## AGNES WOLD: "THERE IS NO EVIDENCE THAT 'ENDOCRINE DISRUPTING CHEMICALS' AFFECT OUR HEALTH"

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Agnes Wold, professor in clinical bacteriology at the University of Gothenburg in Sweden, has frequently accused the Swedish Society for Nature Conservation and scientists of unnecessarily scaring people about endocrine disrupting substances. She does not deny that substances exist that can disrupt the endocrine system, but explains here in detail why she has a problem with the expression 'endocrine disrupting chemicals'.

The Swedish Society for Nature Conservation, together with certain scientists, has successfully hammered home the message to the Swedish people and our politicians that everyday life, even in our safe Swedish nursery schools, is full of poisons. In particular, our health is supposedly threatened by so-called endocrine disrupting (ED) chemicals, which are now a priority area in the Swedish government's environmental policy. Toys and nursery school equipment worth millions are being disposed without any scientific ground that they are in fact hazardous to human health.

Local authority spokespersons are claiming that children's future reproductive capacity is at risk since they play with plastic dolls or sleep on plastic mattresses - an entirely unfounded claim. The term 'endocrine disrupting chemical' is controversial and difficult to define unambiguously. A heated scientific debate has arisen among toxicology researchers in Europe, a debate that we have hardly heard spoken of here in Sweden, where both politicians and the general public have been lulled into believing that "the scientists are in agreement". In this article, the criticism is compiled against the term "endocrine disrupting chemical" and it is explained why European researchers protest – because of the proposition that EDs should receive special treatment and should be banned without ordinarily toxicological testing. Such a policy would nullify decades of successful, scientifically based toxicological risk assessment and turn established toxicological science on its head.

Who has not heard that everyday products – shampoo, perfume and plastic bowls – contain so-called "endocrine disrupting chemicals"? Here in Sweden we seem to believe that it



has been demonstrated that certain substances, such as plasticisers in plastics, exert a negative effect on our health by disrupting our endocrine system in some way. But this is far from confirmed – in reality this theory is not supported by recent reviews of existing research.

Decades of persistent lobbying has convinced Swedish politicians that EDs represent a threat to our health, in spite of the weak scientific evidence. Point taxes are now proposed on PVC floors since they contain plasticisers (phthalates) that "disrupt the ability to have children" according to our own government. Our Swedish nursery schools are to be cleared out of mugs and toys made of plastic that have been used for decades with no sign of negative health effects. Millions of Swedish kroners are being wasted, functional furnishing and toys are being destroyed, plastic floors are being replaced with more expensive and less durable alternatives and parents (and thereby their children) are being scared.

In Europe the term "endocrine disrupting chemicals" is highly controversial. A debate is raging between critics and promoters of the term EDs, the critics believes that the term goes against established science and accepted methods in toxicology. This debate has not been noticed in Sweden, where solitary critics (such as myself) hear the Swedish Society for Nature Conservation, among others, declare that scientists are in full agreement on the issue. If one point out that hundreds of respected European scientists do not agree, the answer could be that they are acting in the interests of the chemicals industry.

I believe that the Swedish Society for Nature Conservation bears much of the responsibility for letting the general public and politicians be given an incorrect picture of EDs, and for letting our children and parents being scared in vain. I shall explain here why "endocrine disrupting chemicals" is a deeply controversial and problematical term and why very many toxicologists in the scientific community in Europe disprove of it (for my part, I do not believe it is because they are all getting paid by the chemicals industry!). The question of whether it should be possible to classify chemicals as "endocrine disrupting", and thereby letting them get special treatment outside of the normal toxicological testing, is one that everyone should care about since it affects the formulation of all future legislation on chemicals.

The main headings and structure of the article are:

# **1**. The term endocrine disrupting (ED) chemicals is confusing and it the term itself is not suited for legislation.

The term EDs is vague and difficult to define, which makes it particularly unsuitable as a basis for legislation and regulations in the society. I will explain why.

# 2. There are no human studies supporting the theory that endocrine disrupting chemicals in our daily lives affect our reproductive capabilities.

There is very little to support the theory that everyday chemicals have any negative effects on people, which the latest review of all human studies also can confirm.

