Plastics and Health Risks

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Abstract

By 2010, the worldwide annual production of plastics will surpass
300 million tons. Plastics are indispensable materials in modern so-
ciety, and many products manufactured from plastics are a boon to
public health (e.g., disposable syringes, intravenous bags). However,
plastics also pose health risks. Of principal concern are endocrine-
disrupting properties, as triggered for example by bisphenol A and di-
(2-ethylhexyl) phthalate (DEHP). Opinions on the safety of plastics vary
widely, and despite more than five decades of research, scientific consen-
sus on product safety is still elusive. This literature review summarizes
information from more than 120 peer-reviewed publications on health
effects of plastics and plasticizers in lab animals and humans. It exam-
ines problematic exposures of susceptible populations and also briefly
summarizes adverse environmental impacts from plastic pollution. On-
going efforts to steer human society toward resource conservation and
sustainable consumption are discussed, including the concept of the
5 Rs—i.e., reduce, reuse, recycle, rethink, restrain—for minimizing pre-
and postnatal exposures to potentially harmful components of plastics.

BRIEF HISTORY OF PLASTICS

PS: polystyrene

Plastics are ubiquitous in modern life. Early uses date back to 1600 B.C. when natural rubber was shaped by human hands and polymerized into objects of utility in prehistoric mesoamerica (46). The exploitation of plastics was jumpstarted in 1839 with the discovery of vulcanized rubber and polystyrene (PS) (3). The first truly synthetic polymer, Bakelite, was produced in Belgium in 1907 (110). Mass production of plastics began in the 1940s and has continued to expand ever since. There are now 20 different groups of plastics, whose worldwide usage was on the order of 245 million tons for the year 2006 (6). Annual world production will likely have surpassed the 300-million-ton mark by the time this article appears in print. The U.S. Environmental Protection Agency's definition of plastics and polymers is shown in the sidebar, Plastics/Polymers. The addition of plasticizers, fillers, antioxidants, flame retardants, and colorings to plastic polymers imparts desired functionalities and creates hundreds of different varieties of plastic materials of differing properties.

This review summarizes the state of science concerning the safety of plastics. It also suggests management and policy strategies for a more sustainable use of this important group of mass-produced materials.

PLASTICS AND HUMAN HEALTH

Plastics are pivotal materials in modern life, public health, and medicine. Owing to their resistance to chemical, physical, and biological degradation, human society relies heavily on plastics. This is particularly true for the health care sector. As with many other modern-day uses of plastics, a key benefit in medicine and public health is the versatility of these materials combined with an extremely low cost, which has enabled the mass production of disposable single-use health care products that are functional and hygienic. The societal value of plastics is immense and has been examined elsewhere in greater depth (3). The rise of polymeric synthetics had been foretold in *Plastics*, a visionary book first published in 1941, in which the authors envisioned a world filled with objects made from plastics (127). In many respects, it accurately depicts the world we live in today.

Owing to the wide usage of plastics and the many additives contained therein, plastics pose a number of potential human health and environmental risks. As discussed below, some appear to be universally accepted now, whereas others are subject to an intense debate involving the many stakeholders of the "plastic age" (110).
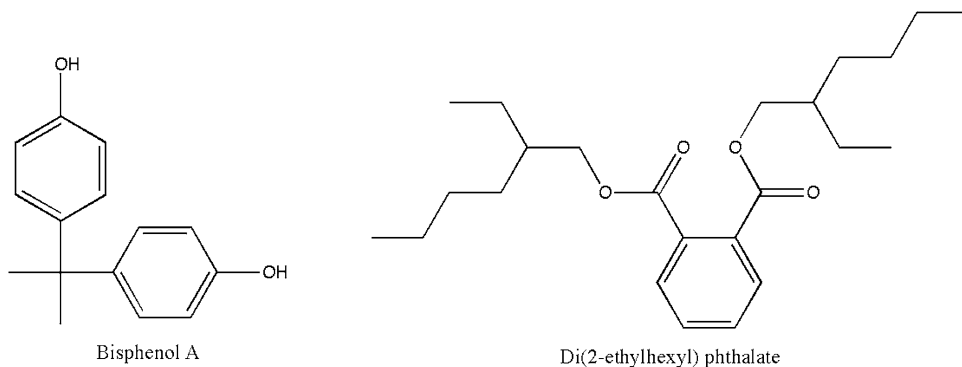
PLASTICS/POLYMERS

Plastics are polymers. The most simple definition of a polymer is something made up of many units. Polymers are chains of molecules. Each link of the chain is usually made of carbon, hydrogen, oxygen, and/or silicon. To make the chain, many links, [sic] are hooked, or polymerized, together.

