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ЗАГРЯЗНЕНИЕ ОКРУЖАЮЩЕЙ СРЕДЫ — УГРОЗА ДЛЯ ДЕТЕЙ

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РЕЗЮМЕ: Фетальный и ранний постнатальный периоды относятся к наиболее уязвимым периодам жизни человека, когда даже относительно незначительные воздействия оказываются достаточными для возникновения стойких повреждений. Влияние поллютантов в окружающей среде на плод и новорожденного остается в настоящее время малоизученными. Исследования показали, что загрязняющие вещества могут оказывать негативный эффект на массу тела новорожденного, на психомоторное и половое развитие, на функционирование эндокринных органов, в частности щитовидной железы, на формирование иммунного ответа и формирование клинической картины заболеваний в дальнейшей жизни. Различают несколько источников поллютантов: 1) промышленность, производящая и использующая загрязняющие вещества, 2) вещества, используемые в домашнем хозяйстве и личной гигиене, 3) пестициды используемые в сельском хозяйстве, 4) добыча полезных ископаемых, 5) транспорт, 6) курение родителей. Среди опасных веществ, сопутствующих промышленному производству, необходимо отметить полихлорбифенилы (ПХБ) и бромированные субстанции (БС), среди веществ, используемых в домашнем хозяйстве и личной гигиене — бисфенол А, фталаты, свинец, метилртуть. Пестициды — ДДТ и фосфорорганические вещества — представляют особый интерес. Несмотря на то, что ДДТ, активно используемый в 50–60-х годах прошлого века, запрещен уже 50 лет тому назад, он и сейчас входит в список опасных субстанций. Транспортные потоки, производящие большое количество газов — таких как NO_2, CO_2, мелкие пылевые частицы (PM 10, PM 2,5) и элементарный углерод, также являются источником поллютантов. Курение — в основном курение родителей — еще один очень важный источник угрозы. Исследования показали, что добыча и плавка никеля сопровождаются продукцией большого количества сернистого газа. Кроме того, это производство приводит к появлению в воздухе большого количества очень маленьких пылевых частиц — наиболее вредного компонента загрязнения воздуха. Хотя теоретически жизнь вблизи предприятий никелевого производства представляется небезопасной, в настоящее время практически не проводится научных работ, направленных на изучение влияния факторов, сопровождающих добычу и выплавку никеля, на здоровье детей. Известно, что практически все поллютанты влияют на деятельность мозга, эндокринной, иммунной и сердечно-сосудистой систем, механизм их влияния может быть различным. Механизм влияния многих веществ остается неизученным. ПХБ и многие другие поллютанты являются разрушителями эндокринной системы, изменяя активность гормонов щитовидной железы и половых гормонов. При этом остается неизвестным, является ли повреждение мозга вторичным по отношению к нарушению деятельности щитовидной железы. Возможен также прямой эффект ПХБ и других поллютантов на развитие органов. Эпигенетические механизмы регуляции экспрессии генов могут быть еще одним фактором повреждающего влияния поллютантов. Изменение активности генов может быть причиной негативных изменений в последующих поколениях. В экспериментах на животных экспериментально доказано наличие эпигенетических механизмов повреждения в структуре токсического влияния пестицидов, причем их эффект был выявлен в четвертом поколении. Такие механизмы, возможно, имеют место при курении.

КЛЮЧЕВЫЕ СЛОВА: плод; новорожденный; поллютанты в окружающей среде; эндокринная система; эпигенетические механизмы.

