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Cincinnati

February 13, 2001

FIELD(title) FIELD(first name) FIELD(last name)  
FIELD(address)  
FIELD(city), Tennessee FIELD(zip)

Dear FIELD(title) FIELD(last name):

Enclosed is the final report from the Centers for Disease Control and Prevention (CDC) on their investigation of the cleft lip/palate cluster in Dickson County. I will summarize the report and its recommendations and summarize what the Tennessee Department of Health and the Tennessee Department of Environment and Conservation are doing. A glossary is included to help explain some terms used in the report.

The CDC has confirmed that the rates of cleft lip/palate were increased in Dickson County between January 1, 1997, and October 31, 2000. They have not identified a cause. They recommend watching the numbers of infants born with cleft lip/palate in Dickson County to see if the cluster continues or if it stops. If the cluster continues, CDC recommends doing a more detailed study to try to find the cause. Please see the attached summary and the attached report from the CDC for details of the investigation.

The families with a child with a cleft lip/palate live in all parts of Dickson County. Most families use water supplied by the cities of Dickson, Charlotte, or Van Leer. Two families have private wells. Sampling of drinking water supplies of ten families has shown no evidence of contamination. The Environmental Assistance Office is sampling four more water supplies. If your water has not been tested and you want it tested, please call the Environmental Assistance Office at (615)687-7000. In addition, the Environmental Assistance Office has sampled many wells in Dickson County; the well and spring in the immediate vicinity of the landfill are the only areas outside the landfill to have shown any contamination.

Because the families with a child with a cleft lip/palate live in all parts of Dickson County, it is difficult to imagine how a source of air pollution could be related to the cluster. However, the Division of Air Pollution Control, in collaboration with the University of Tennessee, is modeling air concentrations of emissions from local industries. The air models predict the concentrations of chemicals in different parts of the county, taking into account such things as temperature, wind direction, wind speed, precipitation, and amounts of chemicals released from industries. Precise

air modeling will give us a realistic picture of air concentrations of various chemicals in different parts of the county. We will let you know the results when we have them.

The Tennessee Department of Health is putting into place the procedures to actively find all new cases of cleft lip with cleft palate, cleft lip only, and cleft palate only that occur in Dickson County and the surrounding counties. If you know of any new cases or want to find out the status of the continuing investigation, please feel free to call me at any time at (615)741-5683.

Sincerely,

Bonnie S. Bashor, Director Environmental Health Studies & Services  
Communicable and Environmental Disease Services

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Summary of the CDC Report:

The ~~EM~~ Tech EM Inc. summarizes what is known about the causes of cleft lip/palate and the rates found around the world. Cleft lip can occur with or without a cleft palate. Cleft lip with or without cleft palate is abbreviated as CL/P; cleft palate alone is abbreviated as CPO. CL/P is thought to have different causes than CPO. Several genes are involved in a complex way with CL/P and CPO.

CL/P is usually found in about 1-2 infants for every 1,000 births; CPO is usually found in about 0.7 infants per 1,000 births (or 7 infants per 10,000 births). Usually 33% of clefts affect the palate only (CPO); 46% affect the lip and palate; and 21% affect the lip alone (67% have CL/P).

The cause of CL/P and CPO is thought to be an interaction between genetic makeup and an environmental exposure during the first three months of the pregnancy. To medical researchers environment means anything except genetics - such as what we eat, drink, and smoke, viruses and bacteria we are exposed to, how we live our lives, the medications we take, and the chemicals we are exposed to. Environmental factors known to increase the risk of clefting are exposure of the fetus in the uterus to anti-epileptic drugs and isotretinoin (a medication for severe acne) taken by the mother. Other environmental factors that may increase the risk of clefting are maternal cigarette smoking, stress, obesity, diabetes, and exposure to some organic solvents. Use of multivitamins by the mother during the first trimester may decrease the risk of clefting.

The Preliminary Results section discusses how the cluster was confirmed, the results of the medical records review, and the result of the interviews. The Centers for Disease Control and Prevention (CDC) and the Tennessee Department of Health (TDH) found 18 infants born between January 1, 1997, and October 31, 2000 with CL/P or CPO in Dickson County. All mothers were living in Dickson County at the time of birth of the infant. The discussion of finding rates of clefting in Tennessee and Dickson County before 1997 is very involved. The result of the discussion is that no one can be sure what the rates of clefting are in Tennessee or were in Dickson County before 1997. The eighteen cases of clefting are more than we would expect, and the cluster is real.

Eleven (61%) infants had CL/P and 7 (39%) had CPO. This is very close to what is found around the world (67% with CL/P and 33% with CPO). The type and severity of clefting ranged from mild to severe.

Staff from the CDC completed interviews with 15 of the 18 mothers. The following table summarizes the information about possible risk factors for clefting.

Some risk factors related to clefting were found among the 18 mothers. But no one factor seems to account for the cluster in Dickson County. It is interesting that six infants were born prematurely, but that may be the normal rate among infants with CL/P.

Other studies of cleft lip and palate have shown clustering in geographical areas and over time, without an obvious explanation. CDC does not know if the cluster in Dickson County is due to

some unidentified exposure, a normally high rate, or if it is a statistical variation that will disappear.

CDC recommends that we continue to follow the numbers of infants born with CL/P to see if the high rate continues or stops. If the rate continues to be high, CDC recommends a more detailed study to try to find the cause.

