Mini Review—Developments in Reproductive Medicine

Health issues and the environment—an emerging paradigm for providers of obstetrical and gynaecological health care

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Although ongoing study is required to winnow environmental ideology from scientific fact, existing evidence from recent research demonstrates a definitive link between chemical toxicants and potential health sequelae, including congenital affliction and gynaecological disorders. Amid media clamour of health risk and biological peril associated with various environmental toxicants, a spectrum of responses has emerged: some have embraced the environmental cause, some have summarily dismissed it as piffle and perhaps the majority has remained disinterested. Although journals devoted to toxicological and environmental health concerns have become prominent in academia with voluminous numbers of scientific reports being published, there has been limited exploration of the relationship between contemporary chemical exposure and reproductive medical issues in mainstream obstetrics and gynaecology literature. Providers of obstetrical and gynaecological health care need to acquire knowledge of taking an exposure history, instruction in details of precautionary avoidance, skills to provide preconception care and necessary tools to investigate and manage patients with toxicant exposure.

Key words: congenital anomalies/endocrine disrupting chemicals/environmental health/human exposure assessment/toxicology

What you don't know has power over you; knowing it brings it under your control, and makes it subject to your choice. Ignorance makes real choice impossible.

Abraham Maslow

There are many opinions, beliefs and urban legends about the risks of various environmental exposures and insufficient research to conclusively establish fact from fancy on many related issues. Although advocates have staged demonstrations and press conferences to draw attention to the plight of the environment, some writers and commentators, at times radiating a smug sense of cerebral superiority, have allegedly debunked fanatical activists who rant about environmental pollutants. Credible scientific study is emerging, however, which raises disquieting evidence about the potential for environmental toxicants to profoundly affect the health and well-being of individuals at all stages of life—from the microscopic embryo within the amniotic sac to the toddler on the playground; from the child in a classroom to the robust adolescent and from the young adult in the workplace to the senior in a nursing home. In this article, recent research exploring the impact of adverse exposure on reproductive health will be surveyed, and recommendations for integration into obstetrical and gynaecological care will be discussed.

A historical perspective on chemical exposure

Medical professionals have long been aware of the importance of various chemicals in the day-to-day functioning of the human organism. The study of human biochemistry, a requirement for medical students, involves the exploration of myriad biochemical reactions that constitute the basis for the functioning of the human species. With the objective of ameliorating human suffering, medical pharmacology includes the study of how therapeutic agents interact and modify human biochemistry in dysfunctional states. Toxicology, on the contrary, involves the pursuit of understanding how, where and which chemical agents adversely affect inherent biochemistry and endeavours to correlate exposure to specific toxicants with consequent morbidity and mortality. The recognition that numerous toxicants with a wide variety of chemical structures have the potential to adversely affect biochemical functioning is well documented.

The revered Hippocratic Oath, crafted as a template for ethical practice in medicine, was conceived in an era when toxic chemical tonics of bribed medical practitioners were frequently used to poison unsuspecting political or business rivals. Hippocrates admonished practitioners to avoid using their practical skills of chemical intervention to inflict injury or harm. Centuries later, the familiar phrase 'mad as a hatter' arose from the observation of individuals occupationally exposed to mercury, a well-recognized heavy metal toxicant (Fraser-Moodie, 2003). In the production of felt hats, once

popular in North America and Europe, a mercury compound was applied to the animal fur—as well as direct ingestion by licking the brushes, the fumes of this compound were consequently inhaled by hatters working in poorly ventilated workshops. These labourers often developed a sequence of symptoms including trembling (known as 'Hatter's Shakes'), slurred speech, loss of co-ordination, irritability, anxiety, depression and various personality changes which cumulatively became known as the 'Mad Hatter Syndrome'.

