Breast Cancer, Pesticides and YOU!

Meriel Watts, PhD

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Introduction

Poisoning from exposure to pesticides is a problem the world over, but most especially in developing countries and particularly for women. Women in Asian countries are severely over-exposed to pesticides, and acute pesticide poisoning kills, maims or incapacitates many millions of Asian women each year.

While an estimated 99 percent of acute poisoning deaths are believed to occur in developing countries[1], there is no accurate data on the true extent of the effects of pesticides. Often, symptoms are not recognised by either victims or medical personnel as resulting from pesticides. Underreporting is endemic in all countries, especially in poorer nations where few workers have access to medical personnel. In Central America, for instance, the under-reporting rate has been documented as 98 percent[2]. Meanwhile, estimates of acute poisoning of agricultural workers vary, ranging from one to five million[3], to 25 million in developing countries alone[4], and even from 50 to 100 million[5]. These figures do not include poisonings resulting from household or public authority use, non-agricultural occupational exposures, or 'bystander' exposure. Nor do they include chronic effects such as cancer.

Women account for more than 50 percent of the agricultural labour force in Asia[6]. In Bangladesh, Cambodia, China, India, Lao People's Democratic Republic, Viet Nam, and India, more than 70 percent of women are employed in agriculture, with this figure rising to 98 percent in Bhutan and Nepal. In the Pacific Islands, women's engagement in agriculture varies from a low of one to three percent and a high of 80 to 85 percent. In Australia, the figure is only four percent and in New Zealand, six percent[7].

No attempts have been made to estimate how many of these women are affected by chronic poisoning caused by exposure to pesticides. How many suffer and die from breast cancer,

Image: heppykanippy / FreeDigitalPhotos.net

to which pesticides have contributed, will probably never be known.

Women in poorer developing countries are much more vulnerable to exposure to pesticides than other agricultural workers for many reasons, including lesser control over their ability to avoid pesticides, and greater susceptibility to the effects of those pesticides. They are the ones most affected by economic policies rooted in structural adjustment programmes, World Trade Organization trade rules, privatisation of community resources, and other programmes discriminatory to the marginalized, particularly women.

These policies are part of the global economic agenda of giant transnational corporations and western G8 governments to intensify corporate control over land and agriculture. They have caused increasing unemployment and displacement of women in agriculture. They have resulted in the loss of women's skills and control over the seeds, which for centuries have been their domain and conferred their status in society. Thus, control over their own lives have been further eroded. Women who were once self-sufficient farmers have become displaced menial workers in the most marginal positions in the workforce, driving them further into poverty. Women currently comprise an estimated 70 percent of the world's 1.3 billion 'absolute poor.' It has been found that the number of rural women living in poverty has almost doubled in the last 20 years[8].

Globalization

The conditions of rural women are intricately linked with the international and national contexts. The WTO and its agreements, hand in hand with the International Financial Institutions such as the World Bank and the IMF, have emerged as the institutionalized face of globalization imposing neoliberal policies and "conditionalities" on developing countries. Even though the present negotiations in the WTO have stalled, the US and other G8 countries are intensifying efforts to enter into bilateral free trade deals with Asian countries. These bilateral agreements push developing countries to provide maximum concessions and further liberalise trade and investments.

These agreements and conditionalities are systematically dismantling national policies and regulations safeguarding the rights of people, their health, environment and livelihoods and making natural resources, i.e. land, water, genetic resources into commodities for sale. It is also reducing public expenditure for social services, such as health and education, by the government and moving the control for these services to corporations at the expense of rural poor communities. National policies are being amended to fit into the dictates of liberalized trade.

Globalization is described as economic integration in trade investments and finance and takes the form of liberations, privatization and deregulation.

Image: Tenaganita

In food and agriculture, this translates to increased control of land and productive resources by transnational and local corporations, landlords and elites in the country. The large-scale conversion of rice fields, vegetable and fruit gardens, and small mixed farms into cash crops for exports as well as land grabbing for industrial purposes, tourism and infrastructure projects only benefit the large TNCs, landlords and local elites.

These incidences have far-reaching implications and affect women disproportionately. Stakes have become higher for rural women as they become exploited as workers in corporate farms that are expanding into rural areas. As they become informal workers, low wages make them exist far below the poverty line. Women face more and more hazards with highly toxic chemicals and forms of hazardous technologies brought about by monocultures and high-input agriculture. As a result, women's reproductive and health rights and well being are being sacrificed in the altar of globalization. This set-up also results in massive displacement and forced migration of local rural and farming communities who have lived in those lands for decades. Rural women suffer mounting hunger and food insecurity, escalating unemployment and are forced into bonded forms of labour. Forced migration and trafficking of women is also on the rise where these women have few rights and face brutal exploitation, abuse and harassment.

Because rural women are also subjugated by cultural, social and patriarchal norms that have become institutionalised, they are caught in a web of exploitation. In such an unjust system, women peasants, agricultural workers, Dalits, fisherfolk and indigenous women are doubly oppressed and marginalised.

CASE STUDY: PARAQUAT SPRAYERS

The case of paraquat sprayers in oil palm plantations is an example of how neo-liberal globalization aggravates women's risk to pesticide exposure, and consequently, breast cancer.

While the use of many synthetic pesticides classed as "highly hazardous pesticides" (HHPs) have been banned in developed countries, it has increased exponentially in developing countries in Asia. Through bi-lateral and multi-lateral trade agreements facilitated by states and institutions such as the World Bank and the World Trade Organization agrochemical corporations have aggressively penetrated the markets in developing countries and pesticide use has risen tremendously. Asia for instance, has become the largest agricultural pesticide consumer, accounting for over 30 percent of overall consumption in the world.

One of these HHPs still in prevalent use in Asia is the herbicide paraquat. It is in widespread use in oil palm plantations in Southeast Asia, especially Malaysia and Indonesia. Paraquat is acutely toxic, and cannot be used safely, especially under common working conditions. As little as 17 milligrams has been known to kill a human, and there is no antidote. Because of its immediate and long-term hazardous effects, it has been banned in 32 countries including Switzerland, the base of operations of its manufacturer, Syngenta.

And yet, paraquat is used in an industry that is considered as one of the major sources of economic growth in Malaysia and Indonesia. These two countries account for 83 percent of global oil palm production and 89 percent of global exports. Pushed by multi-lateral institutions

to adopt export-oriented agriculture (replacing food crops with cash crops), the Malaysian and Indonesian governments radically expanded its oil palm plantations since the 1970s. The World Bank assistance facilitated investments in large-scale private plantations through measures such as cheap credit and access to government-controlled public forest land. Today, oil palm is planted in over 4 million hectares in Malaysia, and in 7.3 million hectares in Indonesia.

Women and children, the majority of pesticide and fertilizer sprayers in oil palm plantations, are most at risk. There are over 30,000 women working as plantations sprayers in Malaysia, according to the women's group Tenaganita. They are in daily contact with toxic chemicals such as paraquat, often bringing their spraying equipment inside their homes. Hot and humid conditions make wearing personal protective equipment nearly impossible.

In a 2002 report by Tenaganita and PAN entitled Poisoned and Silenced: A study of Pesticide Poisoning in the Plantations, a study among 72 women sprayers in 17 plantations in Malaysia revealed symptoms of acute pesticide poisoning, such as fatigue, vomiting, back pains, nausea, breathing difficulties, skin disorders, eye irritation, headaches, tight sensations in the chest, burning sensations in the vagina, and inflammation in the breast. Such inflammation can be a key event in cancer development. Other evidence also points to a possible link between paraquat and breast cancer including mammary tumours in laboratory animals, mutagenic and genotoxic effects, and oxidative stress and formation of free radicals.

Despite growing alarm over the effects of paraquat—including possible long-term effects such as breast cancer that have not yet been fully uncovered—the Malaysian government in 2006 temporarily lifted a ban on the herbicide, apparently under pressure from Syngenta, the palm oil industry, and its own drive to maintain existing neo-liberal economic policies.

Women's exposure to pesticides

Many rural women have been driven into the plantation sector or into other forms of corporate cash cropping (such as floriculture) where their exposure to pesticides has increased dramatically. In some countries, women make up 85 percent or more of the pesticide applicators on commercial farms and plantations, often working whilst pregnant or breastfeeding. There are an estimated 30,000 women pesticide sprayers in Malaysia alone that spray pesticides, and frequently highly toxic ones like paraquat, on an average of 262 days per year. Eighty percent of the spraying is carried out with leaky hand-held equipment. An incentive of extra

Sri Lanka: Woman washes in water that flows off farm fields where pesticides are highly used.

Image: Vikalpani

50 cents per day is enough to encourage these impoverished women to spray[9].

Even if they do not directly apply the pesticides, women work and raise their children in a toxic environment. They mix pesticides, weed while pesticides are being applied, wash out pesticide containers, or harvest pesticide-doused crops. They wash pesticide-soaked clothing and store pesticides in their homes.

Data collected from developing countries show that women's exposure to pesticides is significantly higher than is formally recognized, and that pesticide poisonings are greatly underestimated. A study of Vietnamese farmers found that they suffered 54 cases of moderate pesticide poisonings per month, but that only two of these cases were treated and reported at the local health centre[10]. Given that most episodes of acute pesticide poisoning appear to escape the attention of medical authorities—and this is more recognisable than chronic effects—it is not surprising that so little is known about the relationship between exposure to pesticides and breast cancer.

Women Farmers spraying pesticides in Viet Nam. *Image: CGFED*

Women more susceptible to pesticides

These problems are compounded by gender biases in epidemiology[11]. Most researchers looking at links between cancer and farming have concentrated on male farmers[12]. Moreover, as will become evident in Chapter 4, there have been very few epidemiological studies investigating a potential link between exposure to pesticides and breast cancer, especially those pesticides in current usage.

- **Women's greater vulnerability to pesticides is also overlooked in the toxicological risk assessment of pesticides[11].**
- **Women's higher proportion of body fat provides a greater reservoir for fat-loving pesticides, some of which are known to be hormonally active and/or carcinogens, and are associated with breast cancer.**
- **Women may also absorb pesticides through their skin more easily than men. For example, dermal absorption of the organochlorine lindane is three times greater for women than for men[13]. And once there, fat-loving pesticides may reside in the body longer in women than in men[14].**
- **Women's higher level of hormonally sensitive tissues make them more vulnerable to the effects of pesticides, especially those that are hormonally active known as endocrine disruptors. These pesticides are capable of causing profound changes to hormonally sensitive tissues, such as breast tumours. Increased fat exchange, for example during pregnancy and lactation, together with the cyclic nature of hormonal changes, also add to that greater sensitivity[15].**

Lastly, where there is poverty, there is malnutrition, especially for women who eat 'last, the least and the left-overs.'

Malnutrition can enhance the adverse effects of pesticides. Low levels of dietary protein enhance vulnerability to organophosphate insecticides[16]. Low levels of dietary protein also increase the toxicity of diuron, a known mammary carcinogen[17].

In laboratory tests, the toxic effects on liver, kidneys and muscle tissue of a mixture of monocrotophos, hexachlorocyclohexane (HCH) and endosulfan were aggravated by malnourishment[18] — HCH and endosulfan are also associated with breast cancer.

Malnutrition leads to weakened immune systems. Malnutrition of the pregnant woman leads to underdevelopment of the unborn child, paving the way for chronic ill health later in life[19]. These effects can contribute to an increased risk of breast cancer.

Women's exposure to pesticides has increased as their poverty and marginalisation deepened. At the same time, poverty has also increased their vulnerability to pesticides, and to the development of chronic diseases such as breast cancer.

Corporations selling pesticides are also selling breast cancer drugs

Not surprisingly, the corporate economic agenda that has driven women into this position has also failed to do anything to stop the escalating epidemic of breast cancer to which pesticides are undoubtedly contributing. The corporates have certainly contributed to the breast cancer research programme—but usually only in ways designed to enhance their own returns from the sale of screening equipment and expensive drugs. Whilst billions of dollars are being poured into an attempt to develop a vaccine against breast cancer, these corporates are contributing almost nothing to prevent breast cancer. With the vast majority of breast cancer thought to be caused by environmental and lifestyle factors, this is a preventable disease. But most government breast cancer programmes, driven by the self-interest of drug companies and specialist medical sectors, continue to focus on understanding the genetic factors that underlie less than 10 percent of breast cancer cases, on early detection, and on treatment with increasingly expensive and sophisticated drugs. For example the USA's National Breast Cancer Awareness month was founded and sponsored by Zeneca Chemicals, which ironically earns millions from sales of carcinogenic pesticides such as acetochlor on the one hand, and as Astra Zeneca, from the breast cancer treatment drug tamoxifen (which is itself carcinogenic) on the other hand[20]. Zeneca was a subsidiary of ICI chemicals. Zeneca/ICI pesticides that increase the risk of breast cancer include lindane, permethrin, cypermethrin and captan. Zeneca also purchased the largest for-profit chain of cancer treatment centres in the US, Salick Health Care Inc.[21], neatly assuring profits from both the causing and the curing of breast cancer.