Table  
Risk Factors Associated with Clefting

Possible Risk Factor	# Answering Yes	# Answering No
Vitamin use before pregnancy (protective)	2	13
Prenatal vitamin use (protective)	13	2
Smoking throughout 1st trimester	4	11
Some smoking in 1st trimester	7	8
Alcohol use in 1st trimester	0	15
Use of anti-epileptics or isotretinoin *	0	15
Obesity (BMI > 30) *	2	13
Gestational diabetes	2	13
Occupational exposure to relevant chemicals	0	15
Family history of clefting	1	14
Family history of tooth agenesis *	2	13
Preterm delivery	6	9
Municipal water source	13	2

\* See the Glossary

## GLOSSARY

**22q11 deletion:** an example of short-hand used by scientists to describe an abnormality of the DNA of a gene. 22 refers to chromosome 22; q refers to the long arm of the chromosome; 11 refers to band 11; a band is an area of a chromosome that stains darkly. The short-hand means that a deletion of a part of a gene has occurred in band 11 of the long arm of chromosome 22. This short-hand is said as "twenty-two q one one."

**Alveolar ridge:** the bony ridge where the sockets for teeth and their roots will form

**Anomalies:** Plural of anomaly, marked deviation from the normal, a defect. Used as in congenital anomalies (anomalies that a person is born with).

**Anterior:** in front of

**Anti-epileptic drug:** a medication that prevents seizures

**Bifid uvula:** the uvula is fleshy lobe at the back of the soft palate that hangs down. It is visible in the back of the mouth. A bifid uvula is one that has a split in it.

**Body mass index:** the weight in kilograms divided by the square of the height in meters. Weight in kilograms is equal to the weight in pounds divided 2.2. The height in meters is the height in inches times 0.0254.  $BMI = (\text{pounds} \div 2.2) \div (\text{inches} \times 0.0254)^2$ .

**Case:** a child in Dickson County with a cleft lip/palate born between January 1, 1997 and October 31, 2001.

**Case Mother:** the mother of a child with a CL/P who lives in Dickson County whom we interviewed

**Chromosomal abnormality:** when the chromosome has a mistake in it

**Chromosome:** a structure in the nucleus that contains the genes of the individual; the structure is composed of a long chain of DNA that wraps itself into a spiral or helix. People have 46 chromosomes, arranged into 23 pairs.

**Embryologic:** an adjective of the noun embryo. In people, the developing child is called an embryo from about two weeks after fertilization to the end of the seventh or eighth week of gestation.

**Environment:** to medical researchers environment means anything except genetics - such as what we eat, drink, and smoke, viruses and bacteria we are exposed to, how we live our lives, the medications we take, and the chemicals we are exposed to.

**First trimester:** the first three months of a pregnancy

**Gene:** the unit of heredity found on chromosomes

**Genetic susceptibility:** another way to describe multifactorial disorders - see below

**Hard palate:** the rigid, bony part of the palate that is closer to the teeth

**Incisive foramen:** the area in the embryo where the incisor teeth will develop, including the area where the nerve for the incisor teeth will grow

**Incomplete fusion:** when the sides of the palate that are growing towards each other do not join successfully

**Intrauterine:** within the uterus

**Isotretinoin:** a medication used to treat severe acne; the most common brand name is Accutane

**MACDP:** Metropolitan Atlanta Congenital Defects Program

**Malformation:** abnormal or faulty formation, examples are a cleft palate, heart defect, or leg that does not develop correctly in the embryo or fetus

**Mendelian genetics:** Mendelian genetics are responsible for some diseases. A Mendelian disorder in a person is one that is caused by a defect in one gene in one or both parents that the person inherits; another phrase that means the same thing is, simply inherited. Examples of simply inherited diseases are: color blindness (defect in the X chromosome), sickle cell anemia (the same defect in a chromosome in both parents), cystic fibrosis (the same defect in a chromosome in both parents), and Huntington's chorea (a defect in one chromosome of one parent)

**Mucosal web:** the thin layer of tissue that covers a submucous cleft; the tissue secretes mucous, so it is called mucosal

**Multifactorial disorders:** disorders that are caused by an interaction of multiple genes and environmental factors. Another phrase that means the same thing is, genetic susceptibility. Examples of multifactorial diseases are: cleft lip and palate, congenital heart disease, diabetes mellitus, multiple sclerosis, and hypertension (high blood pressure).

**Muscular diastasis of the soft palate with mucosal integrity:** separation of the muscles of the soft palate, while the tissues covering the palate and secreting mucous are intact

**NBDPN:** National Birth Defects Prevention Network

**Notching of the posterior border of the hard palate:** an indentation or depression at the back of the hard palate

**Obesity:** having a body mass index (BMI) greater than 30.

**Orofacial:** refers to the mouth and face

**Overt:** readily seen

**Palatal shelves:** during embryologic development, the secondary palate looks like shelves as it grows

**Palate:** the partition separating the oral and nasal cavities

**Parity:** number of children that a mother has had

**PDA:** patent ductus arteriosus, an opening between the aorta and pulmonary artery that does not close at birth

**Pharynx:** the area in the throat between the mouth and nasal passages at one end and the larynx and esophagus at the other end

**Primary palate:** that part of the palate that comes from the area in the middle of the face where the nose is developing in the embryo

**Rate:** how often a disease appears among a certain number of people. For cleft lip/palate the rate is usually written as the number of infants born with cleft lip/palate for every 1,000 infants born in a year.

**Secondary palate:** most of the palate, formed when the sides of what will be the palate grow towards each other in the embryo

**Soft palate:** the fleshy part of the palate that is behind the hard palate, toward the throat

**Submucous cleft:** clefts of the hard or soft palate that are covered by a thin layer of tissue called the mucosal web

**Syndrome:** a group of signs and symptoms that occur together and characterize a particular abnormality

**Teratogenic:** an adjective of the noun, teratogen, a factor that causes the production of physical defects in the developing embryo

**Tooth agenesis:** some teeth never come in because the area where teeth are supposed to come in did not develop properly in the embryo

**Velopharyngeal incompetence (VPI):** the soft palate and pharynx do not function as they are supposed to