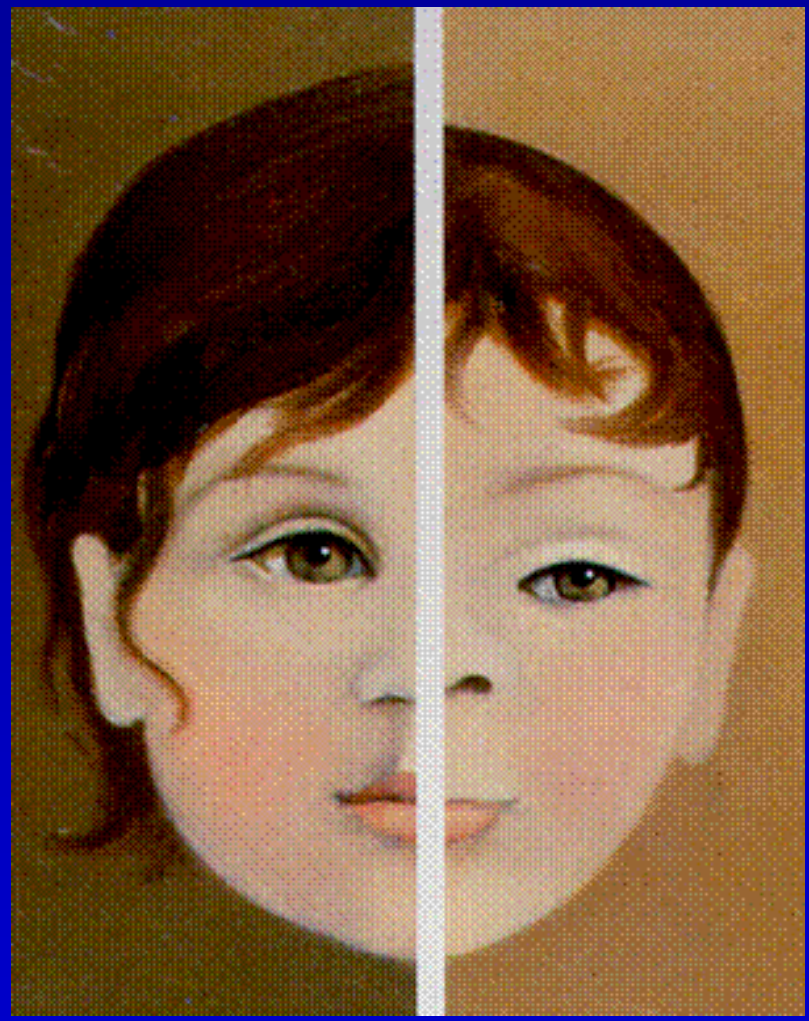

NORMAL FAS

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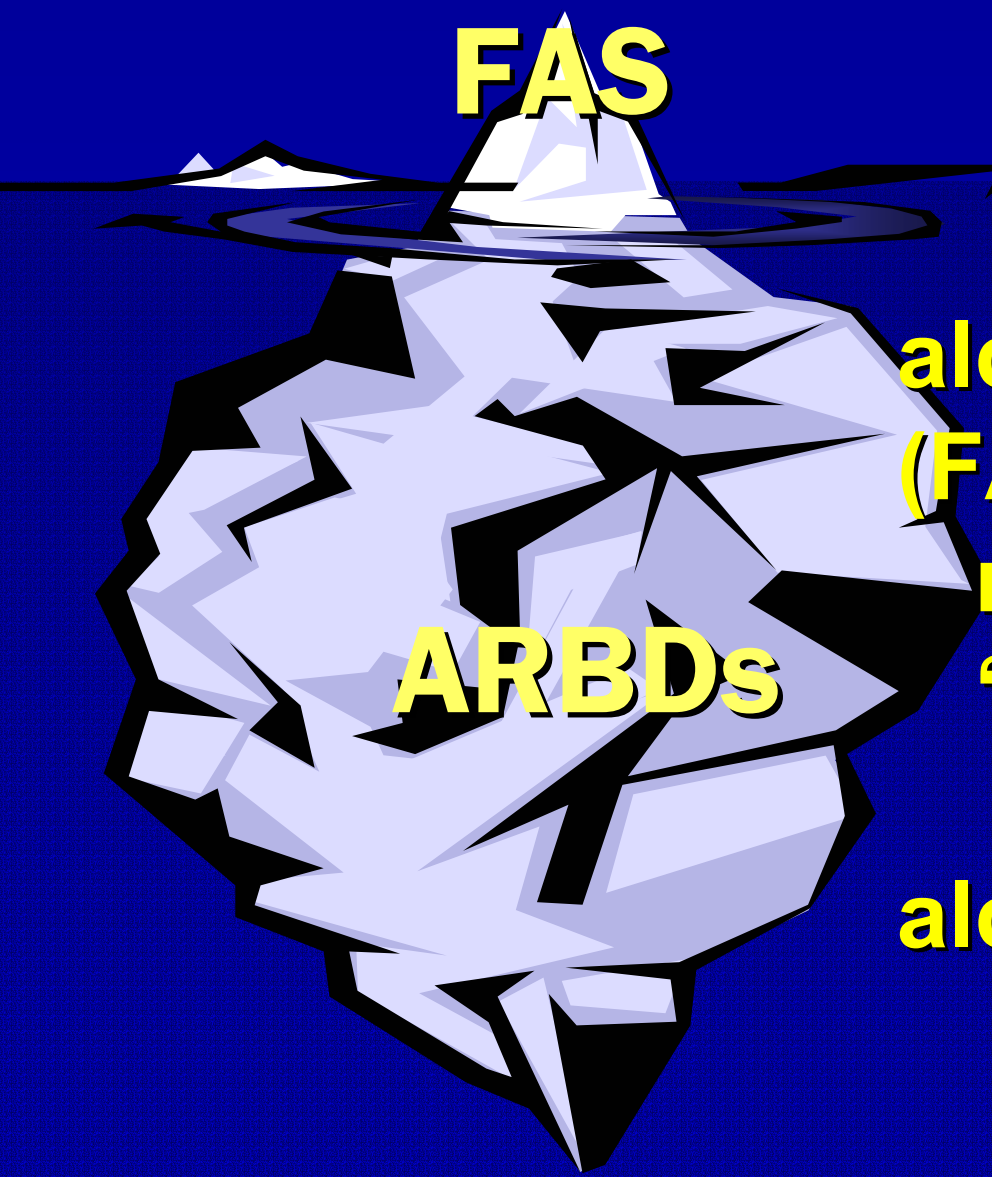

