PRIMAL HEALTH RESEARCH

A NEW ERA IN HEALTH RESEARCH

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UNDERSTANDING HEALTH

FROM FETAL VULNERABILITY TO ADULT ADAPTABILITY

Fetal vulnerability

The six months following conception undoubtedly represent the phase of human life with the highest risks of death. This is one aspect of fetal vulnerability. Today we are in a position to understand another aspect of this vulnerability: anything happening during the phase of intra-uterine formation can have irreversible and life long effects. In other words we learnt in the 1990s that our health is to a great extent shaped in the womb.

The subscribers of our newsletter and those who had an overview of our data bank know that in any field of medecine there have been studies detecting links between what happened during fetal life and health conditions in adolescence, adulthood and old age.

If you are not yet familiar with the concepts of primal health research, just explore the data bank via key words as divers as, for example, life expectancy, obesity, prostate cancer, breast cancer, recurrent miscarriages, schizophrenia, colonic diverticulosis, coronary heart disease, handedness, Parkinson's disease, cancer in childhood, dental caries, etc, and, if your research is prospective, famine, emotional state in pregnancy, seasonality of birth, birth weight, alcohol in pregnancy, anoxia antepartum, abdominal circumference at birth, antipyretics, etc.

In the current scientific context it is clear that all organs and functions have critical periods of development. It appears that many so-called adult diseases are in fact the long term consequences of early developmental defects. For example if there was something wrong during the period that is critical for the development of the pancreas, the main consequence may be, 50 years later, a non insulin dependent diabetes. From an overview of the data bank one can conclude that the growth and development of the fetus is influenced by a great variety of factors such as the emotional state of the pregnant woman, her nutritional habits, and, today, the amount of fat soluble synthetic chemicals which are stored in her adipose tissues.

The very first weeks following conception represent a phase of extreme vulnerability. We previously mentioned an evaluation of urinary gonadotrophin levels during the two weeks

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following implantation (1). According to this study, the incidence of « post implantation loss » is as high as 43%. A recent animal experiment suggests that the maternal diet during the preimplantation period has long term irreversible effects (2). Female rats had a low protein diet during only the four days following mating, that is the preimplantation period. They had a normal diet for the remainder of gestation. There were effects on birthweight, posnatal growth rate, blood pressure and organ/body-weight ratios in either male or female offspring . Preimplantation embryos collected from dams displayed significantly reduced cell numbers, apparently induced by a slower rate of cellular proliferation. The low protein diet reduced insulin and aminoacid levels, and increased maternal glucose blood levels by day 4 of development.

Male fetuses are more fragile than female fetuses. According to an evaluation dated 1983, for 100 abortions of chromosomally normal females there are 132 males (3). Since that evaluation the male/female ratio of fetal deaths has been continuously increasing. This has been well demonstrated in Japan (4). An analysis of the vital statistics of Japan looked at the male/female ratio of miscarriages between 12 and 15 weeks gestation, that is an age when it is possible in most cases to identify the sex of the fetus by routine examination of external genitalia. This ratio increased from 2.52 in 1966, to 3.10 in 1976, to 6.16 in 1986, to 10.01 in 1996 ! The only interpretation one can offer for this alarming phenomenon is intrauterine pollution by hormonal disruptors and more precisely by « oestrogen mimickers ». Hormonal disruption is the effect, in particular, of many families of fat soluble synthetic chemicals. Many of them are polychlorinated substances. That is why there is a spectacular increase of male fetal losses and also, among the survivors, multiple signs of impaired development of the genital tract : lower sperm counts (5,6), more undescended testicles (7), more abnormalities of the penis (8) and also more cancers of the testicle (9). It seems that this sort of cancer is in fact, in most cases, the long term visible effect of intrauterine developmental defects.

The specific vulnerability of male embryos and fetuses has been explained by the fact that all the fetuses have always been exposed to far higher levels of oestrogens than their pregnant mothers.This implies that testicles must develop much faster than ovaries, so that they can produce male sex hormones before their masculinity becomes submerged by high levels of oestrogens. It now seems that sex differentiation begins at conception, and the Y chromosome is involved in accelarating the growth of the male (XY) embryo (10). There is an advantage to win a race so that the testicles are differentiated before there is a high level of oestrogens. In other words male embryos must have a faster growth, that is a higher metabolic rate than females. It has been shown that in pre-implantation bovine embryos total glucose metabolism was twice as high in males compared with females (11). Among humans, after in vitro fertilization, the likelihood of a liveborn male is greater than for a female if at the time of transfer the number of cells per embryo is four or above (12). Finally the main difference between the sexes is that male embryos have a faster metabolic rate. Speed increases vulnerability.