To create polymers, petroleum and other products are heated under controlled conditions and broken down into smaller molecules called monomers. These monomers are the building blocks for polymers. Different combinations of monomers produce plastic resins with different characteristics, such as strength or molding capability.

Plastics can be divided into two major categories: thermosets and thermoplastics. A thermoset is a polymer that solidifies or "sets" irreversibly when heated. They are useful for their durability and strength, and are therefore used primarily in automobiles and construction applications. Other uses are adhesives, inks, and coatings.

A thermoplastic is a polymer in which the molecules are held together by weak bonds, creating plastics that soften when exposed to heat and return to original condition at room temperature. Thermoplastics can easily be shaped and molded into products such as milk jugs, floor coverings, credit cards, and carpet fibers.

Plastic resins are processed in several ways, including extrusion, injection molding, blow molding, and rotational molding. All of these processes involve using heat and/or pressure to form plastic resin into useful products, such as containers or plastic film. (Reproduced from U.S. EPA, **http://www.epa.gov/waste/conserve/materials/plastics.htm**) (113)

Figure 1

Chemical structures of bisphenol A and di-(2-ethylhexyl) phthalate (DEHP), which illustrate the use of endocrine-disrupting monomers and plasticizers in contemporary plastics.

Human health risks from plastics can stem from their monomeric building blocks (e.g., bisphenol A), their additives [e.g., plasticizers (85)], or from a combination of the two (e.g., antimicrobial polycarbonate). A comprehensive treatise of all types and permutations of materials is beyond the scope of this review. Instead, the discussion concentrates on plastics components and additives of principal concern such as bisphenol A and phthalates (**Figure 1**).

BISPHENOL A

Bisphenol A (BPA) is best known as the monomeric building block of polycarbonate plastics. However, it is also used frequently as an additive to other plastics such as polyvinyl chloride (PVC). It was first synthesized in 1891 (26). A 2003 estimate puts the worldwide annual output of BPA at more than 2.2 million metric tons. A sizable fraction of this mass comes into contact with food. Because the polymerization of BPA leaves some monomers unbound, BPA molecules can be released from beverage and food containers into drink and food over time. The leaching process is accelerated by repeated washing of containers and when storing in them acidic or basic items that break down the polymer. As a result, reusable water bottles, baby bottles, and the inner linings of food cans, all made by using BPA, are known to leach the controversial monomer into food over time,

particularly at elevated temperatures (12, 54, 82, 86). Whereas food is considered the major exposure source (e.g., up to 99% of the total exposure in school children), additional environmental exposures can occur primarily via inhalation (123). As a result of worldwide production of the compound, an estimated 100 tons are being released into the atmosphere each year by synthesis alone (114). Additional airborne exposures can occur during off-gassing of the substance from consumer products and volatilization from contaminated water.

The body burden of BPA is routinely assessed in blood serum and urine as either the free, unconjugated BPA level or the combined total concentration. Levels of unconjugated BPA in human blood and tissues are in the range of 0.1 to 10 μg/L (47, 94). Levels detected by enzyme-linked immunosorbent assay (ELISA) in amniotic fluid were in a similar range (126). Bisphenol A is also present in human milk at low μg/L levels (62, 105) and further has been detected in human colostrums with a mean concentration of 0.46 μg/L (67). In 2005, the Centers for Disease Control and Prevention (CDC) assessed the body burden of BPA in a reference population of 394 American adults (14). Ninety-five percent of urine samples showed detectable levels of BPA, as determined by isotope dilution gas chromatography/mass spectrometry (ID-GC/MS). Average concentrations found in