As Dr. Devra Davis[22], a then Senior Adviser to the World Health Organisation, put it:

"investments in controlling and studying avoidable environmental contributions to cancer remain scandalously low... fuelled by a sophisticated disinformation campaign of the tobacco industry—just confirmed by the WHO—we wasted 50 years debating the importance of cigarettes. We cannot afford to make the same mistake again."

Certain pesticides may contribute to breast cancer epidemic

Pesticides that are carcinogenic, disrupt hormones, or in other ways disrupt the development of the mammary gland, are a significant environmental factor that contributes to the global breast cancer epidemic—one that has long been ignored.

Numerous laboratory studies show that animal mammary carcinogens and pesticides which mimic oestrogen, or otherwise disrupt natural hormones, may be increasing breast cancer risk [23 24 25 26 27 28]. Pesticides can also contribute to breast cancer by undermining the immune system, interfering with intercellular communication, and interfering with metabolic activities.

Increasing, though still insufficient, attention is now being paid to

some industrial and household chemicals—such as phthalates, bisphenol A, polyvinyl chloride (PVC), polychlorinated biphenyls (PCBs), polycyclic aromatic hydrocarbons (PAHs), and dioxin—as known, probable, or possible causes of breast cancer[28]. However, scant attention is being paid to the role of pesticides. Generally, only the organochlorine insecticides like DDT have been linked with breast cancer. But even this review has, conservatively, identified 98 pesticides as potentially increasing the risk of breast cancer. Most of these are not organochlorines and are still in widespread use in many countries.

A number of these pesticides are found as residues in women's breast milk, indicating exposure, not only to the women, but also to the newly-born child transferred in breastmilk. However this ***does not*** mean that breastfeeding should be replaced with bottle-feeding. Breastfeeding should be maintained because, despite the residues, it confers health benefits on both the infant and the mother. For example, it reduces the risk for mothers of developing uterine and breast cancer. Breastfeeding confers substantial benefits on babies, in the form of vital nutrients, growth factors and immunological components passed from the mother to baby. It reduces the risk of infant death and the incidence and severity of infections. It helps prevent the development of allergies, obesity, hypertension and diabetes. Breastfeeding enhances cognitive development and significantly develops the bonding process between mother and child. It is the cheapest and best available food for newborn infants: it provides complete nutrition for the first six months and many benefits thereafter for the first two years and more of the child's life. This is vital for all infants, but especially those in households that do not have enough to eat and where women and children are often nutritionally deprived. Therefore, in spite of concerns regarding chemical contamination, the advice from scientists and health professionals is to continue breastfeeding[29].

The solution to the problem of transferring residues to the infant is not to stop the breast-feeding but to stop the contamination of the breast milk in the first place, by stopping the use of the pesticides. In March 2004, the World Alliance for Breastfeeding Action (WABA) and the International POPs Elimination Network (IPEN) issued a joint statement[30], which acknowledged that:

"The contamination of breastmilk is one symptom of the environmental contamination in our communities. Responsibility for this problem belongs to the industrial sources of contamination, not to breastfeeding women."

Stop the contamination of breast milk!

Image: Mohammad Rakibul Hasan, WABA

Government regulations fail to protect women from exposure to carcinogenic pesticides

Most of the pesticides implicated in breast cancer are still in common use because of the prevailing regulatory failure to access up-to-date independent scientific research, and to apply the precautionary principle. Instead, regulators invariably rely on toxicological data provided by the pesticide manufacturers as 'proof' that a pesticide is 'acceptable' because it doesn't identify effects such as breast cancer. This regulatory approach, which determines national and international chemicals policy, applies the paradigm of 'science-based' decision-making.

'Science-based' decision-making is erroneously taken to mean quantitative risk assessment, or proof of a causal link between a pesticide and an 'unacceptable' effect before action should be taken to remove that pesticide. In the words of Dr. Janette Sherman, Adjunct Professor in the Department of Environmental Sciences, Western Michigan University in Kalamazoo, this "grant[s] to chemical companies the right to claim their product 'innocent' until proven guilty beyond the shadow of a doubt"[31]. The burden of proof then falls on the community and those who

Decision-making based on quantitative risk assessment and the need for causal proof is in fact really politically-based, not science-based, because it implicitly places more importance on the commercialisation of pesticides than it does on the community's health

Precautionary approach: The key to preventing pollutants[32]

A precautionary approach is more thorough and more 'scientific' than the standard risk assessment process because it requires recognition of the limitations of science, such as uncertainty about the chronic effects from ongoing low-dose exposure to mixtures of chemicals; recognition of the lack of knowledge about casual links; recognition of the value judgements involved in risk assessment; and attention to other factors involved, such as the availability of less harmful alternatives.

Essentially, the precautionary approach puts the protection of health and the environment over and above business interests.

It should replace the current system of decision making that demands generation of extensive scientific data and requires exhaustive analysis of risks as preconditions to policy formulation and action. With the precautionary principle, there is recognition that long-term impacts of toxic chemicals are difficult to predict and often impossible to prove. Efforts to regulate, restrict or prohibit the production, sale and distribution of toxic chemicals to protect health and the environment are often considered "trade restrictions" and are challenged by the chemical companies or by countries where these companies are based. This situation is obviously biased in favor of business interests highly disadvantageous to people's health and the environment. The precautionary approach attempts to change this unjust situation. It puts the burden of proof of safety on the polluter. Prevention is the major activity, not mitigation. Avoidance of exposure is the major concern, not defining the limits of exposure as in the risk assessment approach. The question asked is not how much exposure is allowable but whether the exposure is necessary in the first place.

Affected communities need not carry the burden of proof of harm. Citizens should use the precautionary principle to push for preventive action and policies and resist the corporate push for hazardous chemicals. Pollution prevention is the only logical option.

Unlike in risk assessment where uncertainty is given the benefit of the doubt, the precautionary principle considers uncertainty as a potential threat. While the risk assessment paradigm often considers absence of evidence as evidence of absence of harm, the precautionary principle considers absence of evidence as no evidence of absence of harm. Infinitesimal uncertainty factors often preclude demonstration of cause and effect relationships and probabilistic characterization of risks. To be meaningfully protective, therefore, an assessment process looking into the potential environmental and health impacts of a chemical should consider uncertainties as a warning signal. Addressing the knowledge gaps pertaining to that chemical should be made an obligatory matter for the chemical manufacturer to the people's satisfaction before any chemical is allowed to be released into the environment.

The evaluation process using a precautionary approach is not just an arbitrary procedure based on mere speculations and unfounded fears. It is based on the best available scientific evidence and guided by technically sound analytical procedures. There is a wide array of available scientific data that could provide sufficient basis to make a sound judgement as to the potential risks that a chemical poses to human health. However, for existing chemicals in commerce where scientific data is lacking or is inappropriate or impractical to generate (such as direct experimentation on humans), precautionary action protective of human health and environment should be taken even if there are doubts that the chemical in question poses unacceptable risks, making use of the best available knowledge and taking into account not only scientific but also socio-cultural factors.

With the precautionary principle, there is recognition that long-term impacts of toxic chemicals are difficult to predict and often impossible to prove

work in the public interest to prove that a pesticide does cause unacceptable effects such as breast cancer.

The current situation is a no-win situation for the community. Chronic effects are complex and difficult to link back to pesticide exposure and, especially, to prove. They usually arise from ongoing low-dose exposures to pesticides that do not result in acute poisoning.

Thus, the real effects of that exposure often lie below the radar. As breast cancer can have a very long latency period, linking its onset to an original pesticide exposure is extraordinarily difficult. Studies that do show a link between pesticide exposure and breast cancer, or laboratory studies that show a pesticide can cause mammary tumours in rodents, should never be dismissed, simply because other studies do not. Conversely, studies that fail to find a link between exposure to a pesticide and breast cancer, do not prove that the pesticide cannot be linked to breast cancer. Rather, the precautionary principle must be applied to these findings, and women's exposure to pesticides, which may be contributing to the escalating global epidemic of breast cancer, must be dramatically reduced.

INCIDENCE OF BREAST CANCER

GLOBAL PREVALENCE

Of the 10 million new cases of invasive cancer worldwide each year in both males and females, approximately 10 percent are breast cancer, which makes it the second most common cancer after the lung[33].

Breast cancer is by far the most common form of cancer in women throughout the world, and the leading cause of cancer death amongst women[34].

An estimated 1.15 million women have breast cancer, and the incidence rate continues to climb in all age groups[35]. There are an estimated 4.4 million women alive who have had breast cancer diagnosed within the last five years[36]. Whilst there has been a minor decrease in the mortality rate from the disease in some countries, the tragic reality is that there are still an increasing number of women dying from breast cancer each year.

Men can also develop breast cancer, although the incidence rate is very low compared with women and male breast cancer is regarded as a rare disease. It accounts for less than one percent of all breast cancer cases[37].

The *reported* incidence rate for breast cancer varies enormously between countries. Reported rates are highest in the USA, Europe, New Zealand, Canada and Australia, and lowest in Asia and Africa. Using the age-

Using the age-standardised incidence rates reported by the International Agency for Research on Cancer, the country with the lowest incidence is Mozambique (3.9 cases per 100,000 population) and the highest is the USA (101.1). Other countries with high rates—over 90 cases per 100,000 population—are Belgium (92), France (91.9), New Zealand (91.9), Israel (90.8), and Iceland (90.0). Mortality from breast cancer parallels incidence. Mortality is reported to be highest in the countries with the highest incidence rates, and lowest in Latin America and Asia.

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Mortality from breast cancer parallels incidence. Mortality is reported to be highest in the countries with the highest incidence rates, and lowest in Latin America and Asia[33].

Strikingly, these pesticides did not come into prominence in Asian countries until the excesses of the Green Revolution (1970s to 1980s), during which pesticide usage soared, and after which breast cancer rates began to follow suit

Under reporting of breast cancer likely

This apparently huge regional variation in breast cancer incidence may not be all it seems. It is likely that there is substantial under reporting in many developing countries—for some of the same reasons that hinder the collection of accurate poisoning statistics. Many poor rural women simply cannot afford to go to doctors, so their breast cancer may never be recorded. Additionally, not all countries have adequate breast cancer registries even for those cases that do get seen by a doctor. Not surprisingly then, it has been observed that the introduction of breast screening results in a rise in the *reported* incidence rate of detected breast cancer[39]. So countries in which health structures and services are inadequate may in fact have a significantly higher rate of breast cancer than the currently available statistics reveal. Therefore, it is advisable not to place too much emphasis on the differences in reported incidence rates between countries.

GLOBAL TRENDS

Breast cancer incidence is increasing almost everywhere. From the 1970s to the 1990s, reported breast cancer incidence rose 30 to 40 percent in most countries, with the most marked increases among women aged 50 years or older[33]. The incidence of male breast cancer has meanwhile increased by 26 percent in the last 25 years in the US[40].

However, although the incidence rates continue to climb in 'western' countries, they are climbing more rapidly in 'non-western' countries[33 35].

- Whilst the global increase in incidence rate is about 0.5 percent annually, in China it is 3 to 4 percent, and "not much less elsewhere in eastern Asia"[35].
- There has been a rapid increase in years of potential life lost to breast cancer in Japan, increasing five-fold over the fifty years from 1950 to 2000[41].
- Mortality from breast cancer in Kazakhstan has been rising steadily, and this increase accelerated in 1995 to 1997[42].
- Rising incidence rates have been observed in Hong Kong[35].
- There has been a striking recent increase in breast cancer in Taiwan, with a relatively young median age (45 to 49 years) at diagnosis. Whereas the increase in the incidence rate in the USA slowed down between 1980 and 1999, in Taiwan it continued to escalate, with the incidence rates of Taiwanese women born after the 1960s approaching that of Caucasian Americans[43].
- In India, the incidence of breast cancer is rapidly increasing, with an estimated

GLOBOCAN 2002:

The following data is sourced from the GLOBOCAN 2002 database developed by the International Agency for Research on Cancer (IARC 2002), using incidence data from national cancer registries and mortality data from other national registrations. The quality of the data varies considerably. The data covers the entire national population or is based on samples from selected regions.

Cancer data are always collected and compiled some time after the events to which they relate, so that the most recent statistics available are always 'late' by varying degrees. GLOBOCAN 2002 presents estimates for the year 2002. However, although the populations of the different countries are those estimated for the middle of 2002, the disease rates are not those for the year 2002, but from the most recent data available, generally two to five years earlier. Incidence and mortality rates by age group (0 to 14,15 to 44,45 to 54,55 to 64,65+) were estimated for as many countries as possible. The numbers of cases and deaths are computed by multiplying the estimated rates by the year 2002 population estimates for the corresponding country.