ENVIRONMENTAL POLLUTANTS, A THREAT FOR CHILDREN

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ABSTRACT: The fetal and early postnatal are the most vulnerable periods of life, when even relatively small disturbances can lead to permanent damage. Relatively unknown risks for the fetus and young infant are environmental pollutants — compounds, present in the environment that can affect human health. Studies have shown that these compounds may have negative effects on birth weight, psychomotor and sexual development, endocrine organs like the thyroid gland, immune responses and the development of diseases in later life. Different sources of environmental pollutants and different products can be distinguished: 1. compounds produced and used шт industrial processes, 2. compounds used in household and personal care, 3. pesticides used in agriculture, 4. pollution caused by mining, 5. air pollution caused by traffic, 6. smoking by parents. Among dangerous compounds produced and used in industrial processes are Polychlorinated Biphenyls (PCBs) and Brominated compounds (BCs), among products which are used in households and personal care — bisphenol A, phthalates, lead, methyl mercury. Pesticides — DDT and organophosphates — are the compounds of special interest. DDT despite it had been used extensively in the 1950s and 1960s and was banned 50 years ago is known to be harmful even now. Traffic, producing gases like NO2, Co2 as well as very small particles (PM 10, PM 2.5) and elemental carbon, is an important source of environmental pollutants. Smoking, mainly by parents, is another very important thread to children. Studies have shown that nickel mining and smelting result in the production of high concentrations of sulferdioxide gas. The air is also polluted by very small particles, the most dangerous part of air pollution. Though theoretically living besides nickel mining and melting plants is dangerous, nowadays studies on the effects of nickel mining on children seem to be lacking. While almost all compounds have effect on the brain, the endocrine system, the immune system and the cardiovascular system, mode of their action might be different. The mode of action of many substances is not well known. PCBs and many other compounds are endocrine disruptors, affecting the thyroid and sexual hormones. It is unclear however if effects on the thyroid hormones are the cause of brain damage. There might also be a direct effect of PCBs and other substances on the development of organs. Another mechanism of action of these pollutants might be to influence gene expression by epigenetics. The activity of genes might be affected, what can have results in next generations. This epigenetic effect has been shown for pesticides in animal studies, effects were seen till the fourth generation. Epigenetics might also been involved in the effects of smoking.

KEYWORDS: fetus; newborn; environmental pollutants; endocrine system; epigenetic mechanism.

Pediatricians are trained to protect, and when needed and possible, to restore the health of children. The most vulnerable period of life, when even relatively small disturbances can lead to permanent damage, lasting till adulthood, is the fetal and early postnatal period. Non-optimal circumstances during fetal life and the first period after birth may cause permanent damage in the infant. Medication given to the pregnant mother might have a permanent effect on the fetus or infant, while no side effects are seen in the mother. Fetal malnutrition is related to an increased risk for cardiovascular diseases, stroke, hypertension and lung diseases in later life. Relatively unknown risks for the fetus and young infant are environmental pollutants. Environmental pollutants are compounds, present in the environment that can affect human health [16]. Studies have shown that these compounds may have negative effects on birth weight, psychomotor and sexual development, endocrine organs like the thyroid gland, immune responses and the development of diseases in later life. Pediatricians have to be aware of these problems and, whenever possible, stimulate efforts to reduce these risks.

Different sources of environmental pollutants and different products can be distinguished:

1. compounds produced and used industrial processes
2. compounds used in household and personal care
3. pesticides used in agriculture
4. pollution caused by mining
5. air pollution caused by traffic
6. smoking by parents

In this paper we will briefly review the existing knowledge about the most well-known pollutants.

COMPOUNDS PRODUCED AND USED IN INDUSTRIAL PROCESSES

PCB's. Polychlorinated Biphenyls or PCBs are compounds that were widely used in industrial processes. These compounds are lipophilic and are hardly degraded, neither by humans nor in the environment. Although the use of these compounds have been banned decades ago in many countries, they are still widely present in the environment and also in humans, due to the resistance to degradation [4]. Levels are especially high in young children. PCBs are transported over the placenta from the mother to the fetus, studies showed almost equal levels in the fetus and the mother [15]. Breast milk is an important source of these compounds, due to the high fat content of breast milk. Many studies have shown that PCB's can have negative health effects, mainly in the fetus and newborn infant. Higher levels of PCBs result in a lower birth weight [11]. Postnatally these infants are more hypotonic. There is a delay in psychomotor development [9]. Levels of thyroid hormones are lower, as well as sex hormones in boys [12]. A higher exposure to prenatal PCB levels is related to a less responsive immune system [12]. The effects on psychomotor development are still present at adolescence [18].

Brominated compounds. When PCBs were banned, they were replaced by brominated compounds. These products are widely used, especially to make clothes, computers, furniture and carpets more flame retardant. Recent studies show that these compounds also have a negative effect on the psychomotor development [18]. More studies are needed to investigate if these compounds also have endocrine disrupting effects.