# 3. Scientists are not at all in agreement – few terms have split the scientific community as deeply as EDs.

More than a hundred European toxicological researchers have protested against the use of the term ED as well as the proposal that traditional methods for determining recommended limits should not apply to chemicals that are classed as an ED. There is no scientific basis for this special treatment of EDs in toxicological practice, and such action could wrecking decades of successful

risk assessment and recommendations of limits for exposures based on established toxicological science.

#### 4. The precautionary principle does not work.

Avoiding everything that might theoretically be hazardous is impossible. Eliminating functioning materials means one have to replace it with something else. A more reasonable objective would be to not use any material that is more toxic than a material which risk we can live with, such as wood. This leads to a more reasonable risk assessment.

#### 5. And the industry?

The industry is the main enemy in the ED critics' rhetoric. But nobody will make more money than the industry if we get rid of functioning materials and replace them with something poorer and more expensive, which also have to be replaced more often.

#### 6. The campaign for non-toxic Nursery Schools has side effects.

Swedish politicians have willingly bought into the ED critics' global picture of our health being threatened by everyday chemicals and launched the Non-toxic Nursery Schools campaign, cheered on by the Swedish Society for Nature Conservation. This campaign scare parents and children and could create a generation with toxicophobia, a fright that affect their well-being. A very serious side effect of the fight against the EDs, whose existence has not even been proved.

## 1. ED is a confusing term that does not lend itself to legislation.

The term ED was launched in the early 1990s. The biologist Theo Colburn suggested that environmental toxins such as DDT and PCBs had hormone-like effects and disrupted reproduction in creatures that live in water. Inspired by this argument, the Danish pathologist Niels Skakkebaek suggested that damage to the sexual function of boys and men could be caused by endocrine disrupting chemicals in the environment. However more recent research gives no support to this theory (see below).

Legislation on chemicals is at EU level, where common rules are decided for how they are to be tested and assessed, what recommended limits should apply and which chemicals should be banned completely. Normally each chemical is treated individually in terms of testing, limits and possible prohibition. But substances that are classified as endocrine disrupting – EDs – are a separate category in two pieces of EU legislation (the regulations on pesticides and crop protection agents).

The burning question is: what is an endocrine disrupting chemical? If the term is to be used in legislation, it must first be defined. The European Commission's proposal means that a substance can be classified as endocrine disrupting in people (and thereby prohibited) if it is known to cause harmful effects. The opponents of the commission and a number of EU member countries include Sweden, which wishes to take a tougher approach to substances that are suspected of being ED and believes that the commission yields far too easily to the chemicals industry.

In my opinion the term ED is vague and useless and should not be included in any legislation at all. The fact that it can be found in EU legislation is probably due to energetic lobbying by scientists and environmental organisations who are supporters of the term. I will explain below why I think that endocrine disrupting chemicals is not a term that should be used

in legislation. It is very difficult to define, since none of the three components of the term - endocrine, disrupting and chemical - can be unambiguously determined.

#### Endocrine relates to hormones, but which hormone?

Let us begin with the first word: endocrine. While exocrine glands excrete their products (such as saliva and gall) from the body, the endocrine glands secrete their products (hormones) into the blood. The purpose of hormones is to control functions that involve many organs; hormones reach every cell in the body (with the exception of the brain, which is protected behind the blood-brain barrier).

The cells that must obey the instructions of the hormones contain a hormone receptor with which the hormone forms a very strong and specific bond. The strength of this bond is a guarantee that only this hormone and no other similar molecule can bind. This binding starts (or stops) processes in the cell. Cells that do not have a receptor for this particular hormone are not affected.

One example is the hormone insulin, which is created in the pancreas when blood sugar rises after a meal. The insulin is carried by the bloodstream to fat cells, for example, which have insulin receptors on their surface. When insulin forms a bond with the receptors, the cells take in sugar and turn it into fat, which is away for the body to store energy for leaner times.

Here we have the first problem with the term endocrine disrupting substances – we have many different hormones belonging to widely diverse classes of molecules: insulin and many other hormones are proteins, others are mini proteins (peptides) consisting of some amino acids, another group is molecules that are as small as a single amino acid, such as thyroxine and adrenalin, which control our metabolism. There are also so-called steroid hormones that are large and rigid fat molecules, which are created from cholesterol. Steroid hormones include sex hormones such as oestrogen, progesterone and testosterone, as well as aldosterone, which controls the salt-water balance and cortisol, which reduces inflammation.