These estimates are based on the most recent incidence, mortality and survival data available at IARC, but more recent figures may be available directly from local sources.

Because the sources of data are continuously improving in quality and extent, estimates may not be truly comparable over time. Care should therefore be taken when comparing these estimates with those published earlier. The observed differences may be the result of a change in the methodology and should not be interpreted as a time trend effect.

Incidence = the number of new cases of breast cancer per year, expressed as either the absolute number of new cases or as a rate per 100,000 persons.

Mortality = the number of deaths per year, expressed as either an absolute number of deaths or as a rate per 100,000 persons.

Crude rate = the number of new cases of breast cancer per year divided by the number of people in the population at risk, expressed as an annual rate per 100,000 persons at risk.

ASR (***age-standardized rate***) = a summary measure of a rate that a population would have if it had a standard age structure. Standardization is necessary when comparing several populations that differ with respect to age because age has such a powerful influence on the risk of cancer. The most frequently used standard population is the world standard population. It is also expressed per 100,000. The ASR (world standard) is calculated using the 5 age-groups: 0 to 14,15 to 44,45 to 54,55 to 64,65+.

80,000 new cases diagnosed annually[44]. The incidence of breast cancer increased by 40 percent between 1965 and 1985[45]. This is thought to be at least in part due to increased life expectancy: in recent years, life expectancy in India increased from 32 years to 63 years[46].

- In Singapore, the increase in incidence of breast cancer was reported to be 5.7 percent per year among premenopausal women and 3.9 percent per year among postmenopausal women by 1992[47].
- In Hawaii, the breast cancer incidence rate increased by 42 percent compared with less than 20 percent over the same time period for areas of mainland USA such as San Francisco Bay area, Detroit and Seattle[48].

Explanations given for these striking increases in breast cancer rates include westernisation of diet, increasing

life expectancy, increasing sedentary lifestyle in urban areas, radiation, alcohol—and increased use of pesticides[47 46 42 45].

Some reviewers have linked this trend to synthetic chemicals, noting that "the increasing incidence of breast cancer has paralleled the proliferation of synthetic chemicals since World War II"[28]. Pesticide use began in earnest post-World War II in western countries, with dramatic increases in the use first of organochlorines, then of organophosphates, and more recently of synthetic pyrethroid insecticides. There is evidence that all of these may be implicated in the global increase in breast cancer.

PREVALENCE IN ASIA AND THE PACIFIC

Breast cancer is the most common cancer for women in many countries in the region, such as Sri Lanka and Thailand, although in others it is second to cervical cancer, e.g. Fiji, India and Indonesia[49 50].

There is huge regional variation, with New Zealand topping the list for age-standardised incidence rates (91.9), with Israel (90.8) and Australia (83.2) not far behind.

The lowest *reported* incidence rates are in East and South Central Asia, averaging 20.6 and 21.8 cases per 100,000 women respectively. However there is a major exception, and that is Pakistan. Pakistan has an incidence rate of 50.1 cases per 100,000 women—well in excess of comparable countries such as Afghanistan (26.8), Sri Lanka (23.6), Nepal (21.8), India (19.1), and Bangladesh (16.6). This may well be because the city of Lahore has a well-developed population-based cancer registry, suggesting that the relatively low figures throughout many parts of rural Asia are due to the lack of a breast cancer registry and diagnosis. The true magnitude of the breast cancer problem in rural Pakistan, as well as the rest of rural Asia, is therefore unknown.

Very little information is available about breast cancer rates in the Pacific Islands. What does exist indicates rates generally higher than in Asia, with Guam topping the list at 50.4 cases per 100,000 women (ASR), and Papua New Guinea having the lowest recorded rate (17.3).

Additionally, the global statistics do not contain a figure for the Gaza Governorates. However, Professor Jamal Safi[51], of the Al-Azha University, provided an age-adjusted incidence rate of 19.3 per 100,000 for female breast cancer from 1990 to 1999. Breast cancer accounted for 34 percent of all cancer cases in women.

MAP: GLOBAL INCIDENCE RATES OF BREAST CANCER IN ASIA AND THE PACIFIC

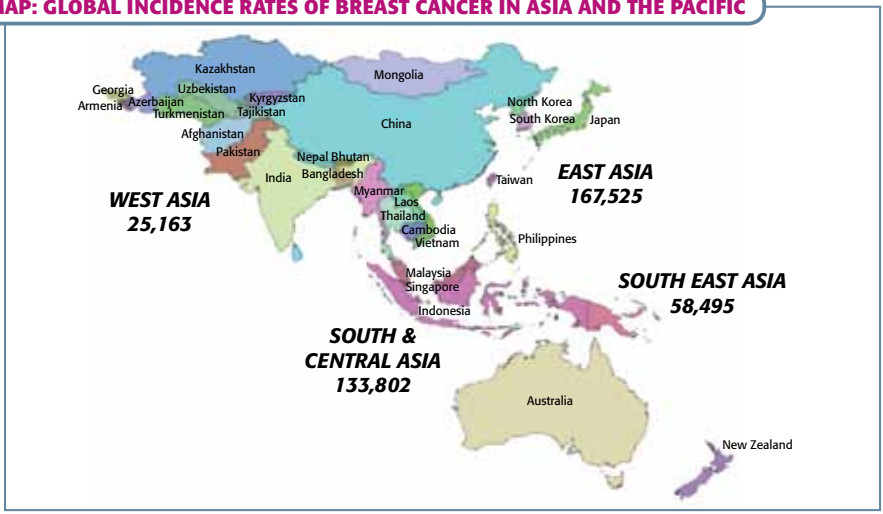


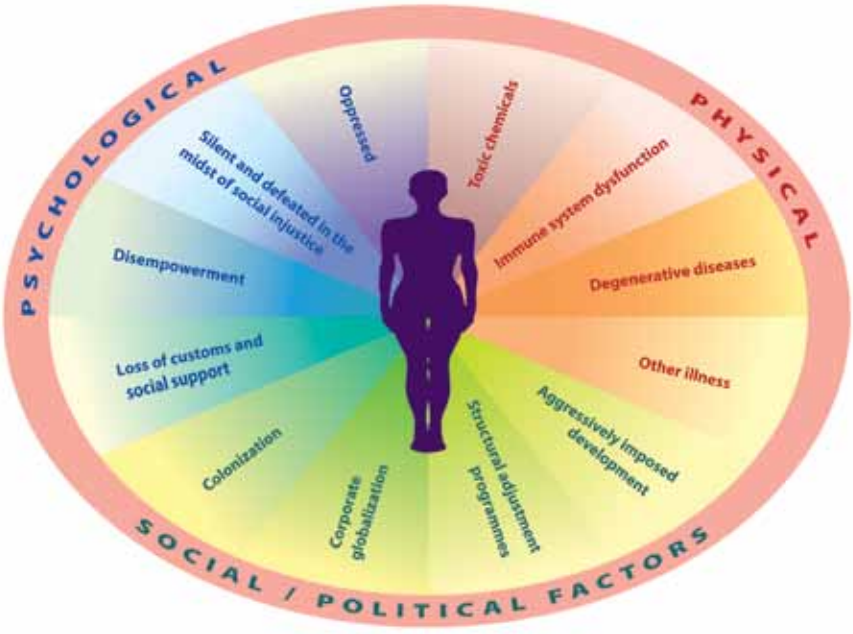
Table 1: Breast cancer incidence and mortality rates in Asia and the Pacific

	INCIDENCE			MORTALITY		
COUNTRY	**Cases**	**Crude Rate**	**ASR(W)**	**Deaths**	**Crude Rate**	**ASR(W)**
World	***1,151,298***	***37.4***	***37.4***	***410,712***	***13.3***	***13.2***
Highest ASR - USA	209,995	143.8	101.1	42,913	29.4	19.0
Highest CR - Sweden	6,583	148.1	87.8	1,516	34.1	17.3
Lowest Cr & ASR - Mozambique	236	2.5	3.9	170	1.8	2.8
ASIA						
East Asia	***167,525***	***22.9***	***20.6***	***47,866***	***6.5***	***5.8***
China	126,227	20.1	18.7	36,630	5.8	5.5
Japan	32,245	49.6	32.7	9,178	14.1	8.3
Korea, N	2,388	21.3	20.4	517	4.6	4.4
Korea, S	5,511	23.5	20.4	1,201	5.1	4.4
Mongolia	64	5.0	6.6	31	2.4	3.5
SE Asia	***58,495***	***21.8***	***25.5***	***26,818***	***10.0***	***11.8***
Brunei	28	17.4	20.6	12	7.5	9.0
Cambodia	1,032	14.7	21.5	453	6.5	9.5
Indonesia	25,208	23.3	26.1	10,881	10.1	11.3
Lao	217	7.8	10.9	94	3.4	4.7
Malaysia	2,974	26.2	30.8	1,292	11.4	13.5
Myanmar	4,117	16.8	20.2	1,800	7.3	8.9
Philippines	13,051	33.5	46.6	7,582	19.5	27.1
Singapore	1,213	59.0	48.7	394	19.2	15.8
Thailand	5,282	16.3	16.6	1,980	6.1	6.3
Viet Nam	5,268	13.1	16.2	2,284	5.7	7.1
S. Central Asia	***13,3802***	***18.0***	***21.8***	***67,165***	***9.0***	***11.1***
Afghanistan	2,021	17.8	26.8	874	7.7	11.7
Bangladesh	7,735	11.1	16.6	3,376	4.9	7.3
Bhutan	170	15.7	21.8	74	6.8	9.6
India	82,951	16.5	19.1	44,795	8.9	10.4
Iran	4,742	13.5	17.1	2,039	5.8	7.4
Kazakhstan	3,447	41.9	38.7	1,687	20.5	18.7
Kyrgyzstan	522	20.4	23.0	258	10.1	11.5
Nepal	1,835	15.6	21.8	799	6.8	9.6
Pakistan	25,719	35.6	50.1	11,194	15.5	22.0
Sri Lanka	2,180	23.2	23.6	948	10.1	10.3
Tajikistan	304	9.9	13.2	135	4.4	6.2
Turkmenistan	349	14.1	17.9	155	6.3	8.5
Uzbekistan	1,755	13.7	17.3	789	6.2	8.2
W Asia	***25,163***	***26.1***	***33.3***	***10,738***	***11.2***	***14.3***
Armenia	1,162	59.8	51.6	561	28.9	24.5
Azerbaijan	1,295	31.6	31.5	557	13.6	13.7
Bahrain	91	32.4	40.2	40	14.3	17.7
Cyprus	349	87.7	67.2	157	39.4	29.6
Georgia	1,901	70.1	51.8	1,003	37.0	25.1
Iraq	2,497	21.0	31.7	1,081	9.1	13.9
Israel	3,382	106.3	90.8	978	30.8	24.0
Jordan	509	20.4	33.0	223	8.9	14.6
Kuwait	194	23.2	31.8	83	9.9	14.0
Lebanon	816	44.4	52.5	362	19.7	23.4
Oman	100	7.8	13.2	43	3.4	5.8
Qatar	53	25.6	33.3	23	11.1	14.6
Saudi Arabia	1,563	15.5	24.7	677	6.7	10.9
Syria	2,177	25.9	44.8	955	11.4	19.9
Turkey	6,729	19.9	22.0	2,970	8.8	9.7
United Arab Emirates	179	19.5	24.1	77	8.4	10.5
Yemen	1,795	18.0	35.1	787	7.9	15.6
PACIFIC						
New Zealand	2,330	120.0	91.9	670	34.5	24.5
Australia	11,176	114.1	83.2	2,667	27.2	18.4
Melanesia	***474***	***14.5***	***22.2***	***220***	***6.8***	***10.5***
Fiji	104	25.5	31.2	48	11.8	14.5
Papua New Guinea	261	10.8	17.3	118	4.9	8.0
Solomon Islands	39	16.8	29.8	17	7.3	13.9
Vanuatu	16	15.9	24.0	7	6.9	11.1
Micronesia	***99***	***38.0***	***50.4***	***47***	***18.0***	***23.6***
Guam	35	44.9	50.4	16	20.5	23.6
Polynesia	***84***	***28.2***	***34.2***	***38***	***12.8***	***15.8***
Samoa	20	26.5	34.2	9	11.9	15.8

WHAT CAUSES BREAST CANCER?

The wellbeing of humans is closely interrelated with the environment in which we live and function—the physical, social and psychological/spiritual environment. Good health can be seen as a state of harmony between a person and her/his broader environment, and illness as a result of the disruption of that harmony.