PRODUCTS USED IN HOUSEHOLDS AND PERSONAL CARE

Bisphenol A. Bisphenol A (BPA) is a compound used to make plastics more flexible. It is used in many different products, including children's toys, bottles for formula feeding and dummies. It was also used in infusion lines for patients, including newborn infants. Plasma levels of these compounds are especially high in newborn infants. Children are exposed to these compounds through contaminated food and bottles in which formula is given. Another route is the ingestion of contaminated dust and soil. Also, BPA can leak from toys. BPA is readily absorbed by the gastrointestinal tract. Children admitted to a NICU are exposed to these compounds through the use of intravenous and other lines. Higher levels of BPA are related to a lower birth weight, sexual development in boys, increased anxiety and depression and poorer emotional control at three years of age [13]. BPA may also have endocrine disrupting activities, on hormones like thyroid and sexual. This might cause a delay in neurodevelopment. Chronic exposure might cause ischemic heart disease, diabetes and obesity. Finally, concerns have been expressed over that past years that Bisphenol A might induce cancer. Given the risk of BPA, especially for small children, has the use of BPA has been restricted for materials used for small children.

Phthalates. Phthalates consist of a group of compounds also used to make plastics like toys more flexible. They are also used in products for personal care like cosmetics end deodorants. A frequently used product is DEHP. This compound is found to be endocrine disrupting, it is related to affect male and perhaps also female genital development [10]. Also an association was found with a decrease in birth weight. Phthalates are, like all environmental pollutants, transported over the placenta. Levels found in cord blood are almost equal, or slightly lower, compared to maternal levels. High levels of these compounds in the pregnant mother, for instance for DEHP caused by extensive use of cosmetics, therefore is very harmful to the unborn and newborn infant.

Lead. One of the eldest and most studied environmental pollutant is lead. Humans can be exposed to lead via food, drinking water and inhalation. An important source of lead in the environment was the addition of lead to gasoline used by cars. Children living close to a road with heavy traffic showed high plasma lead levels. Food can be contaminated due to lead containing farmland and dairy products from cows consuming polluted food. Smoke from cigarettes also contain lead. The fetus is exposed to lead by the transfer from the mother via the placenta. Many studies have shown that prenatal and early postnatal exposure to lead causes a marked reduction in intellectual development in infants [1]. The addition of lead to gasoline has been banned in most countries, however the land used for agriculture still contains relatively high concentrations of lead. Also, water pipes made of lead are still in use. These pipes are an important source of lead. Infants therefore continues to be exposed with all negative effects on mental development. Recently an accident occurred in the USA where drinking water was heavily contaminated with lead.

Methyl mercury. Studies have shown that methyl mercury has negative effects on the neurodevelopment of the fetus and young infant [20]. Humans are mainly exposed by eating polluted fish. Fish is contaminated through the presence of this compound in water. Levels in fish are high enough to cause damage in infants of mothers with regular fish consumption. On the other hand, is fish consumption very important for the pregnant mother because of the presence of poly unsaturated fatty acids, a-linolenic acid and its derivative DHA in fish. The psychomotor development is higher in off spring of mothers who have taken supplemental DHA during pregnancy as well as in children fed with sufficient DHA [20].

PESTICIDES

DDT. One of the eldest and well known pesticide is DDT and the degradation product DDE. DDT was used quite extensively in the 1950s and 1960s. Then, it became clear that not only weeds and parasites were killed by DDT, but also animals eating these weeds. It caused a dramatic mortality in birds, causing the well-known "silent spring". DDT was banned 50 years ago, but due to its persistence against degradation, it still can be found in the environment, but also in humans. DDT is not only harmful for animal, but also for infants. DDT causes a decrease in cognitive and motor delay in infants, a delay that persist in adulthood [8].

Organophosphates. Organophosphates are a group of pesticides that are quite extensively used in agriculture. These compounds have negative effects on human health. They do not only negatively influence the neuromotor development in children, they might also be able to induce cancer in adulthood [6]. Despite the risk are these compounds still widely used in agriculture due to their high efficacy to protect crops.