Hormones are a so-called functional group, but they have nothing in common in terms of molecular structure - evolution has used many different chemical structures for the messenger molecules in the body. We can make a comparison to media - radio, TV, newspapers, talking books: they are completely different products but they have a common purpose - to distribute information.

Since hormones are chemically diverse, as a result there is not anything in common between their respective receptors, nor between the chemicals that happen to bind to different receptors. Thus a substance that resembles oestrogen can bind only to the oestrogen receptor and exert no effect on an insulin receptor. Compare to then non-existent effect that a radio that is turned off or on has on a newspaper resting on the kitchen table. Thus a collective term, such as endocrine disrupting substances, has no relevance from a biological or scientific point of view. On the other hand, the term has considerable political implications, since legislation is being proposed for all the substances that may cause a risk to affect the function of one hormone.

#### How can we define the term disrupting?

We can read in the papers every day that all sorts of things, from shampoo to gym shoes, are supposedly endocrine disrupting. Articles summarising endocrine disrupting chemicals contain long lists that include both classic environmental toxins such as DDT and TCDD (which is found in dioxin) and substances found in ordinary household plastics.

Has it really been demonstrated that all these substances *disrupt*, that is to say put a roadblock on, our well-oiled and effective endocrine system? Seldom or never. The list of

endocrine disrupting substances should therefore be much shorter. In order to be put on a list of suspected endocrine disrupting substances, it is now sufficient that a chemical binds very weakly to a hormone receptor. Or that it stimulates the growth of cells in a cell culture whose growth is dependent on oestrogen (breast cancer cells for example). Such a chemical is often called *endocrine disrupting* even though nothing is disrupted. It may sound frightening that a chemical stimulates the growth of cancer cells, but the results from one cell culture tell us nothing about whether the chemical might have a cancer stimulating effect in a person or an animal - everything depends on how the chemical is handled in the body: absorbed, distributed, modified and excreted. The concentration of the chemical that is required in order to obtain the effect is also critical - if very high levels are needed, these are perhaps not even attainable in real conditions. Bisphenol A, which is found in some hard plastics, is listed as an ED because it binds to the oestrogen receptor. However, the binding of Bisphenol A to the oestrogen receptor is ten thousand times weaker than oestrogen itself. The relevance of such weak binding in real life is quite unclear. To clarify, ten thousand Bisphenol A molecules would be needed to obtain the same effect as one oestrogen molecule.

This is where we find one of the main conflicts in the ED question. Critics of the term ED insist that a negative effect must be demonstrated if we are to speak of endocrine *disrupting*. Furthermore, it must be possible to observe this effect in a whole, living creature (animal or human), since the effects of a substance are also influenced by absorption, excretion and many other factors that cannot be observed in a cell culture.

I believe that most people who are not specialists in the area interpret the information that a substance is endocrine *disrupting* as meaning that the substance causes hormonal disturbances in animals or people when they are exposed to relevant doses of the substance. Probably these persons also believe that there are at least some indications of negative effects in people who have been exposed to the substance. One might think for example that if phthalates are endocrine disrupting then one should be able to observe endocrinal disruption among workers in the plastics industry, a person who is being exposed to very high doses of such substances every day. As far as I know this has never been reported.

#### What is a chemical?

The last word in the term endocrine disrupting *chemical* also lacks a clear definition. According to the Swedish National Encyclopaedia, a chemical is a molecule that is not produced by nature but by humans. In biological terms this is irrelevant - there is no difference between benzoic acid in lingonberries and benzoic acid that is added to food as a preservative.

There is a widespread misconception that a "natural" substance is generally less dangerous that an industrially produced/synthetic one. Nothing could be more wrong - some of the most toxic substances we know come from plants and animals (the nerve toxin tetrodotoxin from a fish and curare from plants, toxin from the fungus deadly webcap which damages the kidneys, aflatoxins in mould which are carcinogenic and so on). This is because many plants, and also animals sometimes, have developed substances that can kill anything that tried to eat or invade them. And evolution is generally cleverer at creating biologically active molecules than we humans and our industries. Most antibiotics come from fungi or bacteria in soil that use them to defend themselves against other microorganisms; fine heartwood from trees resists attack by algae and fungi by containing toxins. Think about turpentine - a product produced from the tree's toxic terpins.

The detoxification system – the P450 system – that we have in our liver and which quietly and calmly detoxifies and packages foreign molecules for export from the body was obviously not developed to handle the medicines and chemicals that we have produced during the last

100 years. No, it is there to detoxify the plants that have made up a large part of our diet since we left the sea and walked onto the land. However, when we started to produce chemicals and medicines, the P450 system has been taking care of these too.

