Although the impact of environmental contaminants on human health has been widely studied, few reports in the Canadian literature have focussed on the specific vulnerability of children. Because of their rapid growth, physiologic and metabolic immaturity, the fetus and child are often at increased risk from toxic substances in their environments. Furthermore, greater air, food and fluid intakes relative to body weight compared with the adult, increase the child’s potential for excessive exposures. The crawling stage of infancy, the play patterns and short stature of toddlers also serve to increase their exposure to dust and heavy and volatile substances which accumulate near the floor. This article provides an overview of some of the developmental physiologic, anatomic and behavioural features of the fetus, infant and child which increase their vulnerability to environmental contaminants in comparison with adults. Specific examples are given.

**ABSTRACT**

Although the impact of environmental contaminants on human health has been widely studied, few reports in the Canadian literature have focussed on the specific vulnerability of children. Because of their rapid growth, physiologic and metabolic immaturity, the fetus and child are often at increased risk from toxic substances in their environments. Furthermore, greater air, food and fluid intakes relative to body weight compared with the adult, increase the child’s potential for excessive exposures. The crawling stage of infancy, the play patterns and short stature of toddlers also serve to increase their exposure to dust and heavy and volatile substances which accumulate near the floor. This article provides an overview of some of the developmental physiologic, anatomic and behavioural features of the fetus, infant and child which increase their vulnerability to environmental contaminants in comparison with adults. Specific examples are given.

**Children are Different: Environmental Contaminants and Children’s Health**

*Graham W. Chance, MB, FRCP, FRCPC, Eef Harmsen, PhD*

It was not until the 15th century that artists, notably the Italian painter Raphael, began to depict differences in body proportions between adults and children in their paintings. Until then children and cherubs had been painted as though microcephalic. The realization that children are not little adults took much longer to penetrate science. In the context of the potential for adverse effects of environmental contaminants, the differences are especially pertinent. This paper gives an overview of some of the features of growth and development in utero and through childhood, and the characteristics of children’s behaviour which increase risks from both contaminants themselves and exposure to them.

**Developmental characteristics**

Growth and the accompanying anatomic and physiological changes in various organs and organ systems critically differentiate children from adults. Growth in utero proceeds at an extraordinary rate, especially that of the brain. The rapidly changing body to head ratio which occurs in utero was noted in an article published in 1929. The authors reported that early growth of the brain resulted in a 1:1 ratio at 6 weeks gestation, a 2:1 ratio at 12 weeks, and a 3:1 ratio by term, compared with a 6:1 ratio in the adult. Overall growth velocity is most rapid in utero, continually decelerating postnatally until the pubertal spurt. Today we have better understanding of the complexities of this growth.

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**Brain growth**

Research during the past 20 years has revealed the complexity and potential vulnerability of human brain growth. Many different types of neurones exist in groups of similar morphology which are generated at critical times throughout fetal life and early infancy, some of which cannot be replicated, but which may determine intellectual and behavioural performance into adulthood. Early in development neurones are produced in excess but by the process of organization, which includes cell differentiation and migration, and programmed cell death, they are reduced in number to approximately 100 billion by completion of gestation. Axonal growth and synaptogenesis commence in fetal life. Synaptogenesis progresses massively from shortly before, and subsequent to birth so that by age three years a child’s brain has about 1,000 trillion synapses. During later growth in childhood and adolescence synapse reduction occurs, to about 500 trillion in the adult.

At all phases of growth the brain is vulnerable to environmental influence: timing may be critical, as for example determination of visual preference, “fight or flight” responses, or gender specificity. It is now accepted that this phase of brain development is dependent for organization of pathways on incoming electrical impulses. Environmental agents are recognized which interfere with these various phases of growth. A feature of neural tissue growth mentioned above is its finite nature: critical periods missed or critical cell systems lost will not be replaced, unlike in epithelia and other organs where potential for multiplication or hypertrophy persist throughout life.

Other organ systems relevant to this discussion are the lungs, the immune system...
and the genitalia. Whereas bronchial branching in the developing lung is completed early in fetal life, alveolar budding and development continues into late childhood, increasing the alveolar surface area from 3 square metres at birth to 75 square metres in the adult. Although the fetus is capable of mounting a cell-mediated immune response, for example in response to transplacentally acquired viral infection, the immune system is relatively immature at birth. Partial immune protection for the first weeks of life is passively acquired before birth from immunoglobulin (IGG) transported transplacentally in the third trimester of pregnancy, and postnatally from cells and immune globulins (IGM and IGA) secreted in maternal milk. Maturation occurs in the months following birth as the infant is exposed to foreign antigenic substances. The effect of intrauterine exposure to polychlorinated biphenyls (PCB) on the fetal immune system and neonatal leukocyte responses are discussed by Tryphonas on page S51 of this supplement. The phenotypic characteristics of the female and male genitalia develop during organogenesis, being essentially completed by 12 weeks. The female fetus acquires her full complement of primary oocytes by birth; in contrast spermatogenesis is not initiated until puberty.