Many things bring about that disharmony—such as toxic synthetic chemicals that cause cancer, immune system dysfunction, endocrine disruption, reproductive abnormalities, developmental anomalies, degenerative diseases, and other states of ill-health. Inappropriate consumption of tobacco and alcohol, recreational drugs, and inessential pharmaceuticals also disrupt our environment. So do social and political factors like colonisation, corporate globalisation, structural adjustment programmes, and aggressively imposed development. These factors result in a lack of safe drinking water, nutritious food and clean air for many people. So do the various forms of social control and manipulation that distort and destroy the psyche/spirit and leave people disempowered, oppressed, silent and defeated in the midst of social injustice[52].



All these factors may play a role in the genesis and/or development of breast cancer. The role of pesticides in breast cancer-–-a complex, multi-faceted disease—needs to be understood in the broader context of disruption of the human environment. Pesticides disrupt social and psychological environments. This is especially true in Asian countries where pesticides have often been forced on poor and powerless farmers as a conditionality of credit or through coercion or the promise of riches. (For instance, Syngenta's advertising campaign in Thailand gave buyers of paraquat the chance to win a motorcycle or even a truck). Pesticides are also part of the environment, depriving many users of safe drinking water, nutritious food (especially when staple foods are replaced by cash crops), and clean air.

This booklet, however, narrows its focus only to the ways in which pesticides might directly interfere with DNA, the endocrine and immune systems, or other physiological processes. But first, a look at the mainstream understanding of the factors that contribute to breast cancer is necessary.

CONTRIBUTING RISK FACTORS

A number of factors are regarded by mainstream science and medicine as contributing to the risk of breast cancer, but they do not account for the majority of cases.

Inherited breast cancer susceptibility genes—notably the genes BRCA1 and BRCA2, which confer a 60 to 80 percent lifetime probability of breast cancer—are thought to underlie fewer than 10 percent of breast cancer cases[53]. These genes do not cause breast cancer, but they do increase the vulnerability of women to carcinogens and other factors that promote breast cancer.

More than 80 percent of breast cancer is thought to be associated with environmental factors that include exposure to contaminants, lifestyle and diet[54], and exposure to ionising radiation (e.g. x-rays, uranium, nuclear waste). Exposures early in life pose greater risk than exposures later in life[27].

However, factors affecting the ovarian hormones oestrogen and progesterone, and particularly the cumulative lifetime exposure to oestrogen, are regarded as the best-established contributing risk factors for breast cancer.

The mammary gland is a complex organ that undergoes continuous change under the influence of cyclic hormonal stimulation from birth to death, and its development depends on a complex interplay of oestrogen, progesterone and other growth factors[52].

Several epidemiological studies have shown that breast cancer risk is strongly linked to elevated serum levels of the natural oestrogen, 17*beta*-oestradiol[55 56 57].

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Some lifestyle factors that affect the ovarian hormones, and are believed therefore to increase breast cancer risk, include[52 58 25 59]:

- reproductive characteristics such as early menarche (before age 12), late menopause (after age 55), no pregnancies, late age at first full-term pregnancy, and short lactation;
- pharmaceutical hormones: both oestrogen only and oestrogen-progesterone hormone replacement therapy increase breast cancer risk;
- recent, but not long-term, use of oral contraceptives is associated with higher risk;
- alcohol use, lack of physical activity, diet low in fibre and vitamin D;
- low premenopausal body mass index, higher body mass index and weight gain after menopause, and advancing age.

But all these factors, including inherited genes, are thought to

underlie less than 50 percent of the cases of breast cancer. The remaining more than 50 percent of cases are regarded as being 'unexplained' [27 28].

There is now significant international concern that some of the estimated 70,000 synthetic chemicals in our environment today may be making a major contribution to the more than 50 percent 'unexplained' breast cancer cases. Some chemicals have been identified as either mammary carcinogens or likely to be contributing to breast cancer because of their influence on naturally occurring hormone levels. These chemicals are flame retardants, pharmaceuticals, solvents, dyes, benzene, polycyclic aromatic hydrocarbons (PAHs), bisphenol A and phthalates which are used in plastics, parabens, styrene, mercury, and pesticides. The strongest evidence of a link exists for PAHs and polychlorinated biphenyls (PCBs)[60]; and organochlorine insecticides like DDT[52 61 26 34 28] — largely because they have been the focus of research. Many pesticides known from laboratory studies to cause mammary tumours in rodents have been poorly, if at all, studied from a human breast cancer perspective.

As noted earlier, the increasing incidence of breast cancer, and other cancers, has paralleled the global proliferation of synthetic chemicals since World War 1[28].

As developing countries industrialise and take up industrial agricultural practices, their breast cancer rates escalate towards those of the already chemicalised societies of the western world. Many chemicals, including pesticides, persist in the environment, accumulate in body fat, and can now be found residing in the breast tissue of women the world over.

Pesticide exposure, in combination with genetic predisposition, age at exposure, and hormonal condition, has a cumulative effect on breast cancer risk[62]. The lag in time between the chemicalisation of agriculture and the escalation of breast cancer rates is accounted for by the typically late onset of breast cancer—over 78 percent of breast cancer cases occur in postmenopausal women—and the long latency periods typically associated with chemical carcinogenesis in humans[63].

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- **recent, but not long-term, use of oral contraceptives is associated with higher risk;**
- **alcohol use, lack of physical activity, diet low in fibre and vitamin D;**
- **low premenopausal body mass index, higher body mass index and weight gain after menopause, and advancing age.**

HOW PESTICIDES ARE INVOLVED IN BREAST CANCER

There is a growing body of epidemiological evidence, backed by laboratory studies, linking exposure to pesticides with breast cancer. Because of the many factors involved in breast cancer, it is not possible to arrive at an absolute determination of a cause and effect relationship between individual pesticides and breast cancer. What can be done though is to identify how pesticides might be involved. On that basis, it is possible to identify which pesticides are likely to be increasing the risk of breast cancer in the context of multiple contributing causes.

There are a number of ways in which pesticides may be instrumental in the breast cancer epidemic, including:

- As *mammary carcinogens* – initiating cancer, for example

by causing mutations in a gene, chromosomal damage, DNA damage, or formation of free radicals that cause oxidative stress leading to cancer. Pesticides that have caused increased incidence of mammary tumours in rats and/or mice in laboratory studies include alachlor, captafol, clonitralid, 2,4-D, DBCP, dichlorvos, endrin, ethalfluraline, ethylene dibromide, ethylene dichloride, ethylene oxide, folpet, malathion, mancozeb, oryzalin, parathion, paraquat, PFOS, propylene dichloride, sulfallate, and toxaphene[64].

- As *tumour promoters* – promoting the growth of breast cancer cells and hormonally sensitive tumours. Pesticides that promote the growth of breast cancer cells include allethrin, chlordane, chlordecone, cypermethrin, deltamethrin, dicofol, DDT, dieldrin, endosulfan, fenarimol, fenvalerate, heptachlor, lindane, methoxychlor, monocrotophos, omethoate, permethrin, sumithrin, and the adjuvant nonylphenol[63].
- *By affecting mammary gland development* in ways that increase its susceptibility to carcinogens or hormonally active agents, such as by increasing terminal end buds, which are bulb-shaped structures within the mammary gland believed to be the part of the breast most sensitive to chemical carcinogens. Pesticides that have been found to affect mammary gland development include atrazine, DDT, endosulfan, malathion, methoxychlor, and permethrin[63].
- By compromising the *immune system* and affecting a women's defences against cancer. For example, DDT, chlordane, endosulfan, and heptachlor reduce the ability of Natural Killer T-cells to destroy tumour cells[65]; and atrazine suppresses the tumour necrosis factor which is also involved in destroying tumour cells[66].
- By interfering with *communication between cells*, or gap junction intercellular communication (GJIC), which is essential for controlling the growth of cancer cells and tumours. Pesticides that affect GJIC include chlordecone, cypermethrin, DDT, deltamethrin, fenvalerate, heptachlor, lindane, permethrin, and toxaphene[67 68].
- By disrupting the *endocrine system* in ways other than promoting tumours or affecting the development of mammary gland tissue (see below).

Endocrine disruption

Some scientists and many regulators take a narrow view of the role of pesticides (and other chemicals) in cancer, acknowledging only those that actually initiate the formation of cancer cells. However, the importance of pesticides that act as promoters of breast cancer cell development and the spread of tumours, or affect the development or susceptibility of mammary tissue can no longer be ignored.

What are Endocrine Disrupting Chemicals?

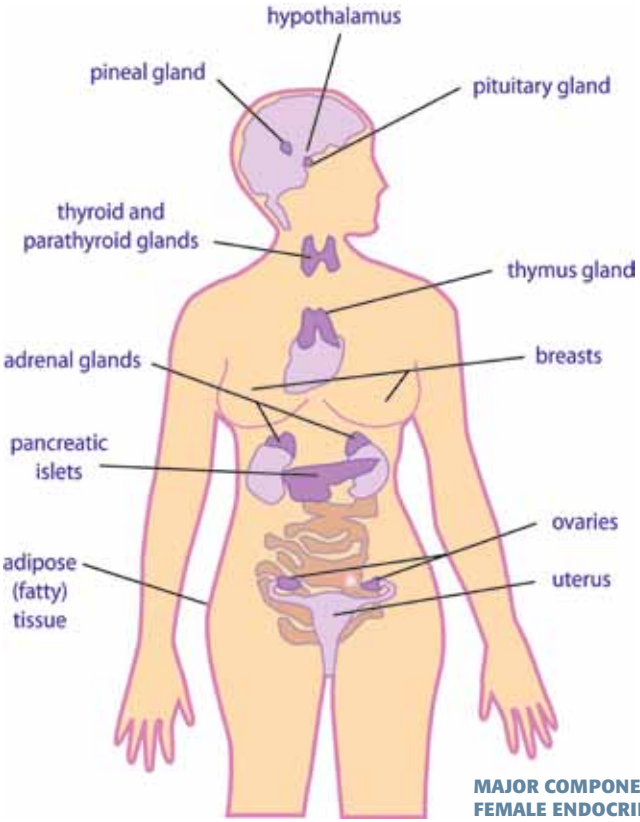
The endocrine system is a complex system that regulates various biological and physical processes. The endocrine system also regulates functions such as physical and mental development, reproduction, metabolism, immunity and behaviour.

It helps the body achieve homeostasis or the ability to maintain internal equilibrium by adjusting its physiological processes.

The endocrine system, mainly consists of a number of glands and hormones.

These glands include among others for example the hypothalamus, pituitary, thyroid, pancreas, adrenal, testes and ovaries.

Hormones are released by these glands in response to the body's requirements.



MAJOR COMPONENTS OF THE FEMALE ENDOCRINE SYSTEM

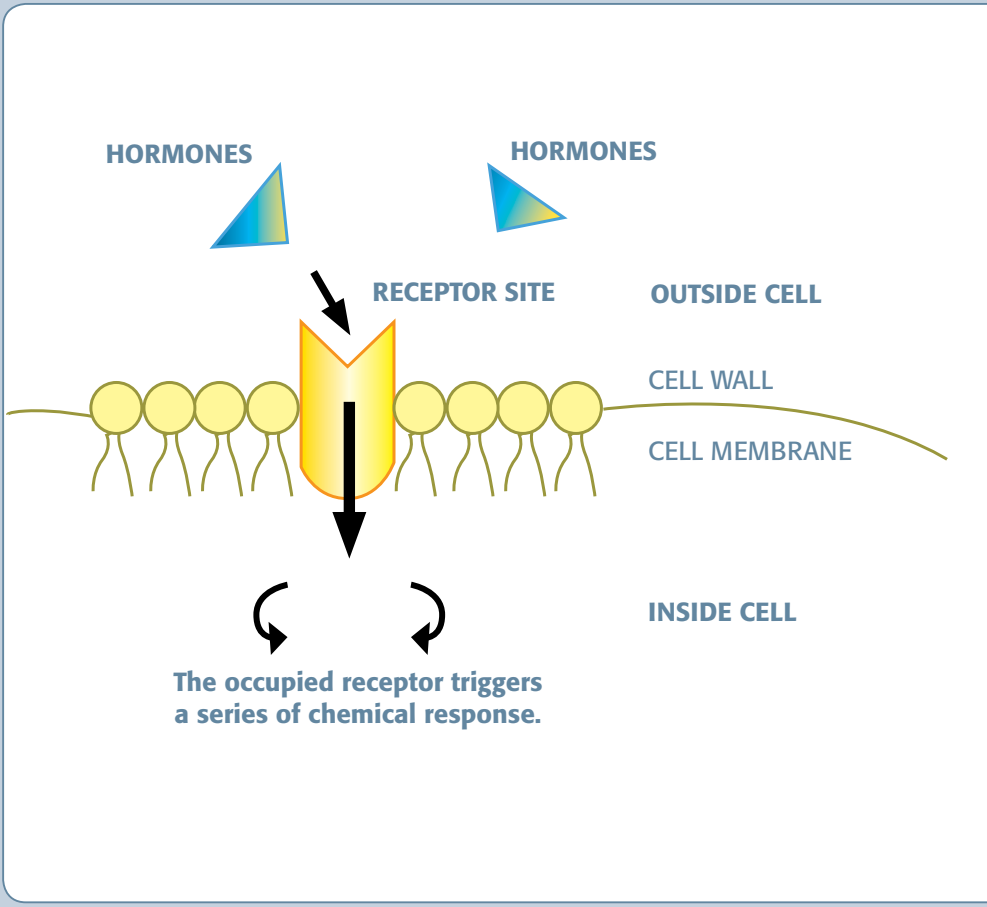
Hormones are released by these glands in response to the body's requirements, carrying chemical instructions or signals for specific actions at specific parts in the body.