Full-blown fetal alcohol syndrome (FAS) represents only the "tip of the iceberg" relative to all alcohol-related birth defects (ARBDs).

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MATERNAL ALCOHOL ABUSE IS THE LEADING KNOWN CAUSE OF MENTAL RETARDATION IN THE WESTERN WORLD

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Children with alcohol-related birth defects typically have:

attention deficits

- language difficulties
- learning disabilities
- impulsive behavior
- poor judgment

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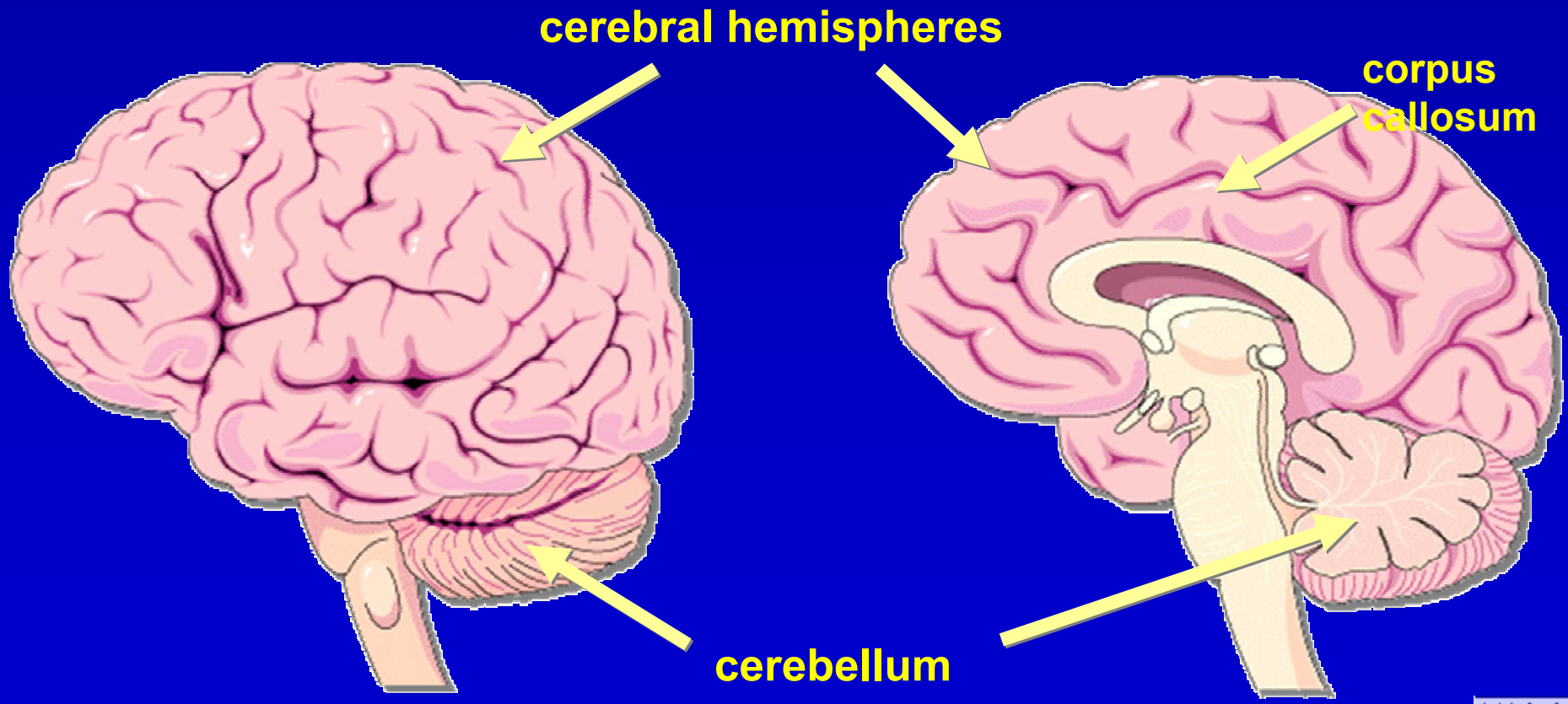
PRENATAL ALCOHOL EXPOSURE CAN PERMANENTLY DAMAGE THE BRAIN, AFFECTING IMPORTANT STRUCTURES SUCH AS THE CEREBELLUM AND CORPUS CALLOSUM, AS WELL AS SPECIFIC CELL POPULATIONS IN MANY OTHER REGIONS OF THE BRAIN

