PRIMAL HEALTH RESEARCH

A NEW ERA IN HEALTH RESEARCH

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Free access to the Primal Health Research Data Bank

Merging

Even at the age of Internet a dinner table is more suitable than a transatlantic exchange of e-mails for initiating fruitful projects. During my last trip to the East Coast I met Cathy Daub and Debra Mendelson, from Birthworks. It appeared (at dinner time) that by merging our sites we could offer free access to the Primal Health Research Data bank. Thanks to the expertise of Paul - Debra's husband - it took only some days to introduce a real data bank in the web. It is already useable. It will be improved in the near future

This bank will be first a tool for researchers interested in the health of the unborn generations. It will contribute to induce a new awareness of the long term consequences of early experiences. Today it is easy to have an overview of all the (apparently) unrelated references and abstracts we brought together. This overview can convince anyone that our health is to a great extent shaped in the womb. Of course the impressive proportion of studies detecting correlations between fetal life and health later in life must be interpreted. There are simple and practical explanations. For example we must take into account the fact that it is easy - and politically correct - to introduce in a computer such indicators of fetal growth as birth weight. But we must go beyond such explanations: the point is that the studies we detected in the scientific and medical literature originate from countless disciplines: cancerology, neurology, cardiology, dentistry, reproductive medicine, endocrinology, gerontology, ophthalmology, psychiatry, etc... This means that today, when we refer to the environmental factors that determine the health and behaviour of human beings (versus the genetic factors), we must focus on the intrauterine environment. The time has come for a radically new vision of human development.

The main implications of this new generation of research is that fetal growth and fetal development must become major public health preoccupations. In the current scientific context some of the factors that influence the quality of prenatal life are better understood. This is the case of the emotional factors. Pregnant women always had the intuitive knowledge that the development of their baby in the womb was influenced by their emotional state.

Today physiologists can interpret this influence. For example when a pregnant woman is unhappy because she feels dominated by somebody (e.g. an authoritarian boss) or by a situation (e.g. unwanted pregnancy) she has a tendency to release high levels of hormones such as cortisol. Yet cortisol is an inhibitor of fetal growth.

The more aware we are of the importance of the emotional states of pregnant women, the more we will take into consideration the possible "nocebo effect" of antenatal care. It seems that many health professionals involved in antenatal care have not realized that one of their role should be to protect the emotional state of pregnant women. In the issues of autumn1994 (vol 2 no 2) and spring 1995 (vol 2 no 4) I had already introduced the concept of nocebo effect of antenatal care. Five years later I find it urgent to reintroduce the topic.

ANTENATAL SCARE

I constantly receive phone calls from pregnant women who are in a state of anxiety - even of panic - after an antenatal visit. I usually reassure them by transmitting the sort of hard data that is easy to find at the age of evidence based medicine. Having analyzed the most common reasons for these phone calls, I have realized that in general ignorance is the basis of the widespread nocebo effect of antenatal "care

Most practitioners seem to be unable to scan the abundant medical literature for valuable epidemiological studies. I found that this sort of blindness is related to a deep rooted cultural misunderstanding of one of the most vital functions of the placenta, that is the placenta as an advocate of the baby: the placenta is constantly manipulating maternal physiology for fetal benefit. The placenta can send messages to the mother via hormones such as HCG or Human Placental Lactogen. It is as if the placenta is telling the mother, for example: "please dilute your blood and make it more fluid, so that it can more easily go where it is urgently needed". The placenta can also ask the mother: "please, increase your blood pressure because we need more blood". It can also tell the mother about an increased need for glucose: this leads to a transitory modification of the metabolism of carbohydrates. The results of epidemiological studies are eloquent reminders of these functions of the placenta.

Let us illustrate these interpretations by looking at three main reasons for panicky phone calls after a prenatal visit.

First example: "my haemoglobin is 9: I am anaemic"

When a woman has a haemoglobin concentration in the region of 9.0 or 9.5 at the end of her pregnancy, there are two possibilities. More often than not she will meet a practitioner (doctor or midwife) who is not interested in epidemiological studies and who thinks that iron deficiency in pregnancy can be detected via the haemoglobin concentration. She will be told that she is anaemic and she will be given iron tablets. She will understand that there is something wrong in her body that needs to be corrected.