Traffic. Traffic is an important source of environmental pollutants. Traffic produces gasses like NO2, Co2, very small particles (PM 10, PM 2.5) and elemental carbon. Studies have shown that these compounds cause cardiovascular diseases like hypertension and cardiac infarction. It also causes severe lung damage in adults [17]. The life expectancy of an adult living close to a busy road is at least one year less then controls. Unborn and newborn children at especially at risk for negative effects of compounds produced by traffic. Birth weight of children born to mothers living close to a busy road is lower compared to controls. Children exposed to this air pollution show more lung infections and more -severe- asthma. This will likely result in severe COPD at later life. The World Health Organization (WHO) has published upper limits for air pollution. Unfortunately, is the air pollution in many cities in the world, including Russia, much higher than these limits. This results in permanent lung damage in young children and earlier death in adults. Heavy traffic must be banned from cities and schools and other buildings for children must not be built in the vicinity of a busy road. At this moment is air pollution due to traffic one of the main threads to children. That air pollution might be a problem in Russia, is shown in fig 1.

И Smoking, mainly by parents, is another very important thread to children. Maternal smoking during pregnancy results in a lower birth weight. It also leads to a permanent, life long, reduction in lung volume. Smoking by mother and father at home results in more and more severe asthma and also permanent changes in lung growth. Smoking is one of the most serious environmental pollutants for children [7].

Nickel mining. Studies have shown that nickel mining and smelting results in the production of high concentrations of sulferdioxide gas. The air is also polluted by very small particles, the most dangerous part of air pollution. People living close to nickel mining and smelting reported higher incidence of headache, pulmonary infections, palpitations, lower abdominal pain, shortness of breath, constant chest pains, unusual spitting, coughing regularly, loss of body weight, regular constipation, diarrhoea, nausea, vomiting, urinary pain, and unusual genital discharge [3]. Studies on the effects of nickel mining on children seem to be lacking. A study in Russia showed the effect of nickel mining on the environment (fig. 2).

How do these environmental pollutants have effect on the unborn and newborn infant? While almost all compounds have effect on the brain, the endocrine system, the immune system and the cardiovascular system, might mode of action be different. The mode of action of many substances is not well known. PCBs and many other compounds are endocrine disruptors, affecting the thyroid and sexual hormones. It is unclear however if effects on the thyroid hormones are the cause of brain damage. There might also be a direct effect of PCBs and other substances on