BPA: bisphenol A

PVC: polyvinyl chloride or vinyl

males (1.63 µg/L) exceeded those of females (1.12 µg/L). A larger follow-up study by the CDC reported a detection frequency of 92.6% in 2517 of the U.S. participants examined (15). Concentrations of total BPA in urine ranged from 0.4 to 149 µg/L, with a geometric mean of 2.6 µg/L. Geometric means for daily intake of BPA estimated from urinary levels are higher for males than females (53.8 versus 41 ng/kg/day) and higher in children and adolescents (64.6 and 71 ng/kg/day, respectively) than in adults, whose exposure levels decrease with age from 52.9 ng/kg/day in 20–39-year-olds to 33.5 ng/kg/day in seniors 60 years and older (68). Elevated exposure of women of childbearing age and of children are of particular concern because of known windows of vulnerability to BPA that put the developing fetus and children at elevated risk, compared with adults exposed to identical levels of the contaminant (114). Information on long-term trends in BPA exposure is still lacking.

The health risks of BPA are fiercely debated and, after more than 70 years of study, are still not fully understood. The stakes are high because exposure is ubiquitous and BPA-containing products are a multi-billion-dollar enterprise. Estrogenic properties of BPA had been described as early as 1936 (26). Today, monomeric BPA is classified as an estrogen mimic, which binds to both estrogen receptor α (ERα) and ERβ (52, 72, 114); binding to ERβ is about tenfold higher, relative to ERα (37, 66). Compared with estradiol, however, the binding affinity of BPA is ∼10,000-fold lower (66). These data have led to an initial classification of BPA as a very "weak estrogen and endocrine disruptor" (117); however, this classification has been called into question by a number of studies, including one report (125) demonstrating BPA-mediated stimulation of calcium influx in MFC-7 breast cancer cells in culture at levels of 0.023 µg/L, an outcome on par with the effects of the same dose of estradiol (117).

In its determination of a reference dose for humans, the U.S. EPA arrived at a value of 50 µg per kg per day by applying a safety factor of 10 three times over, to account for (a) extrapolation from animals to humans, (b) variability in the human population, and (c) extrapolation from subchronic to chronic exposures (121). This reference dose for BPA was calculated on the basis of the lowest-observable-adverse-effect level (LOAL) rather than the no-observable-adverse-effect level (NOAEL) because adverse responses were found even at the lowest dose tested (114).

Some scientists have argued that neither the calculated EPA reference dose for BPA nor the typical risk assessment approach, which assumes a monotonic increase in the response at increasing dose, are suitable for evaluating BPA's health risks (114, 117). They point to the fact that by the end of 2004, a total of 31 papers in the peer-reviewed literature had reported adverse effects of BPA at doses at or below the current EPA reference dose (117). Adverse effects recorded in animal studies included (a) increased postnatal growth in both sexes after maternal doses between 2.4 and 500 µg/kg/day; (b) early onset of sexual maturation in females after maternal doses between 2.4 and 500 µg/kg/d; (c) altered plasma luteinizing hormone levels and decreased plasma testosterone in males at maternal doses of 2 µg/kg/d; (d) increased prostate size in male offspring following a maternal dose of 2–50 µg/kg/d; (e) decreased sperm production and fertility in males at maternal doses of 0.2 to 20 µg/kg/d from developmental and adult exposure; (f) stimulation of the development of the mammary gland in female offspring at a maternal dose of 0.025 µg/kg/d; (g) during meiosis in oocysts, a significant disruption of chromosome alignment during puberty caused by doses of 15–70 µg/kg/d; (h) increased mortality of embryos following a maternal dose of 25 µg/kg/d; (i) disruption of adult estrous cycles following maternal doses of 100–500 µg/kg/d; (j) alterations in immune function at doses of 2.5–30 µg/kg/d; (k) decreases in antioxidant enzymes of adult males at doses of 0.2 µg/kg/d; effects on the brain such as (l) increases in levels of progesterone receptor mRNA following a dose of 400 µg/kg/d; changes in (m) ERα at a dose of 40 µg/kg/d,

(n) in levels of ERβ mRNA at 40 μg/kg/d, and (o) in levels of brain somatostatin receptors at 400 μg/kg/d; additionally observed were behavioral effects such as (p) hyperactivity at 30 μg/kg/d, (q) increased aggressiveness at 2–40 μg/kg/d, (r) alterations in response to pain and threat stressors at 40 μg/kg/d, (s) impaired learning at 100 μg/kg/d, (t) reversal of normal sex differences and elimination of differences between the sexes in behavior via changes in the locus coeruleus induced at 30 μg/kg/d, (u) decreases in maternal behavior following developmental exposure at 10 μg/kg/d, (v) alterations in play and sociosexual behaviors at 40 μg/kg/d, and (w) altered behavioral response to amphetamine following a BPA dose of 40–300 μg/kg/d (see Reference 117 for primary references and additional information).