The three-fold higher surface area to body mass ratio of the infant, with its resultant excess heat loss, and the increased metabolic needs of growth and activity, result in substantially higher minute volumes of gas exchange in the lungs compared with the adult (Figure 1). As shown, while the metabolic rate is higher in the growing infant, total air intake per kg body weight is maximal in older children because of their activity patterns. Clearly this is a factor of importance with regard to inhaled pollutants and allergens.

**Developmentally based differences between children and adults**

Due to their anatomical and/or physiological immaturity, children differ from adults in many biological characteristics: the distribution of body water changes with age; the total body water and extracellular water are higher in the infant; daily water intake per kg body weight of the infant and young child is almost three times that of the adult; plasma protein binding capacity is reduced in the newborn and young infant compared to older age groups; likewise, the blood-brain barrier begins to develop in the fetus but is significantly less efficient in the young infant, becoming fully effective by about age six months.

Developmental maturation of hepatic and renal function tend to occur concurrently. At birth, Phase 1 reactions in the liver are immature; activity generally increases rapidly during the next few months but patterns of development vary. For example, in rats glutathione reductase activity was shown to follow a biphasic pattern after birth. Activity of the P450 cytochrome family increases after birth, childhood values exceeding those seen in adolescence. Likewise, depending on the particular substrates under consideration, Phase 2 reactions generally appear to increase from low levels of activity before birth to values in the first months to years which are higher than in the adult. Acetylation patterns also seem to vary, peak values being attained fairly early in childhood in some instances. Again, patterns of activity vary considerably with age.

Renal excretion depends on maturation of glomerular filtration, and tubular reabsorption and secretion. The glomerular filtration rate increases following birth to reach adult values by age 5 months, being partly determined by an increase in cardiac output and a decrease in peripheral vascular resistance. Tubular function which also is low at birth increases more slowly in early childhood. Overall, renal function reaches adult capacity by about age 16 months. The ontogeny of hepatic and renal function described above is important in regard to consideration of handling and elimination of many therapeutic and toxic agents. Caffeine clearance, for example, was shown to increase almost tenfold from birth to age six months, subsequently falling to about one third of the six-month level in the adult.

Age-based differences exist in intestinal absorptive capacity. Gastric acidity is low in the newborn, not achieving adult values until several months of age. Most environmental chemicals are absorbed by simple diffusion based on their lipid solubility: low gastric acidity will increase the non-ionised fraction of many of these substances and therefore permit increased absorption. The infant’s low gastric acidity also permits colonization of the intestinal tract by organisms which convert nitrates to nitrites and produce Beta-glucuronidase.
Environmental toxicants have made the fetus and young infant render it particularly vulnerable to environmental contaminants. The small intestine of the newborn and young infant permits absorption of potentially large molecules, including potential allergens. The intestinal mucosa also absorbs substances selectively in accordance with growth requirements, iron and calcium being typical examples. In regard to toxicants, the enhanced absorption and deposition of lead by infants and children appears to parallel absorption of calcium and other minerals. The influence of age on the efficiency of lead is illustrated in Table I.

Other routes of absorption which render the fetus and young child more susceptible than adults to toxicants include the placenta, the skin and the lungs. Dermal absorption, especially of lyophilic substances, is increased when the cornified layer is missing or reduced as in low birthweight and young infants. In the fetus there is a net flow of fluid out of the lungs which increases progressively during gestation, however, fetal breathing movements are such that amniotic fluid contents may reach the distal airways, especially in the stressed fetus.

### Developmental effects

As a consequence of the changes occurring during growth and development, there are numerous possible effects of environmental agents on the fetus and child. The rapid growth and critical developmental changes occurring in the brain of the fetus and young infant render it particularly vulnerable to environmental contaminants. Environmental toxicants have destroyed the concept held for many years that the fetus is fully protected from environmental agents on the fetus and child.

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Average Absorption Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - 2</td>
<td>42 - 53</td>
</tr>
<tr>
<td>2 - 6</td>
<td>30 - 40</td>
</tr>
<tr>
<td>6 - 7</td>
<td>18 - 24</td>
</tr>
<tr>
<td>Adult</td>
<td>7 - 15</td>
</tr>
</tbody>
</table>

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While the effects of mercury, lead, polyhalogenated biphenyls and alcohol are recognized, the full impact of most other environmental agents on fetal development has yet to be assessed. In many instances progress has been delayed by the absence of suitable animal models of the developing human. This lack of knowledge is especially relevant with regard to the long-term effects of exposure during fetal life. Although not caused strictly by environmental contaminants, the tragic results of use of thalidomide and diethylstilboestrol in pregnancy stand as tragic warning of such possibilities. With very few exceptions, current understanding and databases are inadequate to seek subtle associations between sporadic or group exposures to contaminants during fetal life and disorders which appear later in adults.