Examples of the impact of various toxic agents are also evident in literature relating to gestational exposures. In Minamata, a small factory town ~570 miles southwest of Tokyo, a petrochemical and plastics manufacturing company dumped an estimated 27 tons of mercury compounds into the Minamata Bay between 1932 and 1968. Thousands of people whose diet included fish from the bay developed symptoms of mercury poisoning, and numerous neonates succumbed from diffuse central nervous system (CNS) damage following *in utero* mercury exposure (Satoh, 2003).

The problem of limb defects in offspring of some mothers receiving thalidomide to manage hyperemesis is another well-known example of potential damage resulting from gestational toxicant exposure (McBride, 2004). Furthermore, the diethylstilboestrol (DES) tragedy highlighted the potential for delayed sequelae with toxicant exposure. After the administration of this estrogenic agent in pregnancy to diminish miscarriage risk, exposed offspring realized increased rates of reproductive dysfunction, certain cancers as well as (according to some research) long-term psychiatric and psychosexual changes (Ehrhardt *et al.*, 1985; Saunders, 1988; Meyer-Bahlburg *et al.*, 1995; Swan, 2000; Palmer *et al.*, 2002)—effects not readily apparent at birth.

Contemporary regulations regarding pharmaceuticals and safety precautions for selected chemical agents have resulted, in part, as a response to disastrous outcomes resulting from adverse exposures. The current safety recommendations regarding the instillation of carbon monoxide detectors (Runyan *et al.*, 2005), the removal of lead from paint and gasoline (American Academy of Pediatrics, 1987), the restriction of polychlorinated biphenyl (PCB) use in industry (Carpenter, 1998), the discontinuation of asbestos insulation in construction (Robinson *et al.*, 2005) and numerous other examples attest to the recent recognition of toxicant hazards. Yet, many health professionals in clinical practice, including specialists in reproductive medicine, have not fully considered the potential impact of contemporary chemical exposure on the health and well-being of their patients (Kilpatrick *et al.*, 2002; Marshall *et al.*, 2002).

Over the last half-century, more than 75 000 new synthetic chemicals have been introduced, some of which are in widespread daily use (Berkson, 2000). Unlike pharmaceutical regulation, an 'innocent until proven guilty' approach remains in effect for novel chemical agents used for non-medicinal purposes—whereby proof of safety is generally not required before the widespread dissemination of these agents. As a result, individuals are routinely exposed to various chemical compounds through inhalation, ingestion, dermal application, surgical and dental implants and vertical transmission. Consid-

ering historical precedent, it is not a quantum leap to consider that among the vast assortment of synthetic chemicals, some and perhaps many of these compounds may pose a health risk. In fact, emerging research correlates exposure to several chemicals with adverse health outcomes. As some environmental health research has direct application to obstetrical and gynaecological health care, a brief introduction to environmental medicine will be followed by an exploration of toxicant research specifically related to reproductive health.

Overview of human exposure medicine

Health care related to adverse exposure, sometimes referred to as environmental medicine, seeks to understand health problems that arise as a result of the interaction between people and adverse determinants in their environment. According to recent analyses, potential sources of toxicant exposure are ubiquitous: various foods contain toxic substances including contaminated breast milk (Schecter *et al.*, 2003), some baby food (Schecter *et al.*, 2002) and routine foodstuffs (Robbins, 2001; Genuis, 2005); adverse chemical agents may be inhaled in many homes, schools and workplaces (Kilburn, 1998, 2004) and various personal care products and industrial solutions provide dermal exposure to chemical toxicants (Harte *et al.*, 1991; Rapp, 2004).

Although small exposures may seem insignificant and harmless, some chemical agents bioaccumulate within the human body and have the potential to eventually reach levels where clinical illness may ensue. Cumulative exposure from various sources has resulted in the Centers for Disease Control (CDC), finding that the average American child and adult have accumulated numerous toxicants in their bodies (Centers for Disease Control, 2005). At levels measuring in parts per trillion and parts per billion, inherent hormones such as insulin and estradiol (E_2) are bioactive on cells and tissues; exposure to some toxic chemicals also appears to have bioactive impact at seemingly minuscule levels (Welshons *et al.*, 2003).