Meanwhile, additional studies reported binding of BPA to several membrane steroid receptors including a membrane-bound form of ERα (mER) and a transmembrane ER, termed G protein–coupled receptor 30 (GR30) (reviewed in 114). New studies also point to BPA's ability to affect vertebrate development in vivo by inhibiting T3 pathways (42). This finding adds to more than 100 previous in vivo studies (reviewed in 88) and lends further credibility to a previously proposed effect of BPA on thyroid hormone homeostasis (77). In contrast to the conclusions drawn from feeding studies considered by the National Toxicology Program (NTP) (78), a recent study of the effects of BPA exposure on prostate cancer showed that neonatal BPA exposure (10 μg/kg/d) followed by treatment with hormones in adulthood (testosterone and estrogen) caused a significant increase in the incidence and severity of prostatic intraepithelial neoplasias in male Sprague-Dawley rats (44). A recent review article discusses six controversies in the assessment of BPA health risks, and the authors also conclude that a possible connection is strengthening between perinatal BPA exposure and mammary cancer in rodents (114). Finally, epidemiological studies have found associations between blood levels of BPA in women and impaired health, including obesity, endometrial hyperplasia, recurrent miscarriages, sterility, and polycystic ovarian syndrome (9, 30, 87, 89, 119). These types of studies are not suited to drawing conclusions about the causality of these outcomes, however.

In summary, the perception of the safety of BPA continues to shift. No longer regarded simply as a long proven and safe chemical, many scientists today view BPA as an endocrine-disrupting compound whose effects are reason for concern and should be studied further. The rift (117) in the scientific community is exemplified by a number of reports concluding the absence of significant risks or harm posed by BPA to humans (5, 38, 52, 84) and the opposing viewpoint by other experts who favor more studies and possible restrictions in BPA usage (72, 79, 114, 116, 117). As it turns out, the source of funding scientists rely on is an excellent predictor of the conclusions they are prone to reach in their evaluations of BPA's safety profile (117). In the quest for scientific consensus on the subject matter, it will be critical to address the key question, whether the toxicant, owing to proposed nonmonotonic dose-response relationships (reviewed in 114), can cause harm at environmentally relevant low doses but not necessarily at higher ones. Today's concerns about BPA are driven primarily by low-dose effects observed in animals, by epidemiological observations in subsets of human populations, and by the recognition that biologically active levels of BPA detectable in human blood are within or above the range of concentrations demonstrated in vitro to cause changes in the function of human tissues (117).

PHTHALATES

Phthalates are a diverse group of compounds that are heavily exploited in industry. They represent diesters of phthalic acid, a compound also known as 1,2-benzenedicarboxylic acid. Produced in large quantities since the 1930s, phthalates are ubiquitous in our society and can be found in industrial plastics, household items, paints, medical devices, children's toys, and

DEHP:
di-(2-ethylhexyl)
phthalate

DBP: Dibutyl
phthalate

personal care products including cosmetics, lotion, sunscreen, and perfume, to name just a few (53, 69, 75, 91, 92). The properties of phthalates are dependent on the length and branching of the dialkyl or alkyl/aryl side chains, i.e., the alcohol moiety of the ester (69). More than 25 different phthalate esters exist. Phthalates are incorporated into plastics as plasticizers to impart flexibility, pliability, and elasticity to otherwise rigid polymers, such as PVC (18). Phthalates comprise ∼70% of the U.S. plasticizer market (104). Unlike BPA monomers in polycarbonate plastics, phthalates are by design not covalently bound to the polymer matrix, which makes them highly susceptible to leaching. Phthalates are contained in plastics at surprisingly high percentages. For example, they can contribute up to 40% by weight to intravenous medical bags and up to 80% by weight in medical tubing (13).