When travelling or binding to the target sites or cells called hormone receptors, hormones perform various biological processes and functions.

For instance, estrogen and progesterone released by the ovaries and testes, respectively, control menstrual cycles, mammary gland development, fertility and pregnancy in women and sperm production in men. The thyroid plays an important role in the development of the brain and the nervous system, and also in metabolism.

The hypothalamus and pituitary glands in the brain, together with the nervous system, make up the neuro-endocrine system.

It monitors the functions of other endocrine glands and hormone levels in the blood; and also governs the body's responses to stress and other internal and external stimuli.



The Lock-and-Key Model

The Lock-and-Key Model of hormone receptor interaction necessary for a hormone to trigger biochemical activity in a cell.

According to this model, hormones act like a key and the receptor sites act like a lock. A hormone binds to a specific receptor site like "lock and key". After a hormone binds to a receptor site, a series of chemical responses begins so that chemical instructions or signals are sent to specific parts in the body.

This is how the endocrine system communicates with the rest of the body under normal conditions. Some chemicals mimic hormones and bind to the receptor sites, thus disrupting the endocrine system. These chemicals are known as Endocrine Disrupting Chemicals (EDCs). Chemicals identified as endocrine disruptors include synthetic chemicals used as industrial solvents/lubricants and their byproducts, plastics, plasticizers, pesticides, and pharmaceuticals.

Receptor Effects of Synthetic Chemicals (miming the hormone estrogen)[69]

EDCs similar to an estrogen-like chemical can mimic hormones by binding to a receptor site and triggering a chemical response. Some EDCs can act as hormone blockers, for example an anti androgen chemical. EDCs will bind to the receptor sites thus blocking other natural hormones from biding to that particular receptor. For example, the hormone estrogen is fundamental for the development of healthy mammary glands, if EDCs mimic estrogen then it would disrupt the process of proliferation of mammary cells.

Thus, EDCs can also disrupt the endocrine system in several ways by:-

a) Mimicking or blocking chemicals naturally found in the body,

b) Binding to hormone receptors and turning on a biological process at a wrong time,

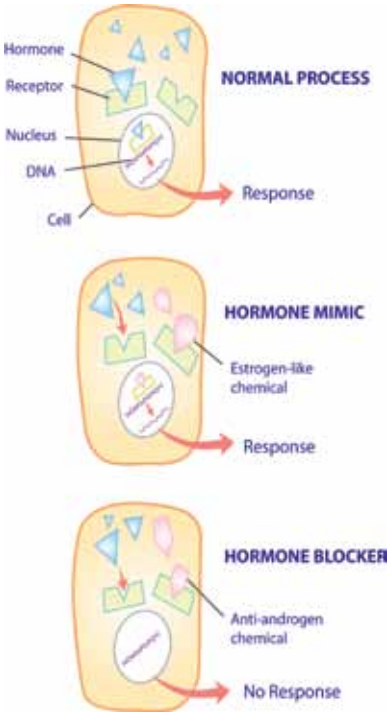
c) Blocking a hormone and shutting off a process,

d) Alter the amounts of hormones the glands produce and release or degrade the quality of the hormones, and thus modify the hormonal signals.

They can alter hormonal levels or degrade the quality of the hormones, and thus, affect functions that these hormones control. Such hormonal disturbances can result in malformed organs, reproductive system abnormalities, cancers, retarded mental growth, behavioural disorders, metabolic-related problems, and a weaker immune system.

Infants, children, and the unborn are particularly vulnerable to endocrine disruptors. Miniscule changes in hormonal levels at the fetal stage and early childhood can affect the organisation of tissues, organs and systems, thus causing lasting damage. Infants and children also absorb higher amounts of pollutants than adults.

Because of the erratic and unpredictable nature of EDCs one should avoid the use of EDCs.



Pesticides that are EDCs:

- ***Aldrin***
- ***Chlordane***
- ***Ddt***
- ***Dieldrin***
- ***Endrin***
- ***Heptachlor***
- ***Hcb***
- ***Mirex***
- ***Toxaphene***
- ***Endosulfan***
- ***For more pesticides refer to PAN Highly Hazardous Pesticide List***

Oestrogen and progesterone affect breast cancer risk by affecting rates of cell proliferation in the breast or by supporting the growth of oestrogen-dependent breast tumours: oestrogen levels in postmenopausal breast tumours can be 10 times higher than in normal circulation (Fan et al 2007). Similarly, hormonally active pesticides, otherwise known as endocrine disruptors, increase breast cells by acting as oestrogen mimics or by disrupting hormonal pathways, which can be critical in the development of breast cancer[25]. Laboratory tests show that oestrogen-mimicking chemicals promote the growth of human breast cells, just as natural oestrogen does[70 71 72 73 74 75].

There are many ways in which pesticides disrupt the natural hormonal system, including:

- interfering with the *metabolism of oestrogen* to increase the forms that cause breast cancer cells and tumours to grow and to decrease the forms that inhibit breast cancer cells – e.g. DDT, 2,4-D, endosulfan and lindane[76 77].
- *mimicking oestrogen,* binding to and activating the oestrogen receptor, which then promotes breast cancer cell proliferation and tumour growth—e.g. chlordane, chlordecone, DDT, heptachlor, lindane[63];
- binding to a hormone receptor but not activating it and preventing it being normally activated, e.g. becoming *androgen receptor antagonists*[78]. Androgens inhibit the growth of hormone-sensitive breast cancer cells, and at least 63 pesticides have been found to have anti-androgen effects or effects that stimulating the manufacture of more *oestrogen receptors*[79]. These include fenarimol, linuron and vinclozolin;
- stimulating the manufacture of more *oestrogen receptors*;
- binding to *proteins in the blood that transport hormones,* thus altering the amount of natural hormone that can circulate;
- increasing the activity of *aromatase,* an enzyme complex that converts androgens to oestrogens, which contributes to the activation of oestrogen receptors—e.g. atrazine, chlordane, cypermethrin, DDT, pirimicarb, propamocarb, simazine, triphenyltin[63];
- increasing *growth factors*, especially TGF-alpha (transforming growth factor) which increases cell division in breast cancer cells; and IGF-1 (insulin-like growth factor) which stimulates the growth of breast cancer cells and their invasiveness;
- binding with *growth factor receptors;*
- interfering with metabolic processes involved in the breakdown of natural hormones such as the cytochrome P450 enzyme complex, a group of enzymes involved in drug and chemical metabolism and the same enzyme complex that breaks down pesticides--e.g. chlordane; heptachlor[63];
- stimulating the release of *prolactin*, which is normally only elevated during lactation. Several studies show a link between elevated prolactin levels and elevated breast cancer risk in humans[80 81]. Pesticides that can stimulate the release of prolactin include atrazine, chlordane, chlordecone, dieldrin, endosulfan, DDE, methoxychlor, methomyl[82], quinalphos, simazine, and the adjuvant nonylphenol[63];
- suppressing *melatonin*, which is a strong anti-oxidant that prevents damage to the DNA[83], and enhances Natural Killer T-cells which suppress tumours[84 85]. No studies could be found showing which pesticides suppress melatonin, but those that do will also play a role in breast cancer;
- interfering with *prostaglandins*, which mediate in inflammatory responses and regulate hormones and cell growth. Pesticides that affect prostaglandins may also affect breast cancer risk.

Thus, the mechanisms involved in the endocrine control of breast cells are complex and there are a number of opportunities for pesticides to influence the development and progression of breast cancer.

The understanding of the real impacts of endocrine disrupting pesticides is still in its infancy. Although some were noted as long ago as 1950, when DDT was shown to cause smaller testes and arrested development of secondary sex characteristics in male chicks[88], it is only very recently that their implications for breast cancer began to be revealed. In 1988, Drs. Ana Soto and Carlos Sonnenscheim identified that nonylphenol was leaching out of plastic laboratory test plates and causing the growth of human breast cancer cells in culture[68 87]. Nonylphenol is used as an inert ingredient in pesticide formulations or as an adjuvant when a pesticide is applied. It is now clearly established as an endocrine disruptor that mimics oestrogen and as such increases breast cancer risk[88].

Critical exposures

There are critical periods during the human life cycle in which the breast is more vulnerable to the influence of carcinogenic and hormonally active chemicals. At these times, exposure to even very low doses of pesticides can cause permanent damage[28]. The critical periods are those times of rapid cell proliferation: the unborn foetus, early childhood, menarche, the age of first childbirth, and perimenopause (the transition years before and after menopause)[34]. During these periods, carcinogens are more likely to bind with mammary cells and trigger DNA damage[92]. Prenatal exposure to pesticides make breast cells more sensitive to subsequent exposures to carcinogens and hormonally active compounds[23]. Additionally, a recent study in the USA[93] demonstrated that pre-menarche females exposed to DDT before the age of 14 developed a five-fold increase in the risk of developing breast cancer many years later.

An inter-generational theory for breast cancer

Exposure to toxic chemicals during embryonic development can result in the modification of the operation of some genes

New studies indicate potential of certain pesticides to cause breast cancer

Since the 1988 discovery by Soto and Sonnenscheim, a large number of pesticides have been identified as having oestrogenic and other endocrine effects. For example, Japanese researchers Kojima et al[77] tested 200 pesticides for their oestrogenic and androgenic activity on oestrogenic receptors in hamster ovarian cells. They found 51 pesticides or pesticide metabolites to have oestrogenic effects, including 34 that were also antagonistic to androgens. Amongst these pesticides were organochlorine and organophosphate insecticides. Another 29 pesticides exhibited anti-androgenic effects alone. The authors expressed concern about potential effects resulting from exposure to these pesticides.

The role of progesterone in breast cancer is not fully established[89 90]; neither, therefore, is the role of progesterone disrupting pesticides such as Roundup, Monsanto's well known formulation of the herbicide containing the active ingredient glyphosate[91].

In conclusion, the mechanisms by which pesticides might increase the risk of breast cancer through their effects on the hormonal system are varied and complex, and not always immediately apparent. Some potential pathways are not yet fully identified. For example, little work seems to have been carried out on the interaction between pesticides and prolactin or melatonin. Most of the potential mechanisms by which breast cancer risk might be increased by pesticides—including endocrine and immune effects, effects on gap junction intercellular communication, and even carcinogenic mechanisms—remain unexplored. Until such time as they are fully explored, it is not possible to give a 'clean bill of health' to any pesticide regarding its relationship to breast cancer.

Image: David Castillo Dominici / FreeDigitalPhotos.net

in the offspring. The DNA itself is not damaged, but the way in which the genes are 'turned off' and 'turned on' can be affected. Thus, an environmental toxin can permanently reprogram an inheritable trait. This is known as epigenetic inheritance. It can lead to alterations to mammary gland development and increase the susceptibility to cancer of mammary epithelial cells, a type of cell in the breast . In studies of the fungicide vinclozolin on rats, it has been shown that the effect can last over at least four generations[95].

Evidence of effects from foetal and perinatal exposure

A number of chemicals, including the organochlorine insecticide dieldrin, have been found to have carcinogenic effects as a result of prenatal or postnatal exposure in animals[96]. A smaller number of chemicals, only a few of which are pesticides, have been studied for the effect of *in utero* exposure on the subsequent risk of breast cancer. However, the herbicide atrazine is one pesticide identified as increasing breast cancer risk with foetal exposure[26 97 98 99] Embryonic exposure to the fungicide vinclozolin has also resulted in breast tumour development in subsequent generations of adult rats[93].

More than 50 chemicals have been identified as causing cancer after perinatal exposure, including the pesticides amitrole, dieldrin, and ethylene thiourea (a breakdown product of dithiocarbamate fungicides that include mancozeb and maneb)[94]. Other studies link an increase in various cancers to prenatal or preconception exposure to ionising radiation, bisphenol A, diethylstilbestrol, saccharin, arsenic, flame retardants, solvents, paints, thinners, plastics, cigarette smoke, polyaromatic hydrocarbons, and synthetic halogenated chemicals[26 100 101].