This new awareness of the importance of prenatal environmental factors has many practical implications. For example when one considers the issue of pollution and health one must keep in mind that intrauterine pollution should be the main preoccupation. This new awareness also leads to re-interpret old studies, such as twin studies : twins share or do not share the same genes, but they always develop in the same uterus of a mother the same age, with the same emotional state, the same diet, the same blood pressure, etc. On the other hand both twins are not exactly in the same intra-uterine environment, because they are not in the same posture ; one of them can receive more blood than the other, etc. In the past, when there were discussions about the comparative role of genetic and environmental factors at the root of a disease or a behaviour, it was as if the environmental factors start at birth. Today the prenatal

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enviromental factors are considered so crucial that we do not even need long and comprehensive studies of the specific vulnerability of the fetus.

Adult adaptability

In contrast with fetal vulnerability, the capacity adults have to recover from adverse circumstances is amazing. During World War II, tens of thousands of human beings were held captive in such conditions of extreme privation that a great proportion of them could not survive. Half a century later we have at our disposal a sufficient amount of data to evaluate the health and the longevity of the survivors.

Significant anecdotes

In a previous newsletter (Winter 1993, Vol. 1, No. 3) we studied the biography of well known people who survived quasi-experimental extreme deprivation during world war II, then came back to active life and died after the age of ninety. These thirteen anecdotes provided sufficient information to demonstrate the extreme adaptability of certain human adults. Because systematic studies are about men, I find it useful to recall the main points of the biography of the two women we included in the list.

Dr Cicely Williams, born in Jamaica and educated in England, was primarily responsible for the identification, in the 1920s, of Kwashiorkor, a nutritional deficiency which has ravaged children in third-world countries. After many years in Africa she went to Malaya. She was conducting a health survey in the remote province of Trengganu when Pearl Harbour was attacked. It took her weeks of danger and deprivation to reach Singapore where she arrived just as the Japanese invaded. She was imprisoned at the notorious civilian Changi gaol. After two years of near starvation, she was taken to the headquarters of the Kempe Tai, the equivalent of the Gestapo. After 'interrogation` she was put in a series of cages which, for the next four months, she shared with dead and dying men, forced to crouch down, and starved.

After the war she went to America and did a post-graduate study at John Hopkins University. In 1948 she became the first advisor in maternal and child health to the World Health Organization. In her nineties she still spoke in Israel, Nepal, Pakistan... 'Retired – except on demand` was the title of her biography published by Sally Craddock. Cicely Williams died aged ninety-eight.

Tsola Dragoicheva was a member of the Bulgarian communist party when she was arrested in September 1923 during an ill-prepared revolt. She was sentenced to fifteen years in prison, amnistied in 1924, but found herself once again behind bars, after the communists had blown up one of Sophia's cathedrals, causing the death of one hundred and twenty prominent Bulgarians. After torture, she was condemned to death and saved from the gallows because she was pregnant. She spent the next nine years in prison, keeping her son with her. The child was later entrusted to party colleagues, who sent him to Moscow. After her release Dragoicheva studied in Moscow and came back to Bulgaria where she was elected to the Central Committee of the Bulgarian Workers'party.

When the Germans invaded the U.S.S.R. in 1941 Dragoicheva was arrested again and sent to the women's detention camp at Sveta Nikola. From there she escaped. After the war she became a prominent figure in party and state and also wrote three substantial volumes of memoirs. She died aged ninety nine...and nine months. The son whose conception had saved her life became a heart surgeon. He should be about seventy six now. It would be interesting to trace him.

Since our winter 1993 newsletter there have been many deaths of famous people whose biographies demonstrate the huge capacity to recover from adverse situations in adulthood. The biography of Cardinal Ignatus Kung, Bishop of Shanghai, is one of the most typical

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recent examples. In September 1955, Kung, along with several hundreds priests, was arrested and emprisoned. Several months later he was paraded in front of an angry mob at Shangai's pre-revolution dog racing stadium. In 1960 he was sentenced to life emprisonment. He was eventually released in 1987 (after 32 years of severe privation in Chinese prisons) and given the permission to travel abroad. After settling in Stamford, Connecticut, and recovering a better health, he travelled to Rome for a private audience with Pope John Paul II. He died in March 2000, aged 98.

All these anecdotes are valuable in that they inspire further research. In fact, more than fifty years after the end of World War II, we are reaching a time when relevant systematic studies can be published.

Systematic studies

In the months after the Japanese invasion of the Malay Peninsula in 1942, more than 140000 Allied servicemen were captured by the Japanese. Conditions in the prison camps were so harsh that by the time the war ended between 25% and 40% had died. These prisoners experienced malnutrition, infections, exhaustion, severe psychological stress and divers neurological syndromes. There have been concerns that the prisoners may have been exposed to slow-acting neurotoxins from plants such as cycads (13), which could have made them more liable to develop degenerative neurological disease. That is why the first large follow-up study regarding these prisoners of war focused on the risk of Parkinson's disease, without ignoring the death rates from other diseases.