Di(2-ethylhexyl) phthalate (DEHP), produced at annual quantities of 2 million tons and widely used in medical devices (69, 91), is one of the principal phthalates causing human health concerns. Attention to DEHP was first drawn in the late 1960s, when reports showed leaching of the compound from medical plastic devices into body fluids and subsequent migration into human tissues (49). Forty years after discovery of this chemical leaching process, the scientific and regulatory communities are still struggling to define and manage potential human health risks posed by DEHP in medical devices. Meanwhile, it has been shown that up to 15% of DEHP contained in medical devices is available for leaching; chemical release was shown to be a function of temperature, mechanical stress, storage time, and chemical composition and geometry of the medical device, as well as the type of contacted matrix employed (reviewed in 111).

Migration of plasticizers and ensuing human exposures have been demonstrated for many additional phthalates and plastics products. Important other additives include di-isononyl phthalate (DINP), dibutyl phthalate (DBP), butylbenzyl phthalate (BBP), di-isododecyl phthalate (DIDP), di-n-octyl

phthalate (DnOP), and di-n-hexyl phthalate (DnHP) (55–61). Among the nonmedical applications of phthalate-containing plastics, usage in children's toys and baby care products stand out as being most controversial (20, 91, 92, 99). Di-ethyl phthalate (DEP), di-methyl phthalate (DMP), and DBP are also heavily used in cosmetics, in personal care products, and as enteric coatings of oral medications (91).

Important routes of human exposure to phthalates include, most notably, medical exposures caused by direct release of phthalates into the human body, e.g., through dialysis, blood transfusions, and extracorporeal membrane oxygenation (ECMO); ingestion of contaminated materials, including contaminated food, house dust, or food that has been in contact with food packaging; dermal uptake of phthalates from personal care products; and inhalation exposure from outdoor and indoor air containing phthalate off-gassing from paints, as well as from covering materials for walls, ceilings, and floors (reviewed in 53, 69, 75, 91, 92, 111). Exposure of the developing fetus occurs in utero, from phthalates crossing the placental barrier, from blood and amniotic fluid, and in the early developmental period after birth from ingesting breast milk, infant formula, and cow's milk and from contact with mouthing toys and baby care products (reviewed in 75, 91, 92).

Once incorporated into the human body, phthalates are short-lived and rapidly metabolized with half-lives on the order of hours to several days (34). Phthalate diesters frequently undergo a biphasic metabolism by becoming hydrolyzed or oxidized in phase I and subsequently conjugated in phase II (34). Following initial metabolism in phase I, the resultant monoesters may again be subjected to phase I transformation or may immediately be excreted in urine and feces. Biomonitoring preferably targets the monoesters and other metabolites rather than the parental compound. This approach makes the analysis strategy more robust by minimizing the risk of false-positive detections from background concentrations

of phthalates, which are ubiquitous in indoor air and plastic equipment used in sampling and sample processing. Despite the rapid metabolism of phthalates, single measurements provided fairly reliable estimates of steady-state concentrations in the human body (98).

In 2004, data from the National Health and Nutrition Examination Survey (NHANES) provided a first glimpse of the phthalate body burden on a population-wide basis via analysis of urine from 324 U.S. children ages 6–11 years (97). Monoesters of several different phthalates were found in most of the children monitored. Geometric mean and 10th–95th percentile values (shown in parentheses) in μg/L for the monoesters of the parental compounds were on the order of 5.1 [<detection limit (DL), 34.5] for DEHP, 91.3 (27.2–756) for DEP, 41.4 (15.1–163) for DBP, and 39.4 (9.4–214) for BBP. Additional monitoring studies in children (reviewed in 91) yielded comparable results, the one exception being 54 infants from a neonate intensive care unit, who showed elevated mean and min-max values, again in units of μg/L, for the monoester of DEHP [15 (<DL, 758)] and for two additional metabolites of DEHP not monitored for in the NHANES study: mono-2-ethyl-5-hydroxyhexyl phthalate (MEHHP) [133 (<DL, 3492)] and mono-2-ethyl-5-oxohexyl phthalate (MEOHP) [120 (<DL, 3376)] (39, 122).