Whole brain

Cross-section



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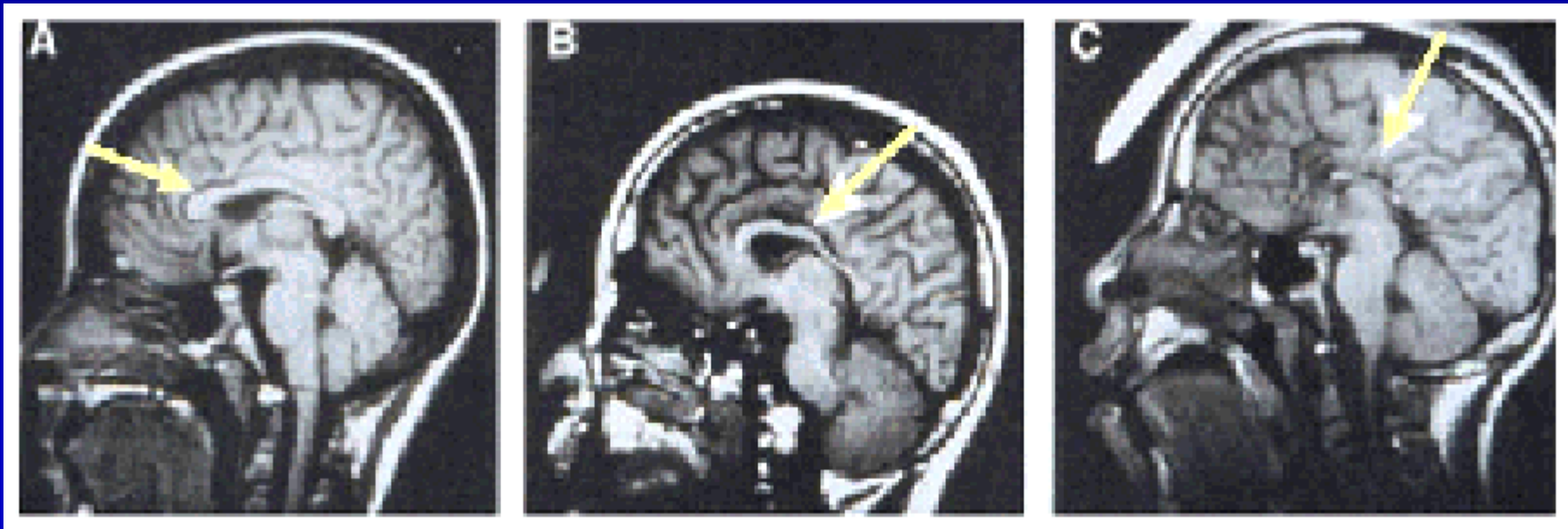
Visualization of the brain of a normal individual (A) and two with FAS (B, C) shows permanent loss of the tissue indicated by the arrows (portions of the corpus callosum)



Normal FAS FAS

Images courtesy of DR. S. Mattson

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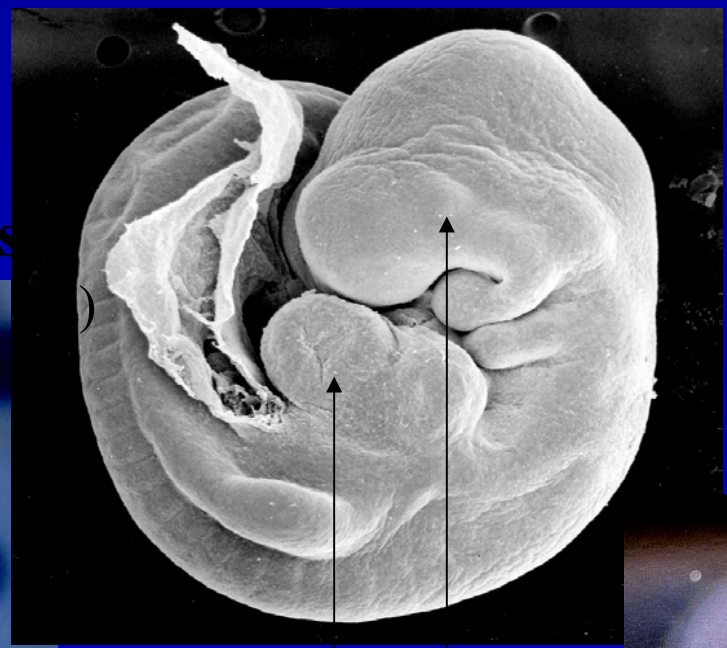
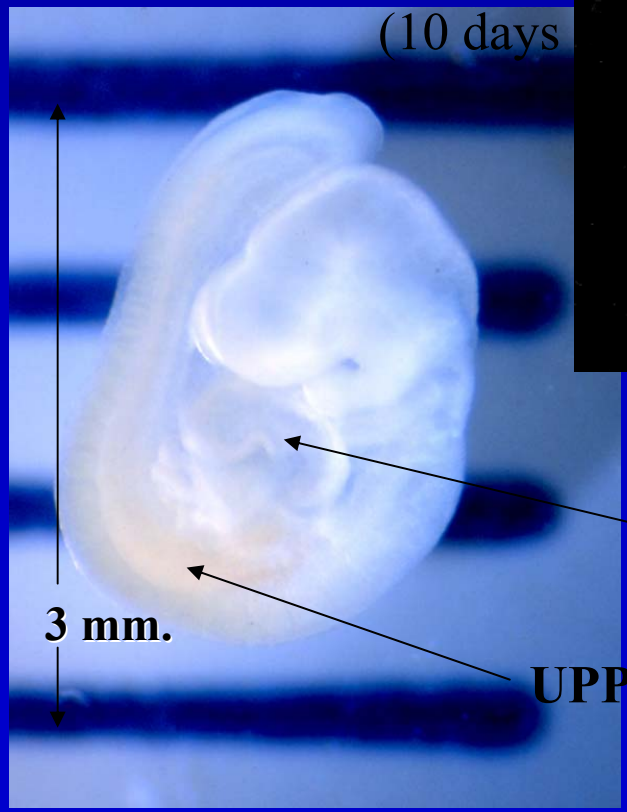
Similarities in mouse and human embryogenesis provide opportunities to study the effects of alcohol on development