It can happen, on the other hand, that a pregnant woman with a similar haemoglobin concentration meets a practitioner who is aware of the most significant epidemiological studies and who is interested in placental physiology. This practitioner has digested the huge and authoritative study by a London team about the relation between maternal haemoglobin concentration and birth outcomes (1). Birth outcomes of 153 602 pregnancies were analysed

(the haemoglobulin measurement used in the study was the lowest recorded during pregnancy). They found that the highest average birth weight was in the group of women who had a haemoglobin concentration between 8.5 and 9.5. Their main conclusion was that "the magnitude of the fall in haemogloblin concentration is related to birth weight".A similar pattern occurred in all ethnic groups. Furthermore it appeared that when the haemoglobin concentration fails to fall below 10.5, there is an increased risk of low birth weight and preterm delivery. Similar conclusions have been reached by other - yet smaller - epidemiological studies (2,3). This sort of practitioner is also probably aware of the many studies that fail to demonstrate that iron supplementation may improve birth outcomes (4). When such a practitioner suspects anaemia, he (she) prescribes specific tests such as erythrocyte protoporphyrin, transferrine saturation or serum ferritin.

The pregnant woman who has access to this evidence based antenatal advice will be offered reassuring explanations. It will be explained that the blood volume of a pregnant woman is supposed to increase dramatically, and that the haemoglobulin concentration indicates the degree of blood dilution. She will understand that the results of her tests are suggestive of effective placental activity and that her body is responding correctly to the instructions given by the placenta . She will be given good news. The antenatal visit will have had a positive effect on her emotional state and therefore on the growth and development of her baby.

All over the world millions of pregnant women are wrongly told that they are anaemic and are given iron supplements. There is a tendency to overlook the side effects of iron (constipation, diarrhoea, heartburns, etc…), plus the fact that iron inhibits the absorption of such an important growth factor as zinc (5).

This misinterpretation of haemoglobin concentration in pregnancy is widespread…beyond belief. A Japanese lady spent the first half of her pregnancy in London, before going back to Tokyo. One of her European friend - who had four babies - warned her long in advance that at the end of her pregnancy she will be told that she is anaemic and given iron tablets. Guess the end of the story.

An authoritative British team of epidemiologists published a study about third stage of labour in a prestigious medical journal. In order to concentrate on low risk pregnancies they eliminated all women whose haemoglobin was below 10(6). Finally the average concentration in the population they studied was 11.1. Afterwards I was given an opportunity to indicate some of the limitations of this study(7).

A lack of interest in placental physiology is at the root of such misinterpretations. There is a tendency to confuse a transitory physiological response (blood dilution) with a disease (anaemia). Obstetrics is dangerous when it is not evidence based.

Second example: "They are giving me drugs to treat my high blood pressure"

In late pregnancy many women have an increased blood pressure. Once more there are two possibilities. More often than not this will be presented as bad news. What's more, certain women will be given antihypertensive drugs. The message is that there is something wrong that needs to be corrected.

However there are practitioners who will not present an increased blood pressure as bad news. These practitioners can perceive and explain the fundamental differences between a gestational hypertension ("pregnancy induced hypertension") as a physiological response and

the disease pre-eclampsia. They can easily offer a reassuring analogy such as: "when you have a brain tumour, you have a head-ache; but when you have a head-ache it does not mean that you have a brain tumour". In the same way when you have pre-eclampsia you have a high blood pressure, but an increased blood pressure in late pregnancy does not mean pre-eclampsia. The explanations given by such practitioners are supported by several epidemiological studies. The most significant study from this regard is an examination of perinatal mortality over two years in the obstetric population at the Nottingham City hospital(8). It demonstrated clearly that the best possible outcomes are among women with gestational hypertension compared with the overall population and, of course, compared with the pre-eclamptic women. Similar results, with smaller numbers, have been presented by Naeye(9), by Kilpatrick(10) and by Curtis(11).