Toxicants remaining within maternal circulation have the potential to affect metabolic activity and also account for the vertical transmission of numerous synthetic chemicals often found in contemporary neonates (Environmental Working Group, 2005). Although individual toxicants have distinct properties, many eventually deposit and become stored within various tissues including bone and fat. Through hormonal mechanisms such as leptin release, fat cells have significant impact on human metabolism, but it remains to be established how stockpiled toxicants affect the physiology of adipose tissue. There is evidence, however, that some toxicants induce insulin resistance (Alonso-Magdalena *et al.*, 2006) and thus may play a significant role in the pathogenesis of myriad chronic afflictions (Cordain *et al.*, 2003). Research continues to uncover various pathophysiological mechanisms whereby chemical agents effect injury.

Mechanisms of toxicity

Chemical compounds can adversely affect cells and tissues through several differing mechanisms. In addition to causing

direct cellular damage to cell membranes or various intracellular components, xenobiotics (foreign chemicals) can also alter communication between cells and thus disrupt cellular and tissue regulation. There is much attention to a pathophysiological mechanism entitled endocrine disruption or hormone deception whereby various agents, referred to as endocrine disrupting chemicals (EDCs) or hormone disruptors, act by direct or indirect action to mimic, stimulate, antagonize, alter or displace the action of natural hormones (Colborn *et al.*, 1993; Brevini *et al.*, 2005). As a result, EDCs may disrupt routine physiological messages from cells and tissues by interference with production, release, metabolism, binding, action or the elimination of inherent hormones (National Research Council, 1999). Dysregulation of myriad inherent physiological processes such as fetal development, routine homeostasis and intellectual functioning may ensue.

EDCs from various sources—from plastics in teething toys to household cleaners, from industrial by-products to pesticides in food and from personal cosmetics to occupational solvents—can infiltrate the endocrine system of unsuspecting individuals and alter hormonal production and physiology. As 'a wide range of hormone-dependent organs (pituitary gland, hypothalamus, reproductive tract) are targets of EDCs disrupting effect' (Brevini *et al.*, 2005), the mechanics of intricate and finely tuned inherent signals may be disturbed, potentially causing developmental changes or health problems, the extent of which is currently under investigation. Although toxicants potentially cause damage in various ways, hormone disruption is a common mechanism by which adverse agents alter the development and functioning of the human organism.

Establishing adverse exposure as causality of disease

Vociferous claims that insufficient proof exists to establish a link between common chemical exposure and harm as well as protestations by some industry that the benefits and expediency of chemical use outweigh the risks have contributed to confusion regarding chemical toxicity. With the gold standard of randomized controlled trials (RCTs) in mind, some health personnel allege lack of proper evidence and remain reluctant to accept that widespread chemical exposure may be the aetiological source of much contemporary affliction. When studying environmental toxicants, there are, most assuredly, distinct challenges in conclusively demonstrating direct causative links with adverse health outcomes.

RCTs are precluded in toxicology assessment because it is unethical to deliberately expose individuals to potentially toxic chemicals. The allegation that clinical trials are the only objective and credible means in medicine to establish efficacy of an intervention or causality of disease is, however, a myth. Just as it would be farsical to require RCT confirmation to establish the efficacy of parachutes 'to prevent death and major trauma related to gravitational challenge' (Smith and Pell, 2003), RCT evidence is not required to reasonably correlate adverse exposure with adverse outcomes; other research methodologies can be effective instruments to establish causality of disease. There are, however, other challenges in conclusively demonstrating causative links.

Individuals have differing genetic vulnerabilities and may exhibit differing manifestations to the same exposure—thus making it difficult to link the outcome with a specific exposure. With variability in effect combined with potentially long lags between exposure and outcome, index of suspicion may be low and correlation hard to conclusively prove. A major breakthrough with the understanding of toxicants and lag times, however, became evident following the DES tragedy: agents can have long-term sequelae without immediate detrimental impact or obvious side effects. Furthermore, individuals often have multiple exposures with the bioaccumulation of varying chemicals in the body (Centers for Disease Control, 2005)—rendering it difficult to link a single specific outcome with a single specific exposure (Hauser *et al.*, 2005).