Many plants contain substances with endocrinal effects. If we do not make the artificial distinction between "natural substances" and "chemicals", we find the greatest quantity of EDs in soya beans, linseed and other things we voluntarily consume. These substances are called phytooestrogens and have an oestrogen effect. One such phytooestrogen, genistein, binds more weakly to our oestrogen receptors than oestrogen does (100 times weaker), but considerably better than Bisphenol A (100 times better). If we worry about small quantities of Bisphenol A that leak out of plastics controlling and adjusting our hormonal system, we should also remove soya beans, linseed and doubtless many other plants from our diet.

Wood contains large quantities of sitosterol, a molecule that resembles our steroid hormones and exert an oestrogen effect on living organisms in bodies of water that are in contact with spill from the timber industry. Another major source of EDs that effect organisms in water is ordinary oestrogen coming from human urine.

Thus it is more probable that completely natural substances in wood and soya beans affect our endocrine system than that the small doses of chemicals from ordinary household plastic will. Perhaps removing plastic toys and plastic floors and replacing them with something "natural" sounds reasonable and good, and every one of us is free to follow his or her feelings in this matter. But basing a policy that affects our entire society on irrational feelings that "chemicals" are more dangerous than natural substances is not an acceptable approach to our amount of time and tax revenues. It should be an unquestionable requirement that the material that is being removed must be more dangerous than what it is replaced with. As far as I am aware, nobody has yet demonstrated that a plastic floor is more dangerous than a wooden one or that plastic toys are more dangerous than wooden toys.

If one reads some of the scientific reviews on EDs and their exerted endocrine effects, one finds that the EDs under study are not only industrially produced substances (such as Bisphenol A and phthalates) but there are also entirely natural products such as genistein from soya beans. Thus an oestrogen-like substance from soya beans is being used to illustrate the dangers of chemicals in our household plastics. Why do this? Possibly because genistein has a much stronger endocrine effect than the substances we are being warned about.

#### Are medicines chemicals?

Another group of substances often found in the lists of EDs are hormone-like medicines, that is to say synthetic hormones manufactured by the drugs industry in order to achieve hormones with a stronger or more lasting effect than our natural hormones. Even though our natural hormones and their respective hormone receptors bind very strongly to each other, the drugs industry has succeeded in creating hormones that bind to the receptors *even better* by slightly modifying the hormone's molecular structure.

In this way, we have synthesised many different versions of our natural antiinflammatory hormone cortisol that exert much stronger effects (prednisolone, betamethasone and others). These are some of our most used and most effective medicines.

The same thing has been done with sex hormones. A strong synthetic oestrogen, DES (diethylstilbestrol), was produced to prevent miscarriage. Appallingly, it proved to give rise to damage to the foetus, probably because of the strong hormonal effect, and it is now banned. However DES regularly turns up as an example of an ED in various articles (see the <u>WHO report</u>). It is easy to be deceived by this and to believe that the terrible effects that are described (from DES for example) are relevant to our exposure to phthalates from plastic containers in the

kitchen. The WHO report, where supporters of the term ED compile the dangerous effects of endocrine disrupting chemicals and urge more stringent legislation, mixes in both natural substances from soya beans and strong (and now banned) medicines when arguing that chemicals in everyday plastics threaten the endocrinal systems of us and our children.

The term ED can of course be used in research if it is found to be relevant. On the other hand, because it has no exact definition, the term ED should not be used in legislation and official documents. Neither should it be used as a basis for regulations in the society. And such a scientifically controversial term should obviously not be used in information to the society, such as brochures and presentations aimed at parents and nursery school staff.

# 2. Studies on humans have so far given no support to theories of endocrine disturbance caused by exposure to everyday chemicals.

The ED issue has mainly been driven forward by environmental chemists and biologists. With a couple of exceptions, doctors and medical researchers have been largely absent. The best known is uropathologist Niels Skakkebaek who in 1993 launched a new syndrome, *testicular dysgenesis syndrome*, TDS, and proposed that this was caused by foetal exposure to oestrogen or oestrogen-like substances. TDS included two malformations, abnormality of the urethra (hypospadias) and undescended testes (cryptorchidism), as well as testicular cancer and reduced sperm production. The term has been severely criticised by other reproduction researchers (Akre, 2009) who believe that the two conditions in TDS have nothing to do with each other and they do not have a common cause.