The misinterpretations of the fluctuations of blood pressure in pregnancy are as widespread as the misinterpretations of the fluctuations of haemoglobin concentrations. A recent review article identified 45 controlled trials that randomly allocated women with mild-to-moderate hypertension to antihypertensive treatment(12). This endless repetition of studies has been called "circular epidemiology". Of course the main effects of an antihypertensive treatment during pregnancy is to restrict fetal growth and to increase the number of low weight babies. Practitioners who have understood placental physiology would not even think of treating with drugs what is a physiological response and would anticipate the dangers.

Third example: "I am diabetic!"

Many practitioners do not realize how powerful the nocebo effect of the term "gestational diabetes" can be. When a woman is given this diagnosis she tends to confuse what is a transitory response to fetal needs with a serious chronic disease. Such a term can transform overnight a happy pregnant woman into a sick person. The point is that this diagnosis is useless. Professor John Jarrett, from London, claims that gestational diabetes is a "non-entity"(13). In a letter to the American Journal of Obstetrics and Gynecology it has been called "a diagnosis still looking for a disease". Today there is a debate on whether pregnant women should be screened for glucose tolerance(14). This diagnosis is useless because, when it has been established, it leads to simple recommendations that should be given to all pregnant women, such as: avoid pure sugar (soft drinks, etc.); prefer complex carbohydrates (pasta, bread, rice, etc.); have a sufficient amount of physical exercises.

We might write volumes about the nocebo effects of antenatal care. Three examples were enough to measure the amplitude of an intriguing phenomenon that is basically the same all over the world. An overview of the Primal Health Data Bank gave an opportunity to realize how serious is the topic.

WHAT IS CUL-DE-SAC EPIDEMIOLOGY?

An overview of our data bank can reveal other intriguing phenomena. One is the contrast between circular epidemiology and cul-de-sac epidemiology. The best way to explain the meaning of these phrases is to offer a reprint of a text I recently published in the Lancet.

REPRINT: Between circular and cul-de-sac epidemiology. Lancet 2000; 355 (April 15): 1371.

In her Feb 12 feature (p 556) Marilynn Larkin reports that Lewis Kuller condemned the continuation of epidemiological studies "beyond the point of reasonable doubt"(1). I have been intrigued for many years by the opposite of what Kuller calls "circular epidemiology". I call it cul-de-sac epidemiology. This framework includes research about topical issues. Despite the publication of this research in authoritative medical or scientific journals, the findings are shunned by the medical community and the media. "Cul-de-sac" epidemiological studies are not replicated, even by the original investigators and they are rarely quoted after publication.

The first example I can offer is a Swedish study, published in 1990 by Bertil Jacobson, leading to the conclusion that certain obstetric drugs are risk factors for drug addiction in adult offspring(2). The results have never been confirmed or invalidated by further research. Yet drug addiction is one of the main preoccupations of our time. Another example is about obstetric medication as a possible risk factor for autism. At the end of his life, the Nobel prize winner Niko Tinbergen studied autistic children with the methods of a field ethologist. He came to the conclusion that there are risk factors for autism in the perinatal period, such as anaesthesia during labour and induction of labour. His observations inspired only one study. Ryoko Hattori (Kumamoto, Japan) found that the "Kitasato University's method" of delivery is a risk factor for autism. This method is characterized by a combination of sedative, anaesthetic agents, and analgesics, together with a planned delivery induced a week before the due date. The curiosity of researchers has not been stimulated by this Japanese study, published in 1991 (3). From my conversations and correspondence with these researchers (including a trip to Kumamoto), I became aware of their similar comments on epidemiology. They all realized afterwards that research may be politically incorrect.

A pessimistic analysis focusing on the difficulties of epidemiology may inspire the simplistic conclusion that politically correct research leads to "circular epidemiology" and that politically incorrect research leads to "cul-de-sac epidemiology". An optimistic analysis would stress that it is possible to break through the dead end of a cul-de-sac and open an avenue. In other words the limits of political correctness are not immutable.

Let us welcome break-through epidemiology.

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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.[15]
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'.[16]
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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