Mous

(10 days)



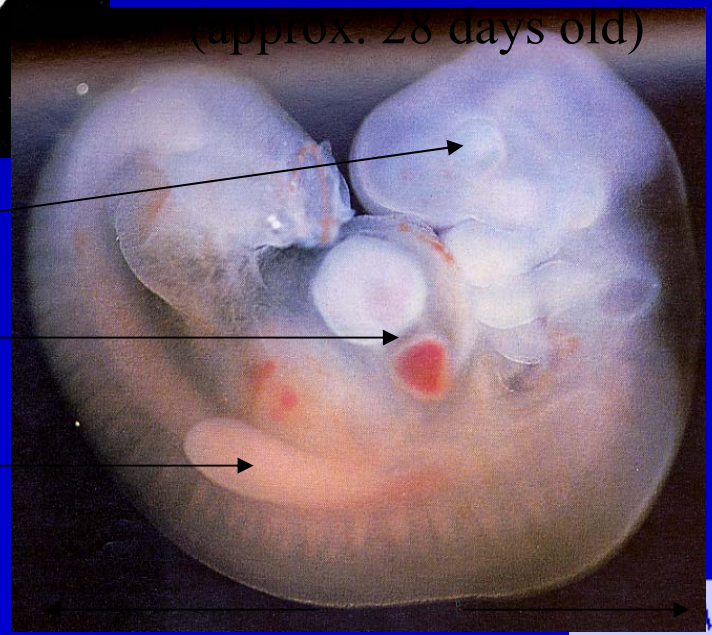
EYE

HEART

UPPER LIMB (ARM)

Human

(approx. 28 days old)



The facial features of Fetal Alcohol Syndrome can be seen in both a child and a mouse fetus that were exposed to alcohol during development.

child with FAS

Narrow forehead

Short palpebral fissures

Small nose

Small midface

Long upper lip with deficient philtrum

mouse fetuses

alcohol-exposed

normal

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The amount and timing of maternal alcohol use determine the type and extent of resulting birth defects.

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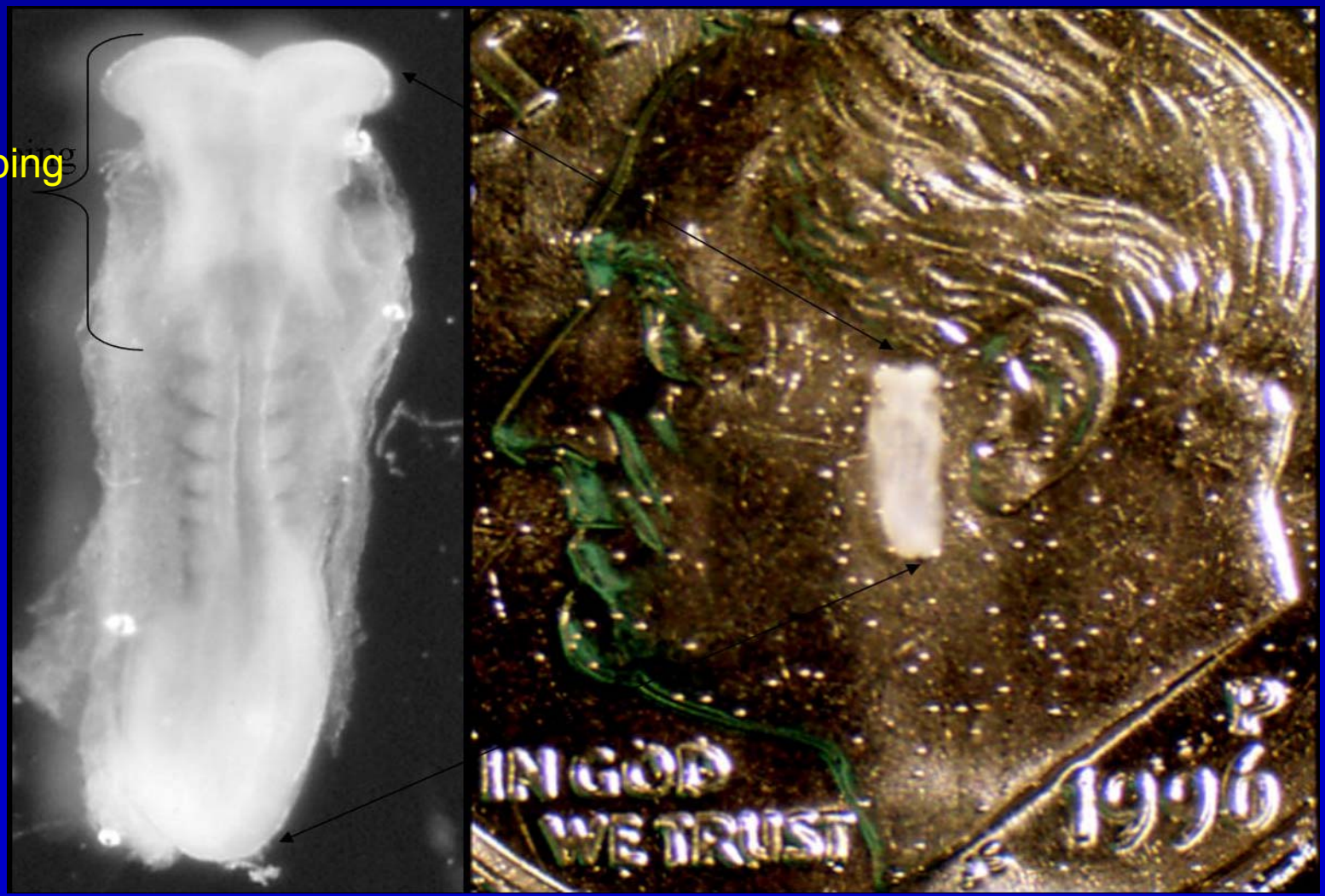
Alcohol can cause malformations and brain abnormalities in embryos that are only three to four weeks old