More work is needed to understand better the trajectory of phthalate exposure levels over time in the general population. A retrospective human biomonitoring study of German adults 20–29 years of age showed constant median daily intakes for DBP and DEHP of 7 and 4 mg/kg body weight (bw)/day, respectively, and a decline in median levels of both phthalates to 1.9 and 2.4 mg/kg bw/day, respectively, from 1996 to 2003 (124). In contrast, increases in daily intake were observed for di-(iso-butyl) phthalate (DiBP) from 1.1 to 1.4 mg/kg bw/day) and for di-iso-nonyl phthalate from 0.2 to 0.4 mg/kg bw/day during the time period of 1988–2003. Fourteen percent of the subjects showed DBP intakes above the tolerable daily

intake value of 10 mg/kg bw/day set by the European Food Safety Authority. Exceedances decreased over the years and were less than 2% by the year 2003.

The occurrence of this body burden in the general population is of concern because phthalates are endocrine-disrupting compounds (reviewed in 69, 75, 91, 92, 111). Among the known and suspected adverse health effects are reproductive outcomes, including testicular dysgenesis syndrome comprising male genital abnormalities that can cause atypical sperm characteristics, which later may develop into testicular cancer (115). Laboratory studies in animals showed phthalates including DBP, DEHP, and BBP to produce malformations of the male reproductive system, cryptorchidism, and testicular injury together with permanent feminization evidenced by the retention of nipples/areolae and demasculinization of the growth of the perineum resulting in a reduced anogenital distance (AGD) (reviewed in 33). A noteworthy, frequently cited human study of 85 mother/infant pairs demonstrated a similar relationship between increased maternal phthalate levels and reduced AGD in male offspring (107). This work has also stirred some controversy (74, 106). Additional human studies (reviewed in Reference 91) reported other adverse outcomes associated with elevated phthalate body burden, including a positive association between premature onset of thelarche in young girls and their serum levels of the phthalates DMP, DEP, DBP, and DEHP and the monoester of DEHP (19), an inverse relationship between phthalate exposure and human sperm quality observed in two (28, 41) of three studies conducted (51), and a positive association between increased phthalate levels and waist circumference as well as an inverse association of phthalate levels with insulin resistance (103). A limited number of reports suggest an effect of phthalates on the thyroid hormone axes and on human immune response (reviewed in 91). The observed development of liver tumors in adult rodents following dosing with high concentrations of DEHP initially suggested DEHP to represent

a "probable carcinogen"; however, in 2000 the International Agency for Research on Cancer (IARC) downgraded the designation to "cannot be classified as to its carcinogenicity in humans" because the identified pathway involving the peroxisome proliferation receptor and its response elements in rodents was deemed by the agency as a mechanism that is not relevant to humans (48, 91).

In summary, 40 years after the first reports of phthalate exposures in humans, human health effects and risks continue to be investigated and the importance of these exposures remains subject to debate. A number of panels and agencies have evaluated the safety of phthalates (reviewed in 53). The Food and Drug Administration's (FDA) safety assessment of phthalates in medical settings concluded that neonates can be exposed to plasticizer levels about fivefold higher than the allowed daily tolerable intake (32).

OTHER PLASTIC ADDITIVES OF HUMAN HEALTH CONCERN

Aside from BPA and the various phthalates, a large number of additional additives to plastics have also raised both human health and ecological concerns but cannot be covered in detail here. The most problematic ones among these are polyhalogenated flame retardants, particularly polybrominated diphenyl ethers (reviewed in 22, 43, 100, 129), polyfluorinated compounds (reviewed in 4, 35, 36, 65), as well as nonyl phenol (reviewed in 11, 31, 95, 101), and antimicrobial compounds, particularly triclosan (reviewed in 1, 7, 16, 17, 128). Human exposures and body burdens of these compounds are driven by many products of daily use that go beyond the applications of plastics.

COMMON USES OF POLYMERS AND ADDITIVES

Consumers alerted by the media to human health and environmental risks from leaching plastics components face a difficult task when trying to minimize unnecessary exposures through informed decision-making. Labeling of plastic consumer products is limited and knowing the type of polymer used, by examining the recycling symbol [labeled with the Society of the Plastics Industries, Inc. (SPI) number], does not inform on the content of potentially harmful additives or on the environmental persistence of plastics. Although universally applicable generalizations are impossible to make, some common patterns in the use of plastics and additives for food packaging and other applications can be noted.