The relevance of these findings is enormous. It demonstrates what has become a critical problem for normal regulatory risk assessment for pesticides: that low dose exposure to endocrine disrupting and/or carcinogenic pesticides during a critical window of development can cause permanent damage. Such health effects only become apparent later in life, and can affect subsequent generations. As Theo Colborn[102] points out, regulatory assessment misses almost all delayed developmental, structural and functional damage of foetal origin.

Evidence of foetal exposure

Evidence that the unborn foetus is indeed being exposed to pesticides comes from the findings of pesticide residues in umbilical cord blood and meconium, the newborn infant's first faeces. A study of umbilical cord plasma samples collected from African-American and Dominican newborns in New York (USA) found a staggering 29 active ingredients or metabolites —see Table 2. There is evidence linking 13 of these to an increased risk of breast cancer (two of the 13 are metabolites of the fungicides captan and captafol). This means that those unborn children in the study were exposed to a cocktail of pesticides that may increase their risk of breast cancer later in life, because these pesticides either have oestrogenic effects or are known to cause mammary tumours. Residues found in the samples were reported to have come from the recent use of pesticides in urban areas. The study did not test for obsolete organochlorine insecticides.

There appear to have been very few studies carried out in the Asia Pacific region on the levels of foetal exposure to pesticides. However, on the basis of repeated findings of pesticide residues in breast milk and blood serum throughout the region, and findings of cord blood and meconium contamination elsewhere, it is highly likely that females in Asia and the Pacific are being exposed *in utero* to a cocktail of pesticides that are implicated in breast cancer. Various organochlorine insecticides have been found in umbilical cord blood in China, India, Japan, Thailand, Kazakhstan and Kyrgyzstan[63]. The meconium of infants randomly sampled from the nurseries of five hospitals in Manila, Philippines, contained the organochlorines chlordane, DDT, lindane, and pentachlorophenol, as well as the organophosphates chlorpyrifos, diazinon, malathion, and parathion[104]. The residues indicate foetal exposure at a time when the developing female is at her most vulnerable to breast cancer stimulants. Pesticides that are also prevalent in breast milk cause additional postnatal exposure.

Table 2: Breast cancer pesticides in umbilical cord blood in New York, USA[101]

Pesticide	Epidemiology	Mammary tumours	Oestrogenic	Carcinogenicity	Other
Triazine herbicides					
atrazine	+	carcinoma	+	+	immune
Pyrethroids					
cis -permethrin			+	+	
trans-permethrin			+	+	+
Organophosphates					
chlorpyrifos			+	+	
diazinon			+	+	
dichlorvos		+	+	+	
malathion	+	carcinoma		+	
methyl parathion			+	+	
parathion		carcinoma		+	
Fungicides					
captan (metabolites)	+			+	
captafol (metabolites)		+		[+	
Other herbicides					
alachlor		+	+	+	
trifluralin			+	+	

Low doses and mixtures of chemicals

It is quite straightforward for genotoxic carcinogens or carcinogens that react directly with the DNA: there is no safe level of exposure. The lowest level of exposure can cause a carcinogenic effect[105 106 107].

However, for non-genotoxic carcinogens—which cause cancer through mechanisms such as promotion of cell or tumour growth and endocrine disruption—thresholds are believed to exist104. These thresholds are essentially unknown. So toxicologists estimate 'acceptable' levels of exposure based on a positive dose–response relationship: that is, the greater the dose/potency of chemicals, the greater the risk of cancer. But there are problems with this approach.

Non-positive, non-linear dose-responses

Attempts to link breast cancer to exposures to endocrine disrupting chemicals are complicated by the fact that their oestrogenic potency is low compared to that of 17*beta*-oestradiol, the naturally occurring hormone. Yet there is concern about the endocrine disrupting effects if exposures take place at times when levels of natural oestrogen are normally low and tissues exquisitely sensitive, such as *in utero,* pre-puberty, and postmenopause.

Additionally, endocrine disruptors do not obey the normal rules of toxicology. Low levels of exposure, assumed by regulators to be non-toxic, can in fact be of profound importance. This is because

Pesticides implicated in breast cancer for which there is evidence of genotoxicity include :-

alachlor, aldicarb, atrazine, captafol, captan, chlordane, chlorpyrifos, cyanazine, cyfluthrin, cypermethrin, 2,4-D, DBCP, deltamethrin, diazinon, dichlorvos, endosulfan, EPN, ethion, ethylene dibromide, ethylene oxide, fenarimol, fenvalerate, folpet, isofenphos, lindane, malathion, mancozeb, maneb, methyl parathion, monocrotophos, omethoate, paraquat, parathion, permethrin, phenthoate, phosmet, simazine, sulfallate, toxaphene, trifluralin, and triphenyltin[63]

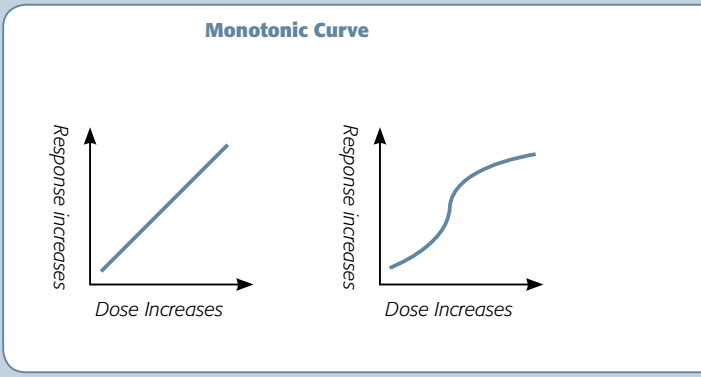
Understanding dose-response relationships[109]

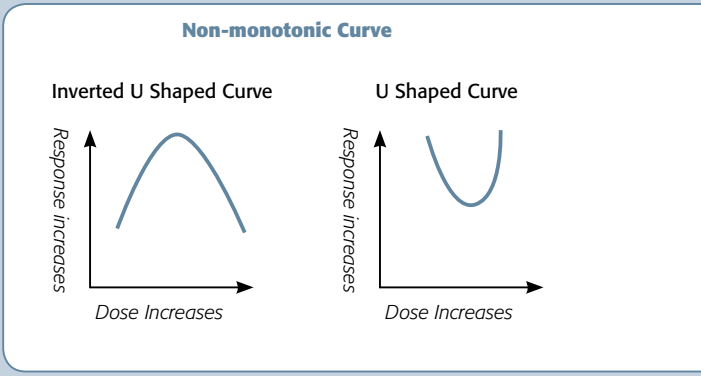
Traditional toxicological models were based on acute toxicity. If the dose of a harmful substance increases, so too does the risk associated with it. Traditional toxicology assumes that dose-response curves are always monotonic: that is, the higher the dose the greater the effect. For example, if you are exposed to high dose of pesticides, then the more likely you are to get affected.

A monotonic curve can be either linear or non linear. A monotonic curve does not change its direction from negative to positive or vice-versa. This would be the traditional way of looking at dose response relationships.

Monotonic Curve

This assumption underpins all regulatory testing: if no effect is found at high levels, then it is assumed that the contaminant is safe. It also usually assumes that there is a threshold level of exposure below which no effect occurs. Therefore, if there are no effects at high doses then it is assumed that the poisons are safe. This may be true for a lot of chemicals based on the old toxicology paradigm but this may not able to explain the effects of endocrine disrupting chemicals. There is a new paradigm shift in regards to the dose and response model. Part of this new paradigm is also the acknowledgment that old assumptions about the nature of the relationship between dose and response may sometimes be different.





Because most regulatory testing has been designed assuming a linear relationship between dose and risk, and tend to test at high doses in order to capture effects, they are likely to have missed low dose effects, which are being reported frequently in research especially for endocrine-disrupting chemicals.

In a non-monotonic dose response curve (NMDRC), the shape of the dose response curve reverses as the level of contamination goes up. Some NMDRC are shaped like U's, with high responses at low and at high levels of contamination. Others are shaped like inverted U's with the greatest response in intermediate ranges. The puzzling but observable fact is that low doses may actually cause greater impact than high doses for

a specific response (cited in Colborn, Dumanski & Myers, 2007).

They then assert that because a chemical did not cause a noticeable effect at high doses it will not cause an effect at low doses at which people are commonly exposed too. The new paradigm assumes that even if you are exposed to a lower dose of pesticides you are also likely to get affected.

"Non-monotonic curves change direction. Over part of the curve, response increases with dose, while over another portion it decreases as dose increases" (cited in Colborn, Dumanski & Myers 2007).

Effects have been observed on animals at very low doses in laboratories[106 110 111], and on fish at or below the detection limits[112]. Prenatal exposure to the organochlorine insecticide methoxychlor results in an inverted U dose-response of adult mice to 17*beta*-oestradiol, with a low dose of methoxychlor increasing uterus weight and a high dose decreasing it[113]. At very low levels, the insecticide allethrin is a moderate oestrogen blocker in human breast cancer cells, but at moderate levels it provokes breast cancer cell proliferation: the dose-response curve has the classic inverted U form[114].

Methoxychlor and allethrin are still in widespread use, and there is every reason to be concerned that low dose exposure to these, and other hormonally active insecticides, may well be contributing to the breast cancer epidemic.

endocrine disruptors do not act in the typical positive dose-response manner upon which toxicologists often rely. A positive dose-response means that the higher the dose, the greater the effect. But with endocrine disruptors, the opposite can happen. Studies have produced dose-response graph shapes that were either low-dose linear; or threshold-appearing; or non-linear (e.g. U-shaped or inverted U-shaped)[108]. These are when the strongest effects can be felt at a low or medium exposure level; or when there are only specific concentrations at which effects occur.

Certain mixtures of pesticides have greater effects than individual pesticides

Women are constantly exposed to chemicals with 'xenoestrogens,' or by-products of industrial and chemical processing that have estrogenlike effects[115].

Through their attraction to fat and their persistence, many of these xenoestrogens accumulate in adipose tissue including breast tissue, in breast milk, and in blood serum.

These chemicals can interact not only with each other but also with natural oestrogens.

Animal studies have demonstrated that mixtures of oestrogenic chemicals can act together to exert an effect even when the level of each individual chemical is too low.

These mixtures have included the pesticides DDT and HCH, and other chemicals such as PCBs, parabens, and bisphenol A[69 116 117 118 119].

One study examined the effects of four herbicides (alachlor, atrazine, metolachlor, nicosulfuron), three insecticides (cyfluthrin, cyhalothrin, tebupirimphos), and two fungicides (metalaxyl and propiconazole) alone or in combinations, on metamorphosis and gonadal differentiation in northern leopard frogs[120].

They found that the mixtures had much greater effects than individual pesticides in inhibiting larval growth and development.

Other studies have shown that mixtures of low doses of pesticides have produced consistent endocrine disrupting effects on thyroid hormone levels[121 122].

Image: maya picture / FreeDigitalPhotos.net

Andreas Kortenkamp[123] summed it up thus:

> ***"breast cancer epidemiology should face the reality of combined exposures and should take account of recent evidence from in vitro models demonstrating that a large number of oestrogen-like pollutants, all present at low levels, can act together to add to the internal oestrogenic load".***

In conclusion, even when adverse impacts of pesticides on health are identified using tests on laboratory animals, the results are often dismissed as being of no relevance to humans, for human exposure is presumed to be at relatively lower levels than those used in laboratories. This is erroneous because a dose-response relationship should not be expected with cancer. If a substance is a genotoxic carcinogen, it presents a health risk at every exposure level. Similarly, endocrine disrupting substances do not always follow conventional dose-response patterns and low or moderate doses can cause greater effects than higher doses. Thus, laboratory tests using the existing standards of toxicity cannot be relied upon to determine the safety of pesticides.

Furthermore, it is crucial to understand that at critical periods of development, mammary tissue is highly sensitive to very small doses of hormonally active substances, and that mixtures of these substances can exert a greater effect than that of individual chemicals.

This sends a simple yet potent message: safe levels of exposure cannot be determined. Women—especially pregnant women and prepubescent girls—should not be exposed to any levels of mammary carcinogens or hormonally active pesticides that may increase the risk of breast cancer.

MAMMARY CARCINOGENS AND HORMONALLY ACTIVE PESTICIDES

Identifying which pesticides might cause or promote breast cancer is not a simple matter, given the complexity of factors underlying breast cancer, and the difficulty of providing absolute proof of a relationship between a pesticide and a specific health effect. The approach taken has been to identify those pesticides that, based on available evidence, may increase the risk or severity of breast cancer.