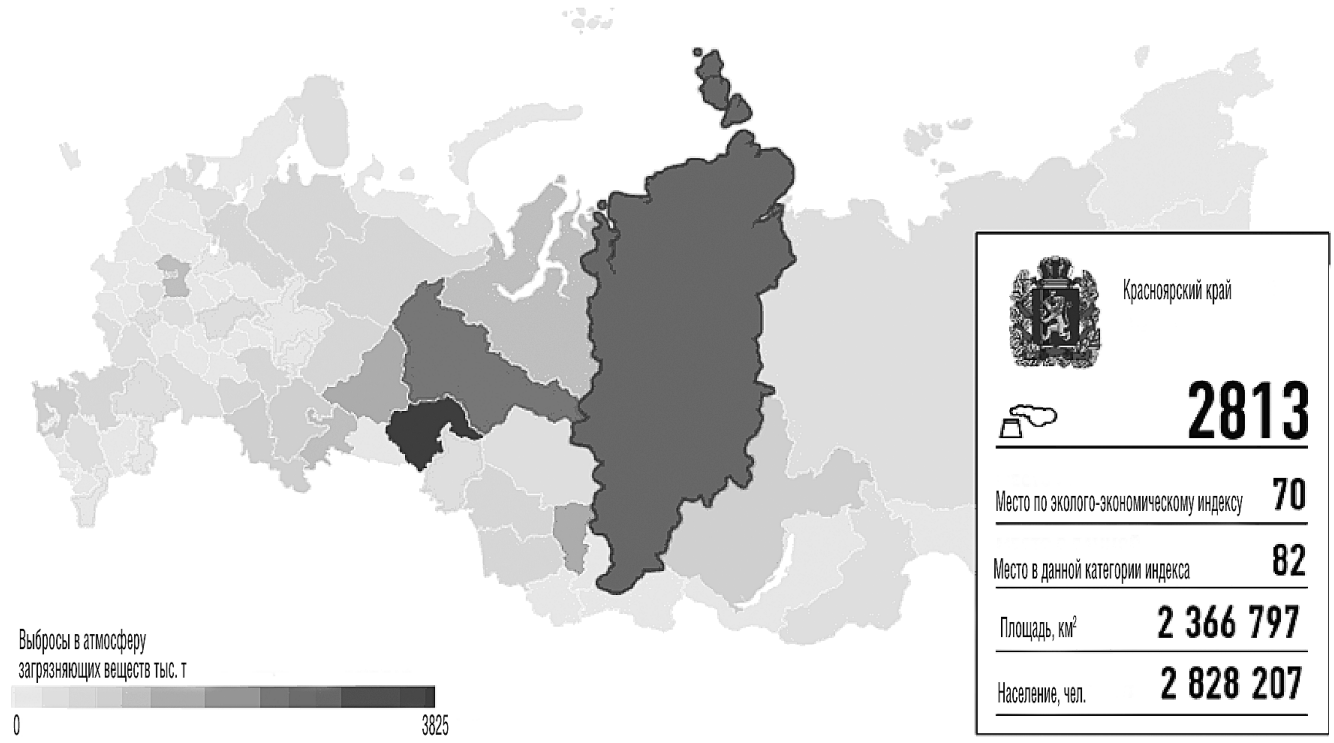

Fig.1. Air pollution in Russia: Krasnoyarsky krai [14]