With several confounding variables and logistical challenges clouding the outcome of toxicant research, some clinicians have remained sceptical of environmental medicine. Recently, however, a number of credible case–control reports, prospective cohort studies and other research work have suggested a causative link between various agents and serious health sequelae. In fact, reproductive abnormalities such as infertility (Greenlee *et al.*, 2003; Claman, 2004), recurrent miscarriage (Sugiura-Ogasawara *et al.*, 2005), preterm birth (Latini *et al.*, 2003) as well as various types of cancer (Harte *et al.*, 1991; Ma *et al.*, 2002; Warner *et al.*, 2002; Ekbom *et al.*, 2003), neurological afflictions (Gorell *et al.*, 1998), endocrine disturbances (Berkson, 2000), immune system irregularities (Baccarelli *et al.*, 2002; Forawi *et al.*, 2004), developmental problems (Siddiqi *et al.*, 2003) and several other maladies have been correlated in some cases with exposure to toxic agents.

Reference values for toxicants

Many agencies and individuals involved in industry and public health have come to rely on so-called reference levels for various chemicals—the predicted daily human exposure dose alleged to be able to occur without deleterious effects during a lifetime. Doses of environmental chemicals asserted to be 'safe', however, are based on many assumptions and are typically derived from animal experiments where the presumed safe dose was never actually tested. Various concerns have been raised with the current construct of safe exposure levels.

Many chemical agents are relatively new, and safety testing has never been performed; accordingly, reference values have not been established. Furthermore, because human exposure medicine is a comparatively new field with incomplete recognition of the totality of adverse effects, existing values may be inaccurate for many reasons including the following: (i) current safety levels frequently reflect testing of a one-time exposure and do not incorporate bioaccumulation and repeated exposures; (ii) animals commonly used in toxicology testing may have inherent detoxification mechanisms not present in people, thus invalidating the application of animal research to humans (Rat Genome Sequencing Project Consortium, 2004); (iii) there can be immense variability in individual response to exogenous chemical agents that may not be adequately accounted for when determining reference values; (iv) in addition to the impact of single exposures, contact with multiple

agents may facilitate synergism of toxicity; (v) analysis of endocrine responses is not part of conventional toxicological assessment and is often omitted (Welshons *et al.*, 2003) and (vi) vested interests frequently have input into determining threshold levels for toxicants (Ziem and Castleman, 1989).

In addition, reference values are based on adult research not fetal impact—*in utero* is a time in the life cycle when there is a particular propensity to respond adversely to chemical agents (Environmental Working Group, 2005; U.S. Environmental Protection Agency, 2005). The immature fetal liver is not sufficiently efficient at detoxifying contaminants particularly during organogenesis and early gestation: the result is rapid fetal bioaccumulation. Furthermore, with higher unbound fractions of bioactive toxicants because of low levels of binding proteins, with undeveloped excretion pathways (e.g. pollutants excreted in urine are recycled into the nose and mouth as amniotic fluid), with high toxicant concentrations by weight in the small fetus (compared with mother), with rapidly developing organs and with an immature and more permeable blood–brain barrier and a proportionately larger brain, there is a much longer half-life of toxicant in the fetus with a greater target-tissue dose and greater access to the CNS (Birnbaum and Fenton, 2003; Makri *et al.*, 2004; Barton *et al.*, 2005). The developing fetus is at particular risk for untoward chemical damage—a reality not usually represented in reference values.