These were selected on the basis of epidemiological evidence linking them with breast cancer, and/or laboratory data indicating oestrogenic activity or mammary carcinogenicity in animals. These pesticides were then reviewed for other effects that might increase the risk of breast cancer, such as effects on the immune system, gap junction intercellular communication, cytochrome P450 enzymes, oxidative stress, genotoxic potential, and for epidemiological evidence of other types of cancer.

We need to consider where the burden of proof should lie, looking at the weight of evidence from a broad perspective and then applying the precautionary principle. We should not wait forever to obtain definitive statistical proof, because in the meantime, women die unnecessarily.

> ***"Not acting to reduce or control our use of such suspected toxic materials is a form of acting"***[124]

— in this instance against the welfare of women worldwide.

Epidemiological Studies

A relatively small number of epidemiological studies have been undertaken in an attempt to explore the link between exposures to pesticides generally and risk of various types of cancer. But the resulting evidence on the relationship between pesticides and cancer tends to be inadequate and contradictory. Cancer risk among women engaged in farming has been particularly poorly investigated. However, some studies have shown elevated rates of non-Hodgkin's lymphoma, leukaemia, multiple myeloma, soft tissue sarcoma, and cancers of the breast, ovary, lung, bladder, cervix, and sinonasal cavities in women in agriculture or with agricultural exposures[125].

Studies Linking General Pesticide Exposure with Breast Cancer

Many studies of cancer and farming do not include breast cancer, and in fact have omitted women altogether, yet announce that they have found no link between pesticides and cancer; or else list cancers other than that of the breast that may be linked to pesticide exposure[126 127 128 129].

Of the few studies that have been carried out on rural women and breast cancer, most have been undertaken in USA or Europe, in markedly different conditions from those of rural women in Asia and the Pacific—particularly with respect to the types of pesticides used, the frequency and duration of exposures, the use or non-

use of protective clothing and its appropriateness, and the presence of other socio-economic factors that can affect health outcomes (such as malnutrition, lack of access to washing water for removing pesticides on the skin or clothes, etc).

Some of these studies have found a positive link between exposure to pesticides and increased risk of breast cancer, and some have found no link or even a decreased risk of breast cancer. The studies below all show a positive link between pesticides and breast cancer.

(a) ***Canada*** – A 3- to 9-fold increase in incidence of breast cancer amongst women with a history in agriculture was found in Ontario[90]. Another study showed that women who developed breast cancer were 2.8 times more likely to have worked on farms than women who didn't get the disease[130].

(b) ***Colombia*** – There were significant associations, in both premenopausal and postmenopausal women, between breast cancer and involvement in crop farming and fruit and vegetable production that was likely to have entailed exposure to pesticides[131].

(c) ***Poland*** – There was a significant association between occupational exposure to pesticides and breast cancer in a study conducted in 1993-1994[132].

(d) ***Costa Rica*** – There was an increased risk of breast cancer associated with heavy use of pesticides[133].

(e) ***USA – Farmers' wives:*** A study of 30,454 farmers' wives in Iowa and North Carolina found an elevated risk of breast cancer among women whose homes were closest to areas of pesticide application[134].

(f) ***USA – Residential use:*** an association was found between self-reported lawn and garden use of pesticides and breast cancer in a study of 1,508 women newly diagnosed with breast cancer on Long Island, New York[135].

(g) ***USA – Women in agriculture:*** There was a possible increased risk of breast cancer in those most likely to be exposed to pesticides—in particular women present in fields during or shortly after pesticide application (80 percent increased risk), and those who did not use protective clothing[136]. Another study showed a potential association between pesticide exposure and risk of breast cancer mortality in three areas in Mississippi. The total number of acres planted was significantly associated with breast cancer mortality rate, and these associations differed by race and type of crop. The strongest correlation was between breast cancer mortality rate for white women and rice crops[137].

(h) ***Belgium*** – A correlation was found between mortality from breast cancer and use of defoliants and potato cultivation[138].

(i) ***China*** – There was increased incidence of breast cancer with high levels of occupational exposure to pesticides in China[139].

Studies Linking Specific Pesticides with Breast Cancer

Epidemiological studies have drawn a link, in some cases rather weak, between 25 different pesticides and increased risk and/or severity of breast cancer. Most of these studies have looked indirectly at exposure, by measuring levels of the pesticide in the blood or fat tissue of women with breast cancer and comparing them with those of women without breast cancer. Often the outcomes are conflicting,

because of the inherent difficulties in getting accurate results from this type of study.

One such difficulty is determining exposure given the long time lag that can occur between exposure and diagnosis of breast cancer (e.g. 17 years[91]). DDT is a classic situation: a roughly equal number of studies have shown a link between exposure to DDT or its metabolite DDE, and studies that did not show a link. However, best available evidence, taking into account the time lag, indicates that exposure to DDT could well increase the risk of breast cancer. **Other pesticides for which there is evidence of a link between residue levels in body tissue or fluids and increased risk of breast cancer include dieldrin, chlordane, endosulfan, heptachlor, lindane, hexachlorobenzene, and mirex[63].**

Epidemiological studies that look more directly at exposure to pesticides provide weak evidence because of the problem of multiple exposures. However, studies have indicated a possible association between breast cancer and exposure to aldicarb, aldrin, atrazine, captan, chlordane, chlorpyrifos, 2,4-D, DBCP, diazinon, dichlorvos, dieldrin, ethylene dichloride (in males), ethylene dibromide (in males), heptachlor, lindane, malathion, methoxychlor, paraquat, parathion, silvex, and toxaphene[63].

To date, epidemiological efforts have focused largely on obsolete, or nearly obsolete, organochlorine pesticides that have left behind evidence of exposure as residues in our bodies. But studies of historically-used persistent pesticides, degraded into various metabolites, may well be too blunt a tool to accurately define the real role of organochlorine insecticides in breast cancer. And they do not clarify the role of the many other pesticides that may be involved in the global escalation of breast cancer rates. It is critical that epidemiological studies focus on currently used pesticides, especially those identified as potentially increasing the risk of breast cancer. Many of these leave no trace in the body soon after exposure. Others that do and have been measured in umbilical cord blood and infant meconium have rarely been studied for their possible role in breast cancer.

Laboratory Studies – Mammary Tumours In Rats

Perhaps of greater importance to linking pesticides with breast cancer are laboratory studies that indicate a pesticide is a mammary carcinogen in animals, a tumour promoter, an endocrine disruptor, or acts in some other way to increase the risk of breast cancer.

There are problems with the relevance of data generated from tests on laboratory animals. There are many reasons why these tests may fail to identify chemicals that cause breast cancer—the numbers of animals in tests are too small to detect nongenotoxic carcinogens, such as those that affect mammary gland development or act as promoters, or have transgenerational epigenetic effects (i.e. cause breast cancer in the subsequent generation); tests are not carried out on the unborn foetus or developing animals which are much more sensitive to carcinogens than older animals; tests are too short to identify mammary carcinogens with a longer latency period; and they fail to identify the effects of chemical interactions because they test only one chemical at a time[140].

However, the most commonly cited concern is that not all chemicals that are carcinogenic in rats are necessarily carcinogenic in humans, and hence animal tests may falsely identify chemicals as mammary carcinogens for humans. This is typically the argument of the pesticide industry and its supporters. Rudel et al[137] commented that:

> ***"disproportionate financial resources have been dedicated to supporting arguments that the carcinogenicity in animal studies is due to toxicity that occurs only at high doses or through biological mechanisms that are not relevant to human exposure scenarios (false-positive) with an aim to reduce regulatory***

constraints and increase public scepticism of the relevance of the animal toxicity studies".

This charge is clearly evidenced by the situation with atrazine: mammary tumours caused by this herbicide were discounted by chemical industry scientists, and subsequently the US EPA, because their underlying mechanism involved prolactin, a mechanism "thought to be of low relevance in humans"[141]. This assumption has subsequently been challenged by recent research that indicates prolactin is important in breast cancer development, and non-normal increases in it may in fact double the risk of breast cancer[142].

But the counter argument is equally valid: not all pesticides that cause breast cancer in humans may be mammary carcinogens in rats, and animal tests may fail to identify them.

Rudel et al[137] continues:

"Conversely, comparable resources are not extended to evaluate how chemical testing and risk assessment as currently practiced may miss critical adverse effects".

Nevertheless, the results of laboratory tests are taken as the best indicators of breast cancer potential in humans currently available.

Table 3 lists the pesticides for which there is evidence of breast cancer potential as identified in *Pesticides & Breast Cancer: A Wake Up Call*[63].

CONCLUSION AND RECOMMENDATIONS

A total of 98 different pesticides, plus one adjuvant and two contaminants, have been identified as having the potential to increase the risk of breast cancer. Breast cancer initiation and development is a complex process not yet completely understood, so the ways in which pesticides might affect that process are also complex, varied and not yet completely understood. Therefore this list should not be regarded as definitive. It may be that, as more is learned about the exact cellular mechanisms of breast cancer and the opportunities for pesticides to interrupt these processes, more pesticides will become implicated. Additionally, studies have not been carried out for many pesticides to fully identify their ability to effect even those mechanisms already identified—such as effects on cytochrome P450 enzymes, gap junction intercellular communication, Natural Killer T-cells other tumour regression factors, progesterone, prolactin, prostaglandins, and melatonin—and their subsequent implications for breast cancer.

The evidence linking these pesticides with breast cancer differs in quality. For some pesticides, such as DDT and dieldrin, there is sufficient high-quality evidence for a number of reviews[27 28] to assert a positive link with breast cancer. Some remain a subject of controversy, e.g. the triazine herbicides because of dispute about the relevance of studies on rodents to humans, or DDT because of the conflicting results of epidemiological studies. For the others, the evidence is slimmer, largely because of lack of studies, and the pesticides do not appear in other review lists. They are included here, on the basis of the precautionary principle, as an early warning that these pesticides possess the ability to interfere with mechanisms involved in the genesis and development of breast cancer.

Exposure to these pesticides at any time of a woman's life may increase the risk of breast cancer. However, there are clearly periods of greater vulnerability: *in utero*, early childhood, menarche, at first childbirth, and perimenopause. One of the most important routes of exposure for these pesticides that have been identified as potentially increasing the risk of breast cancer is maternal transfer to the foetus *in utero*, a time when the unborn child is exquisitely sensitive to minute amounts of carcinogens and endocrine disrupting chemicals. There

IMAGE: AFRICA / FREEDIGITALPHOTOS.NET

is no doubt that such transfer occurs—some information exists for a small number of chemicals measured in umbilical cord blood or infant meconium, and that appears to be just the tip of the iceberg.

There is also concern about the transference of pesticide residues contaminating breast milk to the newborn infant through breastfeeding. The concern is valid, however this ***does not*** mean that breastfeeding should be replaced with bottle-feeding. Breastfeeding should be maintained because, despite the residues, it confers health benefits on both the infant and the mother. Breastfeeding is key to the well-being of the baby, providing the best available sustenance and defence against disease. This is especially important in households that do not have enough to eat and where women and children are often nutritionally deprived.

The solution to the problem of transferring residues to the infant is not to stop the breast-feeding but to stop the contamination of the breast milk in the first place. As Sandra Steingraber said in 2005[143]:

> ***"It should be the right of every child to toxic-free food. Right now no child in the world has that right because breast milk universally is contaminated, and the number one contaminant around the world is still the pesticide DDT, which was first identified in human milk in 1951."***

In order to achieve this, the following recommendation of the UK Royal Commission on Environmental Pollution[144] should be put into effect worldwide:

> ***"We recommend that where synthetic chemicals are found in elevated concentrations in biological fluids such as breast milk and tissues of humans, marine mammals or top predators, regulatory steps be taken to remove them from the market immediately."***

There is no longer any doubt that exposure to toxic synthetic chemicals contributes significantly to cancers worldwide, including breast cancer. The Standing Committee of European Doctors[145] concluded that:

> ***"Doctors believe that the chronic diseases registered by the WHO, in particular cancer, have risen alarmingly; that cancer rates have increased steadily among the populations of the industrialised countries since 1950; that cancer affects all age ranges; and that chemical pollution could contribute to the onset of cancer" and "Doctors have stated that the current proliferation of a number of diseases is a consequence of environmental degradation and that chemical pollution poses a serious threat to children and to the human race."***

PESTICIDE ACTION NETWORK ASIA AND THE PACIFIC, THEREFORE, RECOMMENDS:

1. No woman or girl should be exposed to pesticides that have the potential to increase the risk of breast cancer, and especially not pregnant woman because of the exquisite vulnerability of the unborn child to carcinogens and endocrine disruption.
2. The rights of women to health, including reproductive health, must be given primacy in national and international policies and processes. Each country should develop breast cancer prevention plans that include the rapid removal of pesticides for which there is evidence of a potential to increase breast cancer risk.
3. Women should be encouraged to breast feed their children despite the current contamination of breast milk, and every effort must be made to reduce as fast as possible, and eventually eliminate, contamination of human breast milk, through reduction and eventual elimination of exposures to persistent pesticides and other synthetic chemicals.
4. The precautionary principle must be applied to the evidence indicating a potential increase in risk of breast cancer from pesticides.
5. The continued use of pesticides that are persistent and which contaminate human tissue and fluids should cease completely. Currently some of the persistent pesticides identified here as breast cancer risks are covered by the Stockholm Convention on Persistent Organic Pollutants (POPs). These include aldrin, chlordane, DDT, dieldrin, endrin, heptachlor, HCB, lindane, mirex, and toxaphene. But for some of these pesticides, there are exemptions permitting ongoing use that continues to expose women, children and the unborn foetus. For example, DDT is still widely used for malaria control in Africa, and its ongoing manufacture in India contaminates local communities. Others such as endosulfan are not evenwas added on the POPs list yetin 2011, and therefore: endosulfan should be placed on the POPs list with urgency and all further uses should be eliminated speedily.
6. The burden of responsibility for the potential role of individual pesticides in increasing the risk of breast cancer must shift to the pesticide industry and the regulatory authorities, to prove that individual pesticides will not cause or promote or increase the risk of breast cancer. It should not be left to public interest organisations and independent scientists to provide sufficient evidence of a link with breast cancer before regulatory authorities take action to remove the offending pesticide, because such proof, if it can be gathered to the extent that satisfies the regulatory process, is always too late for many women who will have already died from breast cancer.