After 25 years of research into the effect of chemicals with a suspected endocrine disrupting effect on men's reproduction, a meta-analysis has been published, that is to say a systematic compilation and comparison of research results to date obtained with strict scientific methods (1). The meta-analysis shows that there is no connection between measured exposure to a range of suspected endocrine disrupting chemicals and various disruptions to male reproduction (1). The only exception is DDE, a decomposition product of DDT, which shows a weak association with one of the diagnoses. *Thus there is no support at present for the theory that so-called endocrine disrupting chemicals in everyday plastics cause any damage to boys' and men's reproductive systems.* 

At start, the theory of EDs required that substances should cause damage to the sexual function and reproduction. But as time went by, everything possible has been added into the "endocrinal disrupting" term, from asthma and allergies, via ADHD to overweight and diabetes (usually without clarifying whether a reference to type 1 or type 2 diabetes), in spite of the fact that there is no reason to believe that these diseases and conditions may have been caused by chemicals. On the contrary, for each of these conditions we have good knowledge about the causes and they do not include chemicals. The few studies that show some connections between chemical exposure and these conditions are of relatively low quality and have not taken other, more credible, explanations into account.

It is, of course, of importance to continue research into the relation between exposure to different types of chemicals (including natural substances) and a wide range of health outcomes. But there is no reason to include all possible conditions under the heading of endocrine disruption.

# 3. "The scientists are in agreement" – No, more rarely have scientists been as deeply divided as toxicologists are about the term ED.

The Swedish Society for Nature Conservation claims in its response to my criticism that I am alone in my opinion against a united body of scientists. It has in fact happened before that a united body of scientists has been wrong, and one cannot decide what is true in scientific questions through voting. An argument solely based on the number who think in a certain way is not feasible in a scientific debate, where objective arguments carry more weight than numbers of advocates.

But the Swedish Society for Nature Conservation's claim is also completely wrong. Scientific disagreement similar to that between European toxicologists about the existence of "endocrine disrupting chemicals" has rarely been seen in any field of science. In 2013 essentially the same editorial was published in a number of different scientific publications within toxicology, signed by 18 scientific editors in chief or section editors. It was entitled: Scientifically unfounded precaution drives European Commission's recommendations on EDC regulation, while defying common sense, well-established science and risk assessment principles. (link here)

The article was accompanied by a letter that criticised and dismissed the term endocrine disrupting chemical for defying all previous science, practice and methods in the field. This letter was signed by 88 European toxicological researchers, mostly professors and many with high positions within the toxicological community. (letter here)

Thus a total of more than 100 researchers in toxicology and pharmacology, including many editors in chief of scientific periodicals and heads of supervisory authorities, have protested against the term ED being used as a basis for legislation within the EU. A united body of scientists? Hardly.

Remarkably, the scientific quarrel over the term ED does not seem to have come to the attention of Swedish politicians. Swedish politicians have chosen EDs as a priority area for environmental policy. One could ask whether they would have done this if they really knew how controversial the term is among leading European toxicologists. At least as interesting as the question of any industrial connections among EDs critics the evident silence among the Swedish scientific community. Why is this and what effects has it had?

How could protests towards the term ED not reached Swedish politicians - they must surely have noticed critical voices from other European countries? Perhaps they have been told that all critics of the term ED are hand-in-hand with the chemicals industry; that is the answer that I have been given when reporting the scientific dispute. But can all the scientists and representatives of the authorities that have condemned the term ED really be paid by the industry? Why would they risk their good names and reputations in a scientific dispute in front of the entire European scientific community if they were not serious in their criticism?

Also in this case, it is a question of facts. A scientific field in which reasoned argument is dismissed with the comment that the person presenting the argument has had contact with industry goes against our entire Swedish research policy, which constantly repeats the requirement for researchers to collaborate with industry and interests within the community, and make practical use of their research. Surely Swedish environmental politicians cannot buy into such an argument.

Concerning the question of fact, here is an article to find examples of the ED critics' arguments – arguments that are scientifically sound and sensible in my eyes at least (2).

#### What are the opponents to EDs making a fuss about?

What is the scientific war among European toxicologists about? What causes editors of scientific journals, professors and heads of supervisory authorities to use words like endocrine disruptors are "defying common sense, well-established science and risk assessment principles".