In view of fetal vulnerability, a recent study of cord blood samples taken by the American Red Cross revealing that the average sample contained 287 toxicants (including heavy metals, various pesticide gasoline by-products and fire retardants) (Environmental Working Group, 2005) has raised serious concern about the individual and public health sequelae of *in utero* pollution via vertical transmission. The concomitant statistics that many pregnancies are terminated for congenital anomalies, that ~3% of offspring in America are born with a major birth defect (Arias *et al.*, 2003), that the incidence of paediatric cancer is on the rise (Birnbaum, 2005), that ~17% of children experience developmental disorders (Boyle *et al.*, 1994; Needham *et al.*, 2005) and that an estimated 1 in 12 children and teens has a chronic disability (Cohn, 2002) [some of these problems already having been linked to known environmental exposures (Branum *et al.*, 2003; Needham *et al.*, 2005)] have resulted in the rising attention to prenatal sensitivity to low levels of toxicants.

Obstetrical concerns related to adverse exposure

With recognition that the placenta does not act as an effective filter against many exogenous chemical agents, the teratogenic effect of selected toxicants has become an issue of increasing concern in modern-day obstetrics and gynaecology. For example, alcohol use in pregnancy, referred to as 'the drink that lasts a lifetime', has gathered much attention as the aetiology of fetal alcohol spectrum disorder—a range of life-long developmental, physical and neuropsychiatric disabilities. Cocaine abuse and exposure to other street drugs have also been associated with adverse fetal outcomes. Recently, however, published research has linked obstetrical and paediatric problems with adverse exposure to various household and industrial toxicants during pregnancy. Exploration of a few studies highlights the concern.

In 1999, the *Journal of the American Medical Association* published an article regarding pregnancy outcome following maternal exposure to organic solvents (Khattak *et al.*, 1999). With the recognition that innumerable women of childbearing age are exposed to these agents, this prospective controlled observational study was designed to explore a potential link between fetal outcome and gestational exposure to organic solvents. Pregnant women occupationally exposed to solvents were matched to comparable pregnant women exposed to a recognized non-teratogenic agent. In addition to increased rates of miscarriage, solvent-exposed women were 13 times more likely to have children with major cardiovascular and CNS malformations, leading the authors to conclude that 'occupational exposure to organic solvents during pregnancy is associated with an increased risk of major fetal malformations' (Khattak *et al.*, 1999).

The DES experience of long-term deleterious sequelae without obvious birth defect has been noted with several other prenatal exposures. For example, an important study published in the *Journal of Epidemiology and Community Health* (Knox, 2005) endeavoured to retest previous findings that most childhood cancer is instigated by prenatal exposure to various toxic inhalants. The study explored a potential link between the birth addresses of children who succumbed to childhood cancer in Great Britain over a 15-year period and the location of high atmospheric emissions of different chemical agents. Significant correlation between birth proximity with sites of industrial use of specific chemical agents was confirmed, and the authors concluded that the maternal inhalation of such toxicants was causally related to fatal paediatric cancer in progeny.

Numerous other studies have linked various toxic chemical exposure during pregnancy with myriad afflictions including psychiatric illness and behavioural problems (Vreugdenhil *et al.*, 2002; Sorensen *et al.*, 2003), respiratory disease (McKeever *et al.*, 2002; Miller *et al.*, 2004), neurological disorders (Gilbertson, 2004) and genital abnormalities (Steinhardt, 2004; Swan *et al.*, 2005). Researchers have recently demonstrated, for example, a highly significant relationship between maternal exposure to phthalates (a family of compounds used widely in plastics and personal care products) and alterations in the development of male genitalia (Swan *et al.*, 2005). Furthermore, fetal developmental alterations may not only affect the fetus directly exposed, but the impact may continue through multiple generations (Anway *et al.*, 2005). Animal research has recently demonstrated that toxicant exposure during gestation is able to alter gene regulation and expression by epigenetic changes, an alteration which may persist through successive generations (Anway *et al.*, 2005).