22 day old human embryo (about 2 mm.long, the length of the ear on the US dime)

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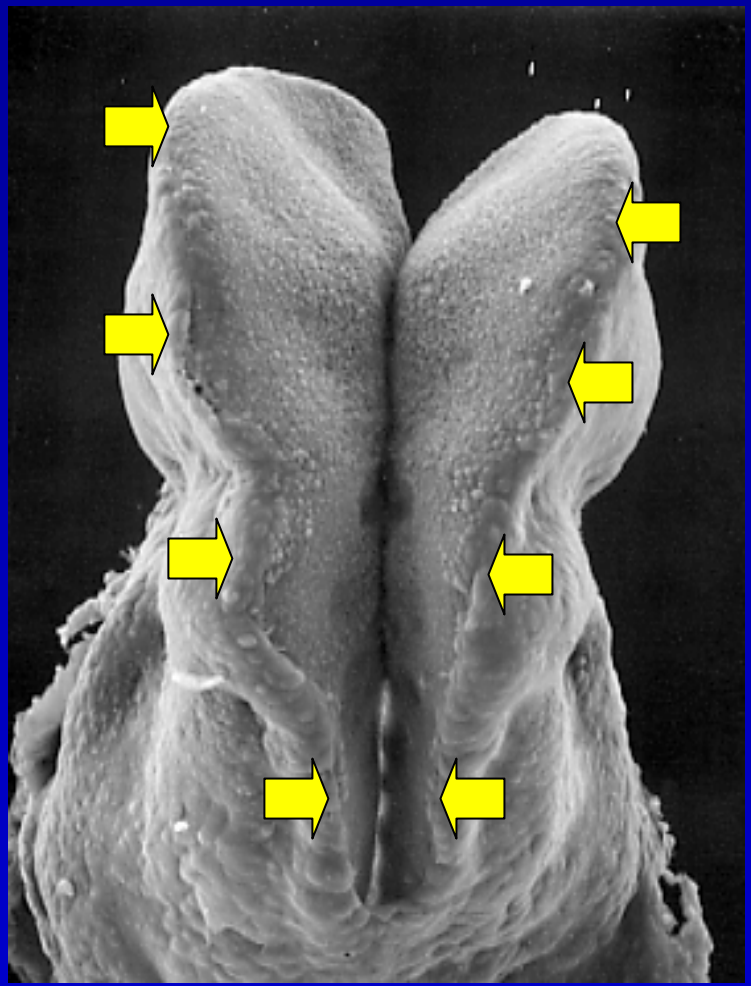
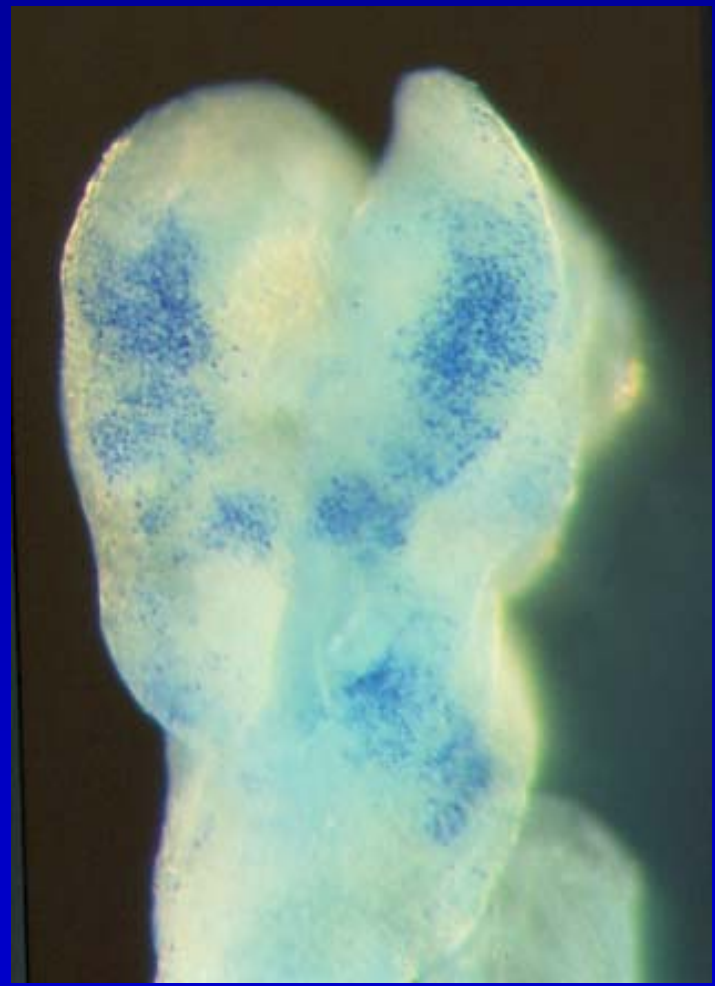
ALCOHOL KILLS SPECIFIC CELLS IN THE DEVELOPING BRAIN



Arrows surround a portion of the brain of a mouse embryo (viewed from the back) that is at a developmental stage corresponding to a 22-23 day human.