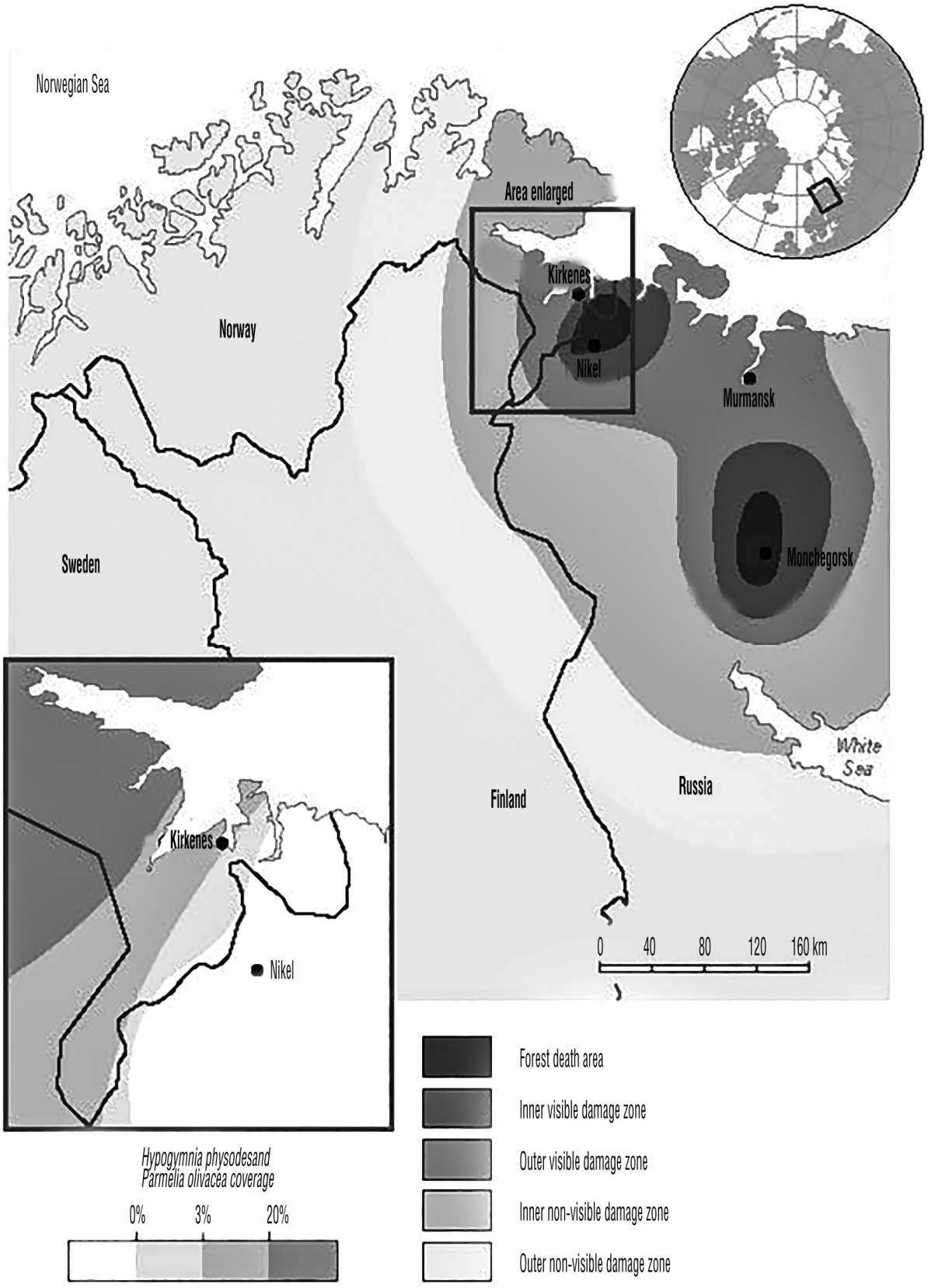

Fig. 2. Effects of Nickel mining and melting (AMAP, 2007) [2]

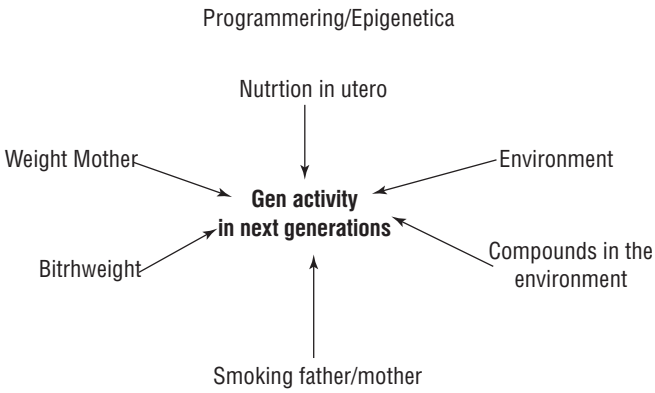

Fig.3. Ways to affect the activity of genes in next generations

the development of organs. Another mechanism of action of these pollutants might be to influence gene expression by epigenetics. The activity of genes might be affected, what can have results in next generations (fig 3). This epigenetic effect has been shown for pesticides in animal studies, effects were seen till the fourth generation [5]. Epigenetics might also been involved in the effects of smoking.

Environmental pollution in Russia. What is known about the environmental pollution in Russia and the effects on children? Not many studies have been published regarding the potential effects of environmental pollution on children in Russia. As far as I could find there were 13 studies on environmental pollution in Russia published in 2014–2015, all in Russian journals. One study showed that he places of work of the parents (wood chemical manufacturing, aluminum plant, petrochemical and chemical plant) influenced the incidence of upper respiratory tract infections in children [19]. There are no indications that the environmental pollution in Russia is very different from other industrialized countries. One study showed the air pollution in Moscow to be at least comparable to other big cities in the world. Another study indicated that the mortality due to air pollution in Russia is higher compares to other countries (fig 4).

Why are these studies important for pediatricians? All pollutants mentioned in this review cross the placenta, so the fetus is exposed to these compounds. The fetal and early postnatal period is the most critical period for the development of organs. Exposure to compounds, also at a low dose, can result in permanent damage in the newborn infant, causing life long effects. Breast milk contains many of the pollutants and is therefore another important source of these compounds in newborn children. Environmental pollutants therefore are more harmful for newborn infants than for adults. It is important that pediatricians realize that the occurrence of diseases in children might be related to the exposure to environmental pollutants.

In conclusion, we must assume that:

- Environmental pollution is widespread in the world
- This is very dangerous for humans, especially for children
- As pediatricians, we must ask our politicians to take care of our environment
- Pollution is costing lives and money
- We are polluting our planet, detrimental for our children and grand children

Fig.4. Deaths from air pollution [21]

- It is possible to prevent this to happen when we all are aware of the problem

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