Polyethylene terephthalate [PET or PETE (SPI #1)] is frequently used in the United States and other countries for the manufacture of synthetic fibers (polyester) and disposable soda and water bottles. PET is produced by esterification of terephthalate or dimethyl terephthalate, monomeric building blocks that are distinct in structure and toxicity from the problematic phthalates discussed above. Whereas plasticizers are not required in PET for softening, this polymer may contain additives. Although it does not represent a noteworthy source of contaminants, some reports have indicated that leaching of plastics' components into beverages from PET can occur (10, 24, 93, 96, 118). Traces of DEHP have been detected in mineral water after nine months of storage in PET bottles (10). The industry position is that PET does not contain orthophthalates, which include DEHP (29).

High-density polyethylene [HDPE (SPI #2)] is frequently used in the production of bottles and packaging for milk, detergent, and oil. Among the contaminants demonstrated to potentially migrate from HDPE into stored materials are antioxidants (50), including nonylphenol, an endocrine-disrupting compound used both as an antioxidant and as a plasticizer (71). Chemical releases from HDPE are limited and not thought to represent a significant health risk.

PVC (SPI #3) has many uses in such things as food wrap, vegetable oil bottles, and medical devices. Products made from PVC are often, but not always, formulated with problematic phthalates. According to a statement by the

American Plastics Council, food wraps and food containers manufactured in the United States do not contain phthalates (29) and instead make use of other plasticizers, such as di-(2-ethylhexyl) adipate (DEHA). The latter compound is being investigated for its ovarian toxicity (120). A hoax circulating on the Internet for several years now suggests that virgin plastics, including PVC, contain carcinogenic dioxins, and additional toxic dioxins are formed during heating of plastics in kitchen microwaves; this claim is without scientific basis, however (83). As stated earlier, PVC medical devices typically have a high content of plasticizers such as DEHP and are subject to extensive phthalate leaching (reviewed in 111). Susceptible populations, such as neonates receiving intravenous liquids and blood transfusions in intensive care units, are at risk from these exposures in the United States (32). A number of countries have banned the use of phthalate-containing PVC in plastic toys and baby care products such as teething rings (reviewed in 25, 75, 91).

Low-density polyethylene [LDPE (SPI #4)] is used in many products including grocery plastic bags, shrink wrap, and garment bags. Migration of antioxidants from the LDPE has been reported, but released quantities were small compared with regulatory limits (27).

Polypropylene [PP (SPI #5)] is used widely for packaging, plastic containers, and bottle tops. Similar to LDPE, migration of additives into surrounding media is limited (27).

Polystyrene [PS (SPI #6)] also finds many applications, including building materials, cups, plates, and throwaway utensils, as well as packaging, dairy containers, and toys. Plastic articles made from PS are known to release styrene oligomers, which can bind to the estrogen receptor and exhibit estrogen-like activity (63, 81). The potency and importance of this activity are subject to debate (80).

Plastics not belonging to the above categories are labeled as SPI #7. These materials include layered or mixed plastics as well as the previously discussed polycarbonate (PC) made from BPA monomers. Reusable water bottles are frequently manufactured from PC and are known to leach BPA in small concentrations (23, 70, 73, 117).

Reacting to consumer concerns, the American Chemistry Council compiles responses to scientific studies on health risks from plastics on its Internet portal (2).

PLASTIC POLLUTION

Looking beyond the essential services that plastics provide to humanity (3) and their associated human health risks (64), evidence abounds for plastics' potential to pollute and disrupt important natural processes and quality of life (reviewed in 109, 110). Plastic fragments, varying in size from macrodebris (>20 mm), to mesodebris (2–20 mm), to microdebris (<2 mm) are polluting the world's oceans (64). Using surface net tows, 334,000 plastic items were collected in 1999 per square kilometer in the North Pacific Subtropical Gyre, a mass equivalent to 5.1 kg (76). Although plankton abundance was about five times higher than that of plastic, the mass of plastic exceeded that of plankton sixfold. Commonly observed plastic debris included thin films, PP/monofilament line, and miscellaneous fragments of unidentified plastics. A similar count performed a decade earlier suggested a tenfold increase in debris over this time period (reviewed in 90). The list of affected wildlife suffering from exposures to plastic debris is long and includes seabirds, seals, whales, and turtles (reviewed in 40). In terrestrial environments, on seashores, and in open marine waters, plastics debris of extreme persistence is accumulating at increasing rates, owing to its environmental longevity, which is estimated to be on the order of centuries to millennia (reviewed in 8). Waste incineration, the single most effective way for removing non-biodegradable plastics from the chemosphere, is known to produce carcinogenic polychlorinated dibenzo-p-dioxins/furans (PCDD/Fs) and additional toxic, persistent organohalogens. Principal precursors of dioxin formation during incineration are in order of decreasing importance: PVC, PET, PE, and PP (108).