Cells killed by alcohol in the brain of a mouse embryo (at a comparable stage of development to that on the left) have taken up a dark blue stain.

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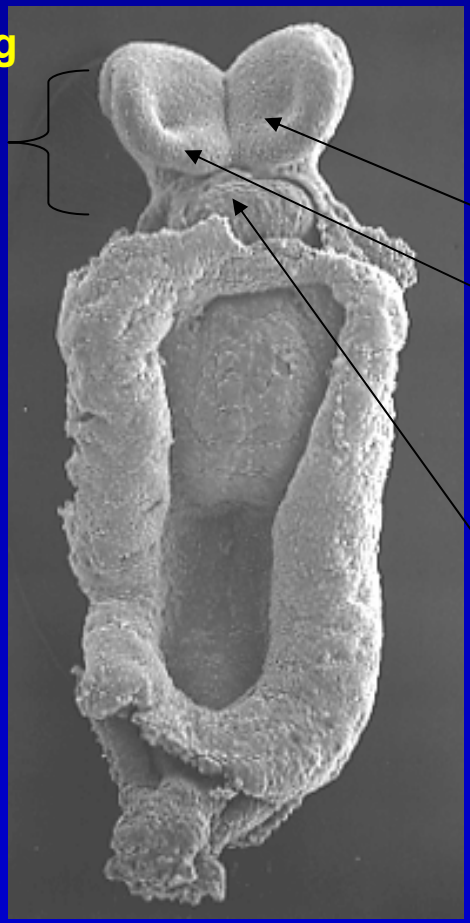
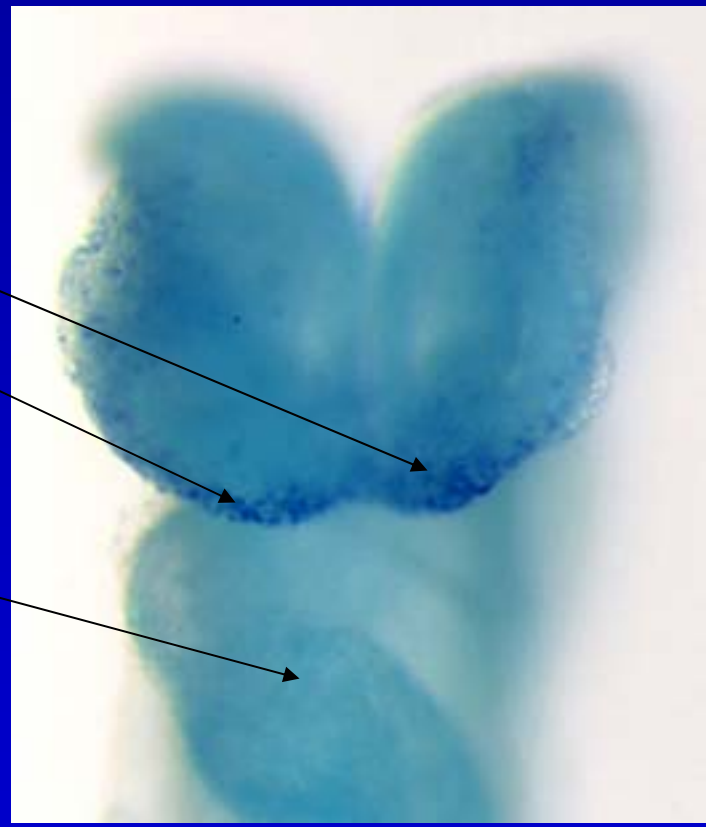
CELLS THAT SHOULD FORM MIDLINE STRUCTURES OF THE BRAIN AND FACE ARE KILLED BY ALCOHOL

Developing brain and face



Heart



Mouse embryo (viewed from the front) at a stage corresponding to a 22-23 day old human.

A close-up view of an alcohol-exposed mouse embryo shows cells killed by alcohol that have taken up a dark blue stain