As well as physical alterations, toxic chemicals have the potential to affect the psyche of developing individuals. Although it may be evident that men and women biologically differ, a major determinant in that difference, both physically and psychologically, is the intricate hormonal balance of parts per billion and parts per trillion of androgens and estrogens present during embryonic and fetal development. The introduction of EDCs (sometimes referred to as gender benders) at critical times of

fetal maturation has the potential, according to various researchers, to affect gender attributes and psychosexual outcome as well as genital formation (Ehrhardt *et al.*, 1985; Saunders, 1988; Collaer and Hines, 1995; Meyer-Bahlburg *et al.*, 1995; Berkson, 2000; Rapp, 2004; Steinhardt, 2004; Swan *et al.*, 2005).

In review, recent medical and scientific literature suggests that toxicant exposure during gestation—a time when fetal cells are rapidly proliferating and differentiating into specific tissues and organs—may have serious implications for the health and well-being of the developing child, with repercussions for families, societies and public health care systems. Although obstetric sequelae resulting from toxicant exposure is a recognized concern, adverse environmental exposures throughout life may also be a determinant of some non-maternity difficulties presenting to the practicing gynaecologist.

Gynaecologic concerns related to toxicant exposure

Although understanding of female endocrine and gynaecologic response to adverse influences is still in its relative infancy, recent scientific literature is beginning to elucidate a possible connection between adverse toxicants and several gynaecological disturbances including bleeding irregularities, precocious puberty, polycystic ovary syndrome (PCOS), subfecundity, infertility, recurrent miscarriage, ovarian failure and more (Falsetti and Eleftheriou, 1996; Berkson, 2000; Cordain *et al.*, 2003; Drbohlav *et al.*, 2004; Mlynarcikova *et al.*, 2005; Sugiura-Ogasawara *et al.*, 2005; Tsutsumi, 2005). Some recent investigation of toxicants related to gynaecological outcome has centred on the prominent role of exogenous estrogen and androgen modifiers in male and female physiology (Cotton, 1994; McLachlan, 2001).

In couples presenting with infertility, for example, male reproductive dysfunction or altered sperm production may be the result of prenatal toxicant exposure (Main *et al.*, 2006) or post-natal interaction with environmental or occupational EDCs which alter testosterone metabolism (Quinn *et al.*, 1990; Egeland *et al.*, 1994; Claman, 2004). Furthermore, it is well recognized that intact estrogen physiology is required for female embryonic development, breast maturation and puberty, normal sexual response, pregnancy as well as healthy vascular, heart and bone function. Anything that disrupts the normal physiology of estrogen—by mimicking or antagonizing the effects of E_2—may facilitate reproductive dysfunction and disorders such as endometriosis (Dubeyl *et al.*, 2000; Tsutsumi, 2005).

Endometriosis and toxicants

With prevalence rates of 10–20% of American women, endometriosis frequently causes chronic pelvic pain and infertility, accounting for incalculable suffering as well as about half-a-million surgical procedures in the United States annually. This increasingly common disorder in industrialized countries (Koninckx, 1999) may afflict very young women and often occurs in geographic clusters. Koninckx *et al.* (1994), for example, found that in addition to having the world's highest incidence of endometriosis, Belgian women also sustain

inordinately high concentrations of dioxin (a potent disruptor of estrogen metabolism) in their breast milk. Furthermore, various researchers have found high rates of endometriosis in animals as well as in individuals exposed to EDCs (Cummings *et al.*, 1996; Osteen and Sierra-Rivera, 1997; Rier and Foster, 2002).

On the basis of these initial observations, work has been done to confirm suspicions that human endometriosis may result from toxic exposure (Rier and Foster, 2003; Louis *et al.*, 2005). A recent case–control study by Heilier *et al.* (2005), for example, assessed the level of estrogenic EDCs as well as synthetic chemicals that operate via other response mechanisms in hospitalized women who were subdivided into groups according to diagnosis. By linear regression analysis and the standardization of variables, the researchers noted a significant association between the body burden of EDCs in participants and the finding of adenomyosis and endometriosis (Heilier *et al.*, 2005). Furthermore, a cohort study investigating the relation between the fetal environment and endometriosis recently found a significant increase in laparoscopically confirmed endometriosis in women previously exposed to estrogen-disrupting DES *in utero* (Missmer *et al.*, 2004).