SUSTAINABILITY

Human health risks aside, the ongoing, increased production of extremely durable plastics of limited recyclability for disposable, short-lived consumer products is unsustainable (45, 102, 109). Plastics production is petroleum based and accounts for 8% of the world oil production, with 4% accounting for feedstock and 3%–4% for energy requirements in manufacturing (109). More than one-third of the production volume of plastics is for disposable items (45). Packaging with extremely durable synthetic plastics is widespread, unnecessary, and unsustainable. Furthermore, many plastic articles have a very short useful life span, measured in timescales of seconds, minutes, or hours (e.g., throwaway cups, utensils, plastic bags). However, upon release into the environment, these products are known to persist and pollute for decades, centuries, or even millennia (reviewed in 8). This mismatch by design has fatal consequences for many plastics-exposed biota. In 2007, Americans produced 254 million tons of trash and an additional 85 million tons of household waste, which was recycled and composted (112). About 4.6 pounds of solid waste are produced per person per day in the United States (112), and plastics represent ~10% of this mass (110). Recycling of present-day synthetic plastics is challenging, however, as illustrated by the fact that many municipalities in the United States accept only plastics from the SPI #1 and #2 categories (21). To address the problem, the widely accepted concept of the 3 Rs, reduce, reuse, recycle, will not suffice. Building on previously proposed efforts (45, 109), a forth R to rethink at the systems level is desirable, as well as a fifth R to encourage measures at the policy and governance level: restrain.

FUTURE ISSUES

Whereas plastics are an essential part of modern society, emerging human health effects and documented ecological impacts demand the development of smarter and safer materials for future use. Contemporary plastics and plastics components of known adverse health and ecological effects should be removed from manufacturing products, e.g., polycarbonate from food containers and DEHP from food and medical equipment, where possible. The observed lack of biodegradability of many plastics deemed safe from a toxicological perspective also demands action. Next-generation replacement polymers and plasticizers should be composed of nonpetroleum-based, carbon-neutral monomers that are nontoxic and will be degradable at a rate sufficient to prevent the ongoing accumulation of plastic debris in terrestrial and aquatic environments. Labeling of materials with longevity estimates could be a first step.

The concept of the 5 Rs, i.e., reduce, reuse, recycle, rethink, restrain, may serve as a guiding principle for consumers, industry, and government for adaptive measures addressing environmental and human health issues posed by plastics. The latter two verbs refer to the need to consider the life cycle of plastics from an earth systems engineering and management perspective (rethink) and to address systematically at the policy and governance level the unsustainable use of plastics (restrain). The need for changes in manufacturing and consumption patterns of plastics is both a public health and an ethical issue. Following the maxim *primum non nocere* (first do no harm), opportunities exist to stir the global market of plastics onto a path toward sustainability. While aiming to protect public health and environmental quality, this common-sense move could also pay large dividends in resource protection and conservation.

CONCLUSIONS

Exposures to plastics, plasticizers, and other additives to polymers are ubiquitous in modern society. Whereas these are often estimated to occur below critical threshold values, exceedances in certain susceptible populations, such as pregnant women and children, are known to occur in some instances. Of principal concern from a human health perspective are

endocrine-disrupting properties of plastic components, such as BPA and DEHP (**Figure 1**). Another issue that may drive changes in production and consumption are the undesirable effects of plastics on the environment and wildlife. The quantity of plastics produced worldwide in the first decade of this century is equivalent to the total world production in the century prior (109). Because many of today's plastics are not biodegradable, continued use at accelerating rates is unsustainable and will cause a significant burden for future generations.

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Contents

Environmental and Occupational Health

Public Health Practice

Social Environment and Behavior

Health Services

Indexes

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