Here is the great line of conflict: *supporters of the term ED maintain that one cannot* (or should not) calculate recommended limits for chemicals that function as an EDs. The ED critics argue against this at this, because this is at the foundation of the profession of toxicology.

The ED supporters argue that normal recommendation limits, which are arrived at by normal, tried and tested toxicological methods (including research on animals) do not apply. Therefore, it does not matter whether children's exposure to Bisphenol A or phthalates is below the TDI (tolerable daily intake - the amount of a substance that one can be exposed to daily without harmful effects). Chemicals that contain suspected EDs must still be eliminated! They are hazardous to us in spite of the fact that all scientific logic says that they are harmless, since our exposure is below the TDI. These are the arguments that cause plastics to be removed from nursery schools even though no children are being exposed to any chemical doses above permitted limits.

The ED supporters use two arguments when they claim that it is not possible to determine a safe chemical exposure concentration, and no therefor TDI for chemicals that are classified as "endocrine disrupting":

1) According to ED supporters, hormones do not show a dose response (that is to say a greater effect occurs with a higher dose and the effect lessens if the dose is reduced). According to them, hormones can actually have a greater effect at a lower dose, or completely different effects at different doses. In other words, we can never arrive at a dose that is so low that it has no effect on hormones.

This argument sounds like something a homeopath might have come up with, but it is actually one of the cornerstones of the ED edifice. If we cannot define a harmless dose, all substances that are classified as EDs can simply be banned without the usual toxicological testing and without regard to whether this is reasonable in relation to the dose we are exposed to or not. One can understand the chemical industry lobbying desperately against such a proposal.

The ED supporters happily tell us that hormones occur in low concentrations in our bodies. Naturally they do, because they bind strongly to their respective receptors so they can achieve their effect even at low concentrations. But this does not mean that a chemical that binds very weakly to the same receptor is active at an equally low dose. If a chemical such as Bisphenol A binds ten thousand times more weakly than oestrogen to an oestrogen receptor, then ten thousand Bisphenol A molecules will be needed to achieve the same effect as one oestrogen molecule. Thus, just because a hormone is active in very low concentrations, it does not mean that a chemical is endocrine disrupting in low concentrations. This depends entirely on its binding strength, which is always many potencies weaker than that of the natural hormone.

To put it mildly, it is unbelievably controversial to claim that hormones do not display any dose response connection. Doubtless most people are not aware of the existence of this theory, which may be because it is concealed behind the code words "non-monotonic dose response" in the numerous articles that the ED supporters regularly produce. The ED supporters publish their consensus documents (where they are in agreement with each other) under the name "The Endocrine Society" which can obviously raise ideas of a professional organisation for endocrinologists: scientists and doctors with specialist knowledge of the human endocrine system.

In normal biology and medicine, it is of course still believed that dose response applies if the concentration of insulin in the blood increases, sugar is stored in fat cells, but if the insulin concentration is reduced, then the uptake of sugar also decreases. In the same way, mucous membranes in the uterus grow when oestrogen levels in the blood increase and recede when the oestrogen disappears. 2) The ED supporters' other argument for the impossibility of determining a harmless dose for endocrine disrupting substances is that, since we already have hormones such as oestrogen in our bodies, a chemical with an oestrogen-like effect will be added to the effect of the existing hormone. This makes it impossible to calculate the sole effect of the chemical and thereby calculate a safe dose.

This argument is incomprehensible. We have many different synthetic hormone-like medicines, such as various cortisone preparations, synthetic sex hormones, thyroid hormones for people with reduced thyroid function etc. etc. With all medicines, including these, the drugs industry has performed comprehensive toxicological testing in order to determine the toxic dose for the substances and then calculate a safe dose based on that. The fact that we have these hormones in our bodies already obviously has nothing to do with this.

Obviously, substances exist that can disrupt our endocrine function and can cause us harm. Radioactive iodine for example disrupts the thyroid gland. But the very term ED means accepting the two highly dubious statements that a substance with an endocrine disrupting effect does not display dose response and that a safe level cannot (and should not) be determined. This is the key questions in the debate.

# There are recommended levels for chemicals in everyday plastics and children are not exposed to hazardous doses in nursery schools.

One of the most important tasks performed by toxicological researchers is, by means of carefully tested models in research animals and other systems, to calculate toxic doses and safe doses for the chemicals that we are exposed to every day.