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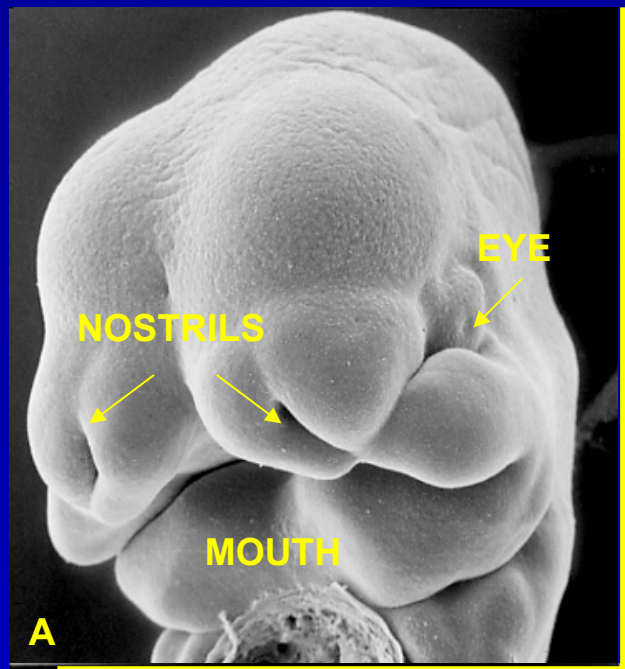
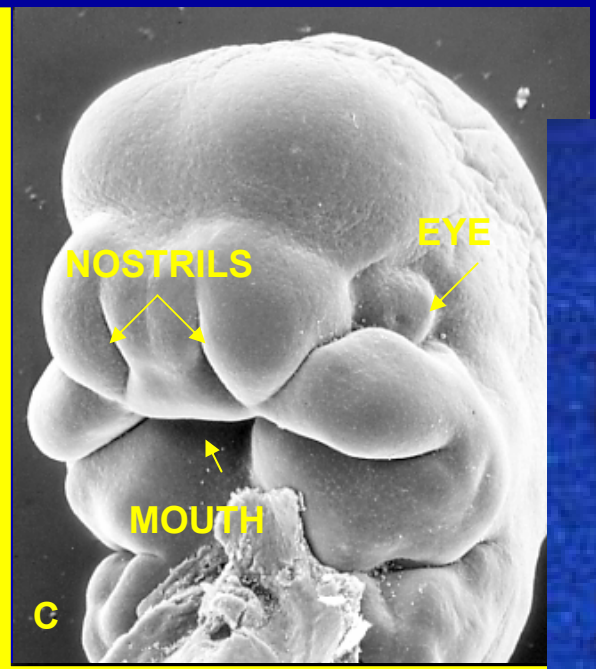
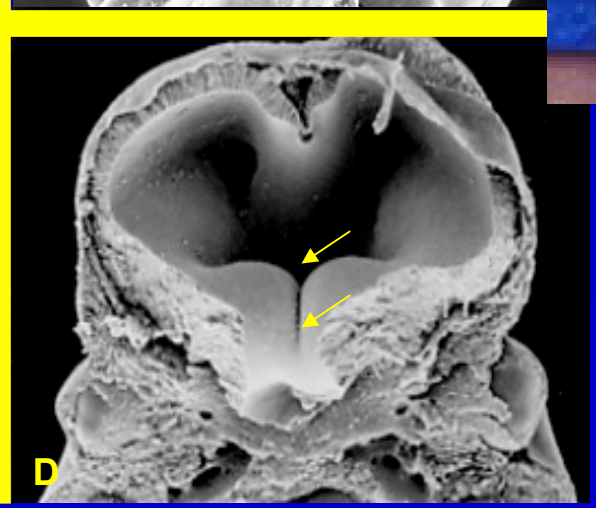
MIDLINE STRUCTURES OF THE FACE AND BRAIN ARE DEFICIENT IN ALCHOL-EXPOSED MOUSE EMBRYOS AND IN INDIVIDUALS WITH FAS





THE FACE OF A CHILD WITH FULL-BLOWN FAS HAS FEATURES THAT CAN BE CAUSED BY DAMAGE TO MIDLINE STRUTURES.



COMPARISON OF THE FACE (A) AND INTERIOR OF THE BRAIN (B) OF A NORMAL MOUSE EMBRYO AND ONE DAMAGED BY ALCOHOL (C&D) SHOWS THAT THE NOSTRILS ARE ABNORMALLY POSITIONED (C) AND THE BRAIN IS MISSING MIDLINE STRUCTURES (D)

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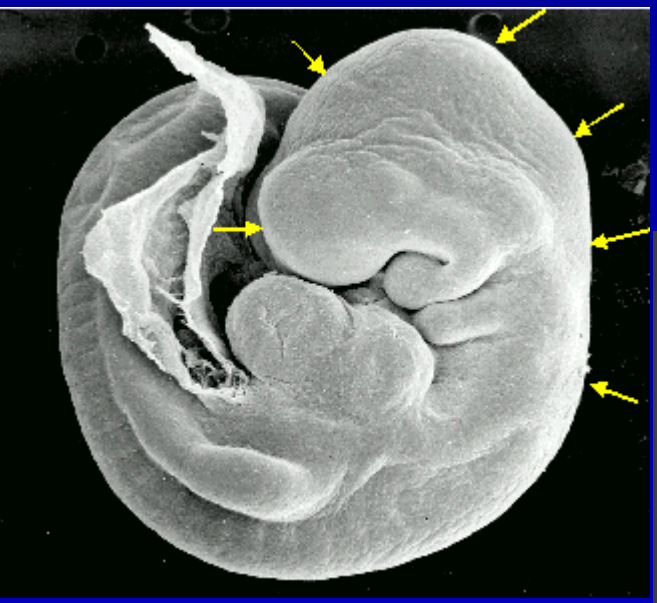
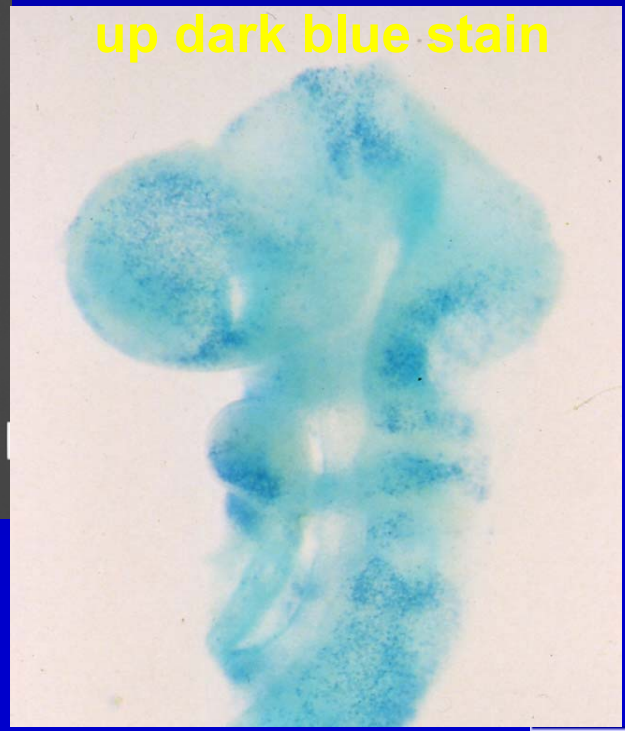
ALCOHOL KILLS SPECIFIC CELLS IN THE DEVELOPING BRAIN



The pattern of cell death varies with the stage of development.