Using records held by the War Pensions Agency, a British team of researchers abstracted data on 11 915 British former prisoners of war held captive by the Japanese (14). 11 134 were traced. The numbers of deaths in this group between 1952 and 1997 were compared with those expected from national rates for the male population of England and Wales. The first amazing conclusion is that the overall mortality was significantly lower than expected : 8796 deaths were expected ; there were in fact 7474 of them. Death rates from Parkinson's disease were slightly below the national average, though this difference was not statistically significant (35 deaths versus 43 expected). A similar pattern was seen for other degenerative neurological disorders (motorneuron disease, multiple sclerosis and dementia). The former prisoners had significantly lower than expected mortality from all major causes of death (coronary heart disease, cerebro vascular disease, all sorts of cancers and respiratory disease). They also had below average rates of death from tuberculosis and suicide. The only exception was the increased mortality from diseases of the liver such as cirrhosis and primary cancer of the liver. This fact can be easily interpreted. A large proportion of prisoners had hepatitis B and probably hepatitis C. Yet it is well known that the chronic carriers of these sorts of hepatitis have a greatly increased risk of both cirrhosis and liver primary cancer.

This British study is by far the most authoritative one regarding the long term consequences of periods of severe malnutrition with frequent infections, exhaustion and intense psychological stress in adulthood. All the other studies were based on much smaller numbers. For example a recent Australian survey of World War II veterans aged 66-86 years compared former prisoners and non-prisoners (15). This study looked at the data regarding only 208 men and therefore could not provide statistically significant results.

The overall conclusions of these anecdotes and systematic studies are easy to summarize. Those who were originally in a state of health good enough to survive the period of adverse circumstances finally had a longer life and were more healthy afterwards than the rest of the population. In other words a period of highly unfavourable lifestyle in adulthood does not alter significantly the life expectancy and the capacity to remain free of diseases.

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The contrast between fetal vulnerability and adult adaptability is a key for understanding the nature of health. What really matters is our 'Primal Health`, that is the basic state of health in which we are at the end of the 'primal period` (16). This basic state of health is determined by a combination of genetic and early environmental factors. A new understanding of the word health, adapted to the current scientific context, indicates what the main preoccupations should be in the future. For those who are interested in the health of the unconceived generations, certain issues should prevail on all the others. This is the case of preconceptional preparation, intrauterine pollution, nutrition during pregnancy and other factors influencing the health and well being of pregnant women, factors influencing the physiological processes in the period surrounding birth, factors influencing the duration of breastfeeding, milk pollution, long term effects on health of early multiple vaccination, in particular.

When looking at the most common topics developed in health magazines and the media in general, it is clear that the recommendations given to adults are presented as important. Adults are offered countless articles on their ideal weight, the best way to take exercise or the latest best diet. Yet we are in a position to claim that the lifestyle in adulthood has only minor effects on health. It will take time to change the focus because health magazines are read by adults and many adults are mostly interested in their own health. I came to similar conclusions when considering the comments inspired by my book 'The Scientification of Love`(17). One of the main theme of the book is that recent scientific advances inspire new questions regarding the development of the capacity to love. They also indicate that early experiences, particularly in the period surrounding birth, are critical in the development of the capacity to love. However many readers only remember the chapter on romantic love. We are in an 'adultist` society…

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GLOSSARY

We propose a vocabulary adapted to the new scientific context.

Primal - first in time and first in importance.
Primal period - the time which included fetal life, perinatal period and early infancy. It is during the primal period that the adaptive systems involved in what we commonly call health reach maturity. It is the time of close dependence on the mother. One can anticipate that any kind of event happening during this period can have irreversible effects.
Primal adaptive system - the subcortical nervous system, the endocrine system and the immune system should no longer be separated and should be understood as a whole (e.g. the brain is a gland, insulin is a neuromediator, lymphocytes can release endorphins, etc.). We call this network the 'primal adaptive system'. Phrases used in the medical literature, such as 'psychoneuroimmuno endocrinological system', 'psychoneuro immunology', immuno endocrinology', etc., should be expressed in simpler terms. A recent review-article in the *New England Journal of Medicine* gave a perfect updated description of what we call the 'primal adaptive system'.[18]
Health - is how well the primal adaptive system works (it is not the absence of disease).

At the end the primal period we are in a basic state of health called **primal health.** The objective of **primal health research** is to explore correlations between the Primal period and what will happen later on.

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