Not all chemicals on the planet have safe limits. But there are limits for many of the most common, such as the various phthalates in soft plastics and Bisphenol A in hard plastic. If these limits are exceeded, then action must be taken. Otherwise, there is no reason to act, since the very concept of a limit is that we should know what dose is hazardous or harmless. But the ED supporters deny the existence of a safe dose for any chemical they class as an ED. That is why they consider that they have the right to force the disposal of millions worth of plastic mugs and toys in Swedish nursery schools. For safety's sake. One might ask how toxicological researchers can quietly listen to the "no safe dose" argument, since it undermines their scientific field and role as expert, which to a great extent concerns risk assessment and determining the limits.

The term "endocrine disrupting chemicals" is difficult to define. And there is no need to if we dismiss the inappropriate idea of basing legislation on what damage mechanisms a harmful chemical has. Substances that harm us must be phased out, whether they attack the liver, the kidneys or some endocrinal organ. The toxicity of a substance must be determined through toxicological studies using established, well documented methods. To determine a substance's toxicity, trials using cultured cells are not sufficient - we must know how an animal or person takes in, breaks down and distributes the substance in the body. We cannot draw the conclusion, based on the behaviour of a substance in a cell culture, that it has negative effects on our health; this depends on many factors, including dose and exposure path. That is what the protesting scientists are against - putting aside all established methods and calculation models in favour of the magic term ED.

Thus the term endocrine disrupting should not be used in the text of laws or in official documents. If a substance is found to be negative because it affects our endocrine system, then it should be treated in exactly the same way as any other substance with a negative effect on our health.

However, by means of energetic lobbying, the ED supporters have received their ED term into two EU regulations (pesticides and crop protection agents). But the opponents are tenacious and have put forward a requirement that a negative effect must be demonstrated in an animal (and not just in a cell culture) in order for a chemical to be classified as an ED. This may be thought to be a reasonable requirement, but it has been interpreted as if they are championing the chemicals industry's cause and opposing legislation that saves people's health. The fight goes on.

## 4. The precautionary principle does not work.

Toxicologists have generally worked on risk assessment and calculating the risks that are seen as tolerable and acceptable (see the term tolerable daily intake, TDI, the dose of a substance that can be absorbed every day of our lives without harm). The ED supporters wish to introduce what they call the "precautionary principle", or in other words banning a substance for safety's sake even though it has not been shown to be harmful.

This sounds good in theory and could be used for substances that have not yet come onto the market. But the principle does not work with substances that already exist - if we remove these substances we must replace them with something else. It is foolish to replace a material that we have been using for a long time without it causing any harm with a new substance that we know nothing about. The possibility that our everyday plastics will harm us is extraordinarily low, given that no injury has been observed among those who are exposed to high doses (such as workers in the plastics industry).

Many people are removing plastic materials and replacing it with wood. Wood feels good and is well tried and tested; I think so too and I have wooden cutting boards, wood panels and wood floors. But if we were to look at wood with the same critical eye as plastic, we can state that sawdust is carcinogenic – nasal cancer is a known occupational cancer among those who work in sawdust - and that wood is full of toxic terpins (think about turpentine, which is made from forestry materials). Also, wood contains high doses of the oestrogen-like substance sitosterol. Fish have been observed to have been affected by such substances after swimming in water containing wastewater from the timber industry.

Obviously, having wood in the home and wooden toys for children is completely harmless. Just as harmless as the plastic objects we have had around us for decades. Instead of the unrealistic zero vision of never being exposed to anything that might harm us (we would not then be able to eat or breathe), there is a better basis: let us not accept plastics and other materials that are more toxic than wood. Because we know wood, we have lived with wood and we accept the minimal theoretical risks from the toxic substances it contains.

The so-called precautionary principle is not cautious, it is unreasonable and would certainly lead to the wrong priorities. Since we would never find anything that is totally without toxins, we choose instead to deny the fact that "natural" materials contain harmful substances. This is okay to do at a personal level; nobody wins if a person is unrealistically worried about minimal, theoretical risks. But we cannot base regulations in the society on this illogical way of thinking.