Cells killed by alcohol have taken up dark blue stain



A cut made through the area outlined by arrows provides a view of the inside of the brain of a 10 day mouse embryo

(corresponding to a 28 day human)

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This child with FAS has a scar from a repaired cleft lip.

Cleft lip can also be caused by genetic or environmental agents other than alcohol.

EXPOSURE TO ALCOHOL DURING DEVELOPMENT CAN CAUSE DAMAGE TO ORGANS AND REGIONS OTHER THAN THE BRAIN

Alcohol also caused cleft lip in this mouse.

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By the ninth week of development the human fetus is about 24 mm. long. Damage caused by alcohol to the brain at this time and until birth can result in abnormal brain function.

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Excessive alcohol exposure can cause damage during all stages of prenatal development.

- **Pre-implantation: first 2 weeks**
- **Embryonic: 3-8 weeks after conception**
- **Fetal: from week 9 until birth**

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Alcohol can cause permanent damage to a baby before most women realize they are pregnant.

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Alcohol–related birth defects last a lifetime

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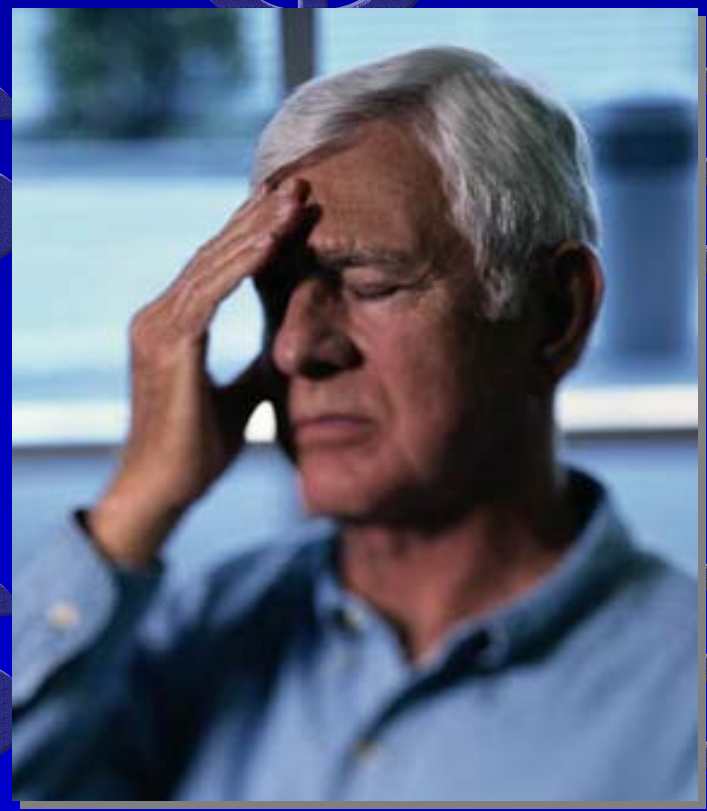
Alcohol-related birth defects are expensive:

- Monetarily – for treatment, care, and lost productivity. Costs are approximately $1.4 million over a lifetime for each individual with FAS
- Socially – relative to delinquency and to emotional drains on involved families.



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How much is too much

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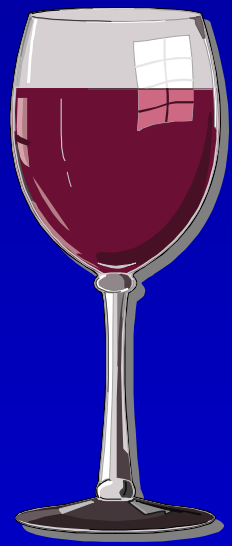
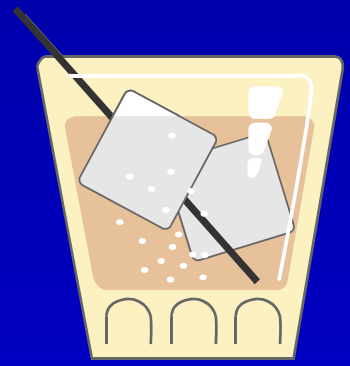
How much alcohol is in a drink?





12 oz beer = 5 oz wine = shot of liquor in a mixed drink

Each contains 0.5 oz of alcohol

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WARNING

Some drinks contain more than a "serving" (0.5 oz) of alcohol.

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NO ONE KNOWS WHAT A "SAFE" AMOUNT OF ALCOHOL CONSUMPTION DURING PREGNANCY MAY BE.

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Health advisories urge women who are planning pregnancy or are pregnant not to drink alcohol.

Despite warnings, frequent drinking among pregnant women appears to be increasing.

Frequent drinking is defined as 7 or more drinks per week or 5 or more drinks on at least one occasion.

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ALCOHOL-RELATED BIRTH DEFECTS ARE PREVENTABLE

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