7. **Regulatory processes must be improved so that they incorporate all the mechanisms by which pesticides may contribute to breast cancer and hence can identify all pesticides that contribute to increasing the risk of breast cancer. Current regulatory processes for pesticides focus on identifying carcinogens that are genotoxic, and tend to ignore those chemicals that promote the growth of cancer cells or tumours, as many of the chemicals reviewed here do. The focus should be on hazard identification and elimination, rather than risk management.**
8. **The substitution principle must be applied and those pesticides that have the potential to increase the risk of breast cancer must be speedily replaced by safer substitutes, particularly by non-pesticide ecological methods of pest, weed and agri-ecosystem management.**
9. **Every effort should be made to support community monitoring of the effects of pesticides and to include the results of such monitoring in national and international pesticide regulatory and management processes. Community monitoring can act as an "alert system", identifying pesticides that are potentially causing health effects including chronic effects, as well as identifying other pesticide problems.**

Breast Cancer & Pesticides: Key Messages

1. **Breast Cancer is escalating throughout Asia in the wake of rising use of pesticides and other chemicals, as it has done throughout the western world.**
2. **Pesticides that cause cancer, disrupt the natural hormone system or alter the development of the mammary gland contribute to the global epidemic of breast cancer.**
3. **There are critical periods when exposure to even very low levels of pesticides can result in breast cancer later in life: the unborn foetus, early childhood, menarche, the age of first childbirth, and around menopause.**

Image: Sujin Jetkasettakorn / FreeDigitalPhotos.net

4. **98 pesticides are linked to breast cancer: they have caused mammary tumours or growth of breast cancer cells in laboratory tests, or elevated rates of breast cancer in exposed women.**
5. **No woman or girl should be exposed to pesticides that have the potential to increase the risk of breast cancer, and especially not pregnant woman because of the exquisite vulnerability of the unborn child to carcinogens and endocrine disruption.**

Table 3: Summary of evidence of potential to increase breast cancer risk

Pesticide	Epidemiology (breast cancer)	Mammary tumours	Oestrogenic activity	Other hormonal effects	Evidence of carcinogenicity	Relevant immune	GJIC inhibition	Mammary gland development
Organochlorines								
aldrin	+		+		+	+	+	
chlordane	+		+	+	+			
chlordecone			+	+	+	+	+	
DDT/DDE	+		+	+	+		+	+
dicofol			+		+			
dieldrin	+		+	+	+	+		
endosulfan	+		+	+	+			+
endrin		+	+			+		
HCB	+			+	+	+	+	
heptachlor	+		+		+		+	
lindane	+		+	+	+			
methoxychlor	+	+	+	+	+			+
mirex	+			+	+	+	+	
toxaphene	+	+	+		+			
Triazine herbicides						+		
atrazine	+	+	+	+	+			+
cyanazine		+		+	+			
propazine		+		+	+			
simazine		+		+	+			
terbumeton		+						
terbuthylazine		+						
terbutryn		+			+			
Synthetic pyrethroids								
allethrin			+	+				+
cyfluthrin			+	+	+			
cyhalothrin		+			+			
cypermethrin			+		+		+	
deltamethrin		+	+	+	+		+	
fenvalerate		+	+	+	+		+	+
flucythrinate		+	+	+				
permethrin			+	+	+		+	+
pyrethrins			+		+			
sumithrin			+		+			+
Organophosphates								
bromophos-ethyl			+	+				
bromophos-methyl			+					
butamifos			+	+				
chlorpyrifos	+		+		+			
cyanofenphos			+					
dichlofenthion			+	+				
diazinon	+		+		+			
dichlorvos	+	+		+	+			
EPN			+	+	+			

ethion			+	+	+			
isofenphos			+	+	+			
isoxathion			+					
leptophos			+	+				
malathion	+	+			+			
methyl parathion			+		+			
monocrotophos			+		+			
omethoate			+		+			
parathion	+	+			+			
phenthoate			+		+			
phosmet		+			+			
pirimiphos-methyl			+					
prothiophos			+	+				
quinalphos				+				
tolclofos-methyl			+	+				
Carbamates								
aldicarb	+				+			
methiocarb			+	+				
pirimicarb			+					
propamocarb			+					
Other herbicides								
alachlor		+	+		+			
chlornitrofen			+	+	+			
2,4-D	+	+	+	+	+			
diclofop-methyl			+					
diuron		+		+	+			
ethalfluraline		+						
fluazifop-butyl			+					
oryzalin		+						
paraquat	+	+			+			
pendimethalin			+	+				
prosulfuron		+						
silvex	+							
sulfallate		+			+			
thenylchlor			+	+				
tribenuron methyl		+	+		+			
triclopyr		+	+					
trifluralin			+		+			
Fungicides								
biphenyl			+					
captan	+				+			
captafol		+			+			
dodemorph			+					
fenarimol			+	+	+			
folpet		+			+			
mancozeb		+		+	+			
maneb				+	+			
triademefon			+					
triademenol			+					
triphenyltin			+		+			
vinclozolin		+		+				

Other pesticides								
bromopropylate			+	+				
chlorobenzilate			+	+	+			
chloropropylate			+	+				
clonitralid		+						
DBCP	+	+		+	+			
ethylene dibromide	+ (male)	+			+			
ethylene dichloride	+ (male)	+			+			
ethylene oxide		+			+			
PFOS		+			+			
propylene dichloride		+			+			
Inerts								
nonylphenol		+	+	+				
Contaminants								
1,4-dioxane		+			+			

Glossary

17beta-estradiol – a naturally occurring sex hormone in women. It activates oestrogen receptors (ERs), which are over-expressed in around 70 percent of breast cancer cases, stimulating growth of breast cancer cells, i.e. too much of the natural hormone can result in breast tumours.

Androgens – the generic name for male sex hormones, the most well-known of which is testosterone; also the precursors of the female sex hormones, oestrogens.

Aromatase – An enzyme responsible for the conversion of testosterone to oestrogen, and so it increases the amount of circulating oestrogen. Aromatase is found in oestrogen-producing cells in the adrenal glands, ovaries, placenta, testicles, adipose (fat) tissue, brain, and breast cancer cells.

BRCA1 – A gene that normally acts to restrain the growth of cells in the breast but which, when mutated, predisposes to breast cancer.

BRCA2 – A gene that normally acts to restrain the growth of cells in the breast and ovary but which, when mutated, may predispose to breast cancer and to ovarian cancer.

Cytochrome P450 enzyme complex – A group of enzymes found mainly in the liver, and involved in many processes, including the metabolism of drugs, chemicals and natural hormones into forms that are easier for the body to excrete.

Epidemiological studies – Epidemiology is the scientific method used to track population health and to find causes of disease in groups of people.

Estradiol – The female steroid hormone produced by the mature ovarian follicle and the adrenal cortex and responsible for sexual receptivity at the time of oestrus. It is also produced in fat cells, the brain and artery walls.

Gap junction intercellular communication – Communication between cells through channels that allow the movement of nutrients, messengers, etc, and so is critical to the life and death of cells. It plays an essential role in the regulation of breast cancer cell proliferation and tumour development.

Incidence – Is the number of new cases per population in a given time period

Globalization – Globalization is described as economic integration in trade investments and finance and takes the form of liberations, privatization and deregulation.

Growth factors – Hormones or proteins produced by the body that stimulate growth, proliferation and differentiation of cells. They also stimulate the growth rate of some cancer cells.

Growth factor receptor – A protein on the surface of cells to which a specific growth factor binds, triggering the sending of a signal that stimulates cell division.

Melatonin – Is a naturally occurring compound found in animals, plants, and microbes. In humans, melatonin is produced by the pineal gland, a gland about the size of a pea, located in the center of the brain but outside the blood-brain barrier. The melatonin signal forms part of the system that regulates the sleep-wake cycle by chemically causing drowsiness and lowering the body temperature. Melatonin also exerts a powerful antioxidant activity. Melatonin has a protective effect against carcinogens, helping to prevent the growth of tumours.

Multiple myeloma – Cancer of plasma cells, a type of white blood cell normally responsible for the production of antibodies.

Natural Killer T-cells – A type of lymph cell that is an essential part of the natural immune system. They target tumour cells and protect against infections. A

lack of NKT cells can lead to the development of autoimmune diseases and cancers.

Non-Hodgkin's lymphoma – A disease in which cancer cells form in a person's lymphatic system and start to grow uncontrollably.

Oestrogens – The main female sex hormones, produced primarily by the ovary and responsible for typical female sexual characteristics. They are also produced by the liver, adrenal glands, breast and fat tissue.

Precautionary Principle – A precautionary approach is more thorough and more 'scientific' than the standard risk assessment process because it requires recognition of the limitations of science, such as uncertainty about the chronic effects from ongoing low-dose exposure to mixtures of chemicals; recognition of the lack of knowledge about casual links; recognition of the value judgements involved in risk assessment; and attention to other factors involved, such as the availability of less harmful alternatives.

Progesterone – A hormone produced in the ovaries, the placenta (when a woman gets pregnant) and the adrenal glands. It helps prepare the body for conception and pregnancy, regulates the monthly menstrual cycle, and is involved in breast development.

Prolactin – A hormone secreted by the pituitary gland. Prolactin stimulates lactation (milk production). It also has many other functions, including essential roles in the maintenance of the immune system. Abnormally high prolactin can delay puberty, interfere with ovulation in women, decrease libido in men, and decrease fertility. It also increases proliferation of pre-invasive breast cancer cells, and increased levels of prolactin increase the risk of breast cancer.

Prostaglandin – One of a number of hormone-like substances that participate in a wide range of body functions such as the contraction and relaxation of smooth muscle, the dilation and constriction of blood vessels, and control of blood pressure. Their relevance to breast cancer is that they mediate inflammatory responses, and regulate hormones and cell growth.

Soft tissue sarcoma – A cancer that begins in the muscle, fat, fibrous tissue, blood vessels, or other supporting tissue of the body.

Terminal end buds – The proliferative structures within the mammary gland that are responsible for the development of virtually the entire ductal system. These bulb-shaped structures are believed to be the most sensitive targets for chemical carcinogens.

Tumor necrosis factor – A member of a superfamily of proteins which are involved in regulation of the immune cells. TNF induces necrosis (death) of tumor cells and so inhibits the formation of tumours; it also can induce inflammation.

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Pesticide Action Network Asia and the Pacific (PAN AP) is one of the five regional centres of PAN, a global network dedicated to eliminating the harm caused to humans and the environment by pesticides and promoting biodiversity-based ecological agriculture.

PAN AP's vision is a society that is truly democratic, equal, just, and culturally diverse; based on the principles of food sovereignty, gender justice and environmental sustainability. It has developed strong partnerships with peasants, agricultural workers and rural women movements in the Asia Pacific region and guided by the strong leadership of these grassroots groups, has grown into a reputable advocacy network with a firm Asian perspective.

PAN AP's mission lies in strengthening people's movements to advance and assert food sovereignty, biodiversity-based ecological agriculture, and the empowerment of rural women; protect people and the environment from highly hazardous pesticides; defend the rice heritage of Asia; and resist the threats of corporate agriculture and neo-liberal globalization.

Currently, PAN AP comprises 108 network partner organizations in the Asia Pacific region and links with about 400 other CSOs and grassroots organizations regionally and globally.

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