The so-called precautionary principle has enormous side effects, as we know from experiments with pregnant women. The Swedish National Food Administration gives out a long list of substances that might pose a tiny risk for pregnant women. For example, women should not eat various cheeses, patés, salmon etc. because of the risk of Listeria infection, which affects 25 persons a year (of 120,000 pregnancies). In other words, 119,975 pregnant women a year are denying themselves good, nutritious food because of the very small risk of being infected with Listeria. There are also a long list of fish that should not be eaten for various reason, which we

know had resulted in many women giving up fish altogether. In the same way, the idea of the precautionary principle for chemicals, which sounds at first so reasonable, takes us into a society of panic, where people see risks in everything.

Since it is well known that people cannot reason statistically when it comes to risk (myself, I am more afraid of flying than of driving a car, even though we know that it is much, much more dangerous to drive a car), we should be relieved from having to brood about the risks of everything. That is why we have the authorities and that is why we must have permitted limits, so that we can feel secure in the knowledge that the risks we are exposed to are not zero, because they can never be that, but they have been reasonable assessed.

## 5. And the industry?

In the world of the ED people's imagination, the industry is seen as an evil force, and it is even enough to have been in a collaboration with the industry to be on the wrong side. But the industry is not evil. Or good. It is interested in making money. If we clear out plastic mattresses and buy new ones (of what material?), industry makes money. If we prohibit plasticisers in PVC floors, industry will produce new, more expensive products that are "phthalate-free". And they will make even more money. The new floor will also be less durable, so there will be a need to be replace them more often; and the industry will make even more money.

I heard a tragicomic story recently about the New Karolinska Solna University Hospital in Sweden, which could well benefit from saving money. They have decided that they should certainly have phthalate-free floors. These floors cost SEK 150 per square metre more than the regular ones. I do not know how many square metres are to be covered with the new floors - a thousand square metres costs 150 thousand more, ten thousand square metres another |1.5 million, a hundred thousand square metres another 15 million. Add to this the fact that Karolinska's new floors will have a shorter lifetime and there will be yet more millions to add.

The irony in all this is that if there is anywhere that soft plastic is used then it is medical articles - all the blood bags, all the tubing that goes into the patients' blood vessels or that is used in dialysis machines - they are all made of PVC with phthalates. So there the patients lie in their wards with expensive phthalate-free floors, surrounded by soft plastic tubing. Unlike the floor, which can become worn and thrown out twice as often due to the more expensive and poorer alternative, the medical plastic must work - lives depend on it. The soft plastic is not being got rid of here.

So the big winner in the wasteful campaign against our plastic products is - industry.

## 6. The campaign for the Non-toxic Nursery Schools has side effects.

In Sweden, the ED supporters have little opposition and we are now seeing a tremendous waste of resources as well as environmental damage when the removal of probably entirely harmless plastics from our nursery schools takes place. Even worse, parents and nursery school teachers are being told that the children's health is being threatened by common, everyday objects, a claim that has a very weak basis in science. The term non-toxic nursery schools is being used as a campaign slogan, which implies that there are toxic substances in the children's everyday life that must be eliminated.

Anyone with the slightest imagination and empathy can imagine what kind of thoughts and fixed ideas children will have. In normal language, a toxic substance is lethal or very harmful in low doses (as in toadstools or potassium cyanide). Is it really appropriate to claim that children's nursery schools are hotbeds of toxic substances that must be cleared out? In an <u>instructive film</u> for the Non-toxic Nursery Schools campaign produced by the City of Gothenburg, a child aged probably about 5 reads the following: "If you ask adults who conduct research about chemicals they will say that they don't really know how this will affect us children in 20 or 40 years' time. But they think that the risk of our suffering from asthma, allergies and cancer will increase, and the possibility of our having children on our own will decrease."

Scaring parents and children in this way is sickening. The scientists and environmental organisations that have contributed to the dissemination of such a partial and frightening message have truly done our society a disservice.

## References

Akre O, Richiardi L. Does a testicular dysgenesis syndrome exist? Hum Reprod 2009; 24: 2053–2060.

1. Bonde JP, Flachs EM, Rimborg S, Glazer CH, Giwercman A, RamlauHansen CH, et al. The epidemiologic evidence linking prenatal and postnatal exposure to endocrine disrupting chemicals with male reproductive disorders: a systematic review and metaanalysis. Human reproduction update. 2016. Epub 2016/09/23.

2. Nohynek GJ, Borgert CJ, Dietrich D, Rozman KK. Endocrine disruption: fact or urban legend? Toxicology letters. 2013;223(3):295305. Epub 2013/11/02.