In view of preliminary data on potential gynaecological outcomes as well as on documented obstetric and paediatric sequelae associated with toxicant exposure, it is important to explore measures that might prevent and ameliorate illness for women and their offspring.

Clinical considerations

Despite compelling evidence that some chemical exposures may have adverse sequelae, there is insufficient proof to directly establish safety or harm for many of the thousands of chemicals in everyday use. How should clinicians approach the issue of environmental toxicants?

As most human activity involves a certain degree of risk, it is important to consider the risk–benefit ratio when providing clinical advice about any health determinant, including the benefits and risks associated with the use of and exposure to specific chemicals. As the *in utero* peril to the fetus from toxicants is manifest, it is recommended that pregnant patients adhere to the 'Precautionary Principle' (Wingspread statement on the Precautionary Principle, 1998) whereby individuals are educated regarding potential toxic exposures and then implement a concerted effort to avoid them. Patients should acquire a thorough understanding of how and where toxic exposure occurs and develop a plan to avoid adverse contact. Accordingly, physicians need to be educated about chemical toxicants to transmit this important information to patients.

Medical practitioners in all clinical spheres need to incorporate exposure evaluation as a routine component of patient assessment (Ott, 1995; Needham *et al.*, 2005; Ozkaynak *et al.*, 2005). To determine potential exposure, past and present, we can use a human exposure questionnaire as an instrument to help in the diagnosis and education of patients. Various assessment instruments are available in the scientific literature (Rea, 1997; Miller and Prihoda, 1999; Steele and Fawal, 2000) and from medical organizations (Marshall, 2002).

To assess the 'body burden' of contaminants, some organizations such as the CDC have performed screening toxicant panels (Centers for Disease Control, 2005)—this type of laboratory investigation can provide definitive evidence of bioaccumulation. Such screening, however, is usually confined to research and is not frequently used in clinical practice thus far. Major drawbacks to blood testing include exorbitant expense as well as frequent false-negative reporting because many toxicants are sequestered within storage sites such as fat and thus not adequately reflected in blood samples.

The process of expelling chemical residue from the body is often referred to as detoxification, a process performed in great part by the liver in conjunction with excretion through routes such as stool, urine, exhaled breath and perspiration. Utilization of specific physical modalities to facilitate toxicant expulsion from the body is not a new concept: Hippocrates used solariums, religious groups used fasting, aboriginal groups used sweat lodges and hot baths, Egyptians used body wraps, specific eastern European groups have used Turkish baths and some Scandinavian cultures have employed saunas and steam baths—all of which allegedly enhance the mobilization of stored metabolic and exogenous toxicants. There has been recent work attempting to utilize biochemical interventions and physical modalities to facilitate and enhance the body's inherent detoxification mechanisms (Schnare *et al.*, 1982, 1984; Kilburn *et al.*, 1989; Shields *et al.*, 1989; Tretjak *et al.*, 1990; Rea *et al.*, 1996; Baker, 1997; Rea, 1997; Berkson, 2000). Although preliminary data suggest clinical improvement after detoxification interventions, this evolving area has not been adequately studied or reported in mainstream medical and toxicology literature (Kilburn, 2004); further research needs to be undertaken to establish definitive evidence-based recommendations.

Conclusion

If individuals and the public are properly educated about chemical toxicants, they will be empowered with the choice to make decisions to protect themselves and their offspring; without knowledge, the choice is precluded. As official advocates for reproductive care in the community, women's health physicians have the distinctive opportunity to assist individual patients as well as to proactively engage in public health education relating to the impact of adverse exposure. With appropriate knowledge and skills of exposure assessment, precautionary avoidance and potential therapeutic options, providers of obstetrical and gynaecological health care may be able to prevent congenital anomalies and ameliorate the life situation for many women.

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