Despite many reports over the past 50 years of adverse effects on wildlife of pesticides, notably DDT and its derivatives, it is only relatively recently that the potential significance of these observations for humans has come into focus. Sex differentiation and gender identity are determined early: there is concern that endocrine disrupters arising from organochlorines and other insecticides can influence this aspect of fetal development. The ultimate effects of the now ubiquitous estrogenic and anti-androgenic breakdown products of these substances on endocrine features of development have yet to be realized. However, the temporal relationship to reduced human sperm counts, and reported increases in the occurrence of hypospadias are of great concern. While the relationship of breast and other cancers to adult exposure to organochlorines has been discussed, possible long-term effects of exposure of female fetuses to these substances appear yet to be adequately explored.

Permanently reduced lung growth may result from the repeated barotrauma of assisted ventilation of premature infant's lung. The lung is an important endocrine and excretory organ in the fetus: these functions of the fetal lung have yet to be fully understood before any effects of contaminant exposures can be determined.

The increased ease with which the young acquire sensitivity to external allergens is well recognized. Asthma is reported to have increased in recent years: hospitalization of young children in Canada for asthma increased by 28% among boys and 18% among girls between the years 1980-81 and 1989-90. While there is debate as to how much of this increase might be due to over diagnosis, there is evidence that visits to physicians, hospitalizations at other ages and deaths due to asthma have also increased, especially in urban populations. It has been suggested that any increase might be due to increased exposure to allergens and to toxicants resulting from the circumstances of modern living. Without appropriate precautions, well-intentioned efforts at energy conservation can lead to poor indoor air quality, especially in older homes.

### Behavioural characteristics

As a consequence of the child’s immaturity, small stature and activities, behaviours specific to children place them at higher risk to certain environmental agents than adults. Childhood, especially infancy, is characterized by dependency on adults and older children, and inability to control one’s environment. Development of safe environments for young children devolves not only on parents, but also on educators, communities and policy makers.

The importance of breastmilk in early nutrition and the need to protect its pre-eminence for infant nutrition cannot be overstated. The caloric requirement per unit body weight in infancy is approxi-
Because of their short stature and early crawling activity, young children, who in Canada spend approximately 90% of their time indoors, “live” much closer to the floor than adults.

Exposure risks

Children are at risk of exposure to contaminants that occurred before they were even conceived. A woman’s full complement of ova is formed at the fetal stage, hence her progeny could have been exposed to contaminants via the grandmother. fanciful though this may seem, measurable quantities of pollutants have been detected in follicular fluid aspirated from ova. In addition to the type of fetal risks described previously, the fetus may be inadvertently exposed to contaminants because of maternal occupational exposure and/or maternal lack of perception of environmental risks. Exposure via breastmilk has been described above, however it is important to state that the vast majority of infants derive major benefits from breastfeeding, and to reaffirm that it is society’s responsibility to ensure the safety of this vital human food.

In the home there are numerous situations which will result in possible exposure to contaminants. Environmental tobacco smoke exposure has been carefully studied. Spraying of insecticide in older homes to treat for infestations places young children at increased risk because of the markedly higher concentrations near the floor, and because of persistence of the spray in carpets. A vast range of contaminants including heavy metals, pesticides, and benzene and other mutagens enter the home in polluted regions in the air, on clothes and especially on footwear. House carpets promote accumulation of many of these materials, especially if cleaned with low efficiency vacuum cleaners. In regard to biological domestic contaminants, while dust mites and animal dander have attracted particular attention as environmental allergens, toxigenic fungi are common in damp areas in homes with poor air quality and are of increasing concern. Those living in inner city environments are clearly placed at increased risk from certain contaminants. Using blood lead levels greater than 20 μg/dL as a marker of probable adverse environmental conditions, a group of inner city children as young as 4 years were recently shown to have blood cotinine levels equivalent to smoking 3 to 4 cigarettes daily, and derivatives of benzene in blood samples from those who participated in afternoon street activities at levels such as might be encountered in workers in the petrochemical industry.

CONCLUSION

Children differ from adults in many important ways as a consequence of their growth and development, with its anatomical, physiological and behavioural characteristics. Potentially these differences render children, especially the fetus and young child, more vulnerable to environmental toxicants than adults. It is therefore essential that policies and standards for the evaluation and use of chemicals in the environment take account of these differences in order to protect the immediate and long-term health and safety of children.

REFERENCES


