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The incidence of autism has nearly doubled over the last 4-years in California. At this current rate of growth, this disease could cost the US Healthcare system $83 billion/year by 2014. Changes and deficiencies in a variety of hormone systems have been associated with this disease.

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The state of California has added DEHP to a list of reprotoxic substances that must be labelled in the state. Products sold in the state with DEHP will require labelling unless manufacturers can prove that the levels found are safe.

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Autism Costs Could Bankrupt Healthcare

Autism in California increased from 2,778 cases in 1987 to 20,377 cases in 2002, with 96% growth for the last four years alone according to a recent study.[1] At this current rate of growth, there could be 300,000 cases of Autism in California by 2014, with an associated cost of $10 billion/year in California, and $83 billion across the US. Other research indicates this same phenomenal growth is occurring around the world.[2]

"This is clearly a public health disaster. It could bankrupt our public services and education systems," said Rick Rollens, co-founder of the Mind Institute, which recently completed the Autism study.[1] "There are a lot of things to look at including endocrine disruptors. There clearly is something in our environment that is causing this. In the past, we spent far too much effort chasing genes. While that may be an important part, unfortunately there is little interest in environmental factors."

A key question is the role environmental factors play in causing changes in brain hormones associated with autism.

California is adding about 11 cases of autism a day to its treatment services, and lifetime costs of an individual with Autism are about $4 million, according to Rollens. Part of this exorbitant cost is that people with autism tend to live full lives, instead of dying off early. The ultimate tab for this lifetime of care may cost California $16 billion over the lifetime of the children that are being diagnosed with the disease this year.

But because of the length of time across which

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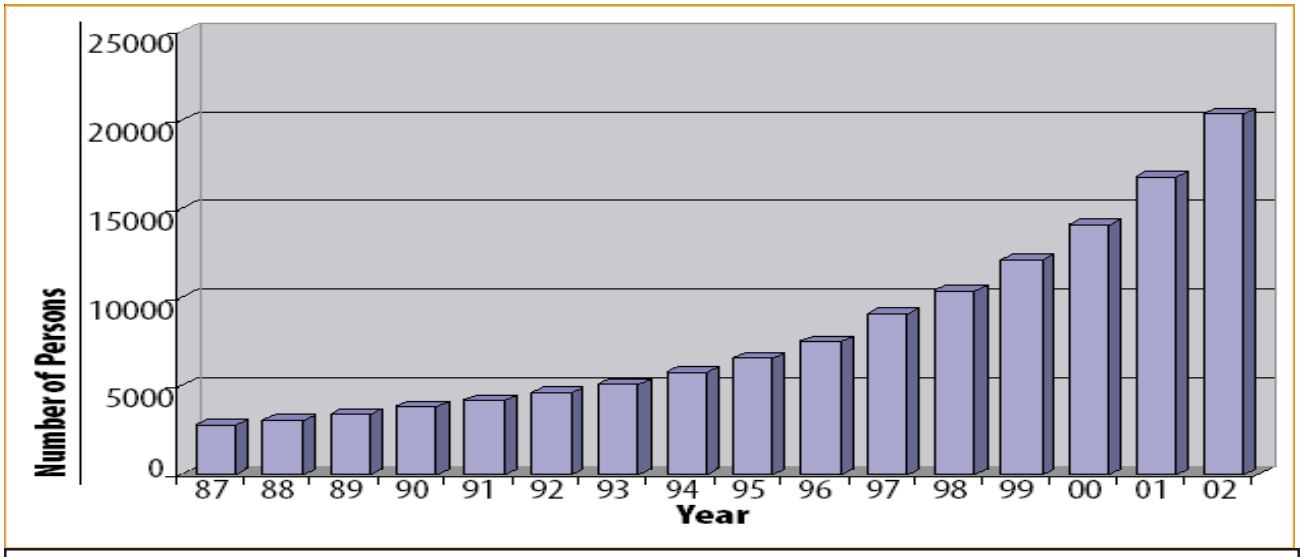

Figure 1. Annual growth in numbers of persons with Autism from December 1987 through December 2002[1]

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care dollars are stretched, the short term costs may seem less significant. For example, California only spent $1.32 billion a year on Autistic care in 2002 based on Rollens' estimated costs, while the additional long term burden was over 12 times that. The state has not had to contend with the huge bill just yet, so the full ramifications of this massive increase in autism are only likely to be felt as a growing number of these youths become dependant on government assistance.

Factors Responsible Uncertain

Whatever is causing this increase is happening universally across the state. Rollens said there is no evidence that points to major changes between different regions or between rural and urban communities. The latest report also rules out questions about the classification and detection of autism.

"This is clearly a public health disaster. It could bankrupt our public services and education systems," -- Rick Rollens, co-founder of the Mind Institute.

Dr Robert Byrd, a researcher with the UC Davis Medical Center, who has been leading this study said, "The research I did was to show that it was not falsely elevated by a variety of things like a loosening of the criteria and misclassification or whether there was an influx of people moving into the state service. A 1999 report came out that showed an increase, but did not give any explanation. In this latest report we did not find out why there is an increase, but did find out it was not just loosely created by people moving into the system. One of the things my study did was to look at the numbers and not say they are just artificially elevated due to factors that are not the real increase.

"Although we did not address the increased utilization because of increased awareness. It is possible that people are coming in because it is recognized more and people are coming into the research center more. But I don't expect that line of research to pan out. One would expect that increased awareness would change the severity of cases, so the more recent cases would be less autistic, but we did not see that."

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One theory is that autism is caused by a genetic component. But Byrd notes, "The curious part is that if genetics is causing this, how do you explain the tripling of numbers, because genes don't change that quickly. Is it caused by a genetic element or environmental interaction? A lot of people have a variety of theories. Until we know what causes it, there is a lot of speculation."

Byrd said that due to the early onset of autism, and certain changes in the head shape and brain chemistry of kids at birth who later develop autism, that the beginnings of the disease are most likely prenatal or even pre-pregnancy as opposed to after birth.

Blood samples taken at birth, which have been analyzed in more detail found that certain neuropeptides and neurotrophins were elevated in kids that later developed autism, as with kids that developed mental retardation. The neuropeptides are groups of protein particles that act at the synapses of the brain. Neurotrophins are hormones that operate on brain neural tissue.

Its not clear if these changes cause autism, predispose them towards the disease, or are simply coincidental. No one has done a study across a large group of healthy children to see if these changes exist.

One NIH study[3] found that vasoactive intestinal peptide (VIP), calcitonin gene-related peptide (CGRP), brain-derived neurotrophic factor (BDNF), neurotrophin 3 (NT3), and neurotrophin 4/5 (NT4/5) were higher in children in the autistic spectrum and in those with mental retardation without autism than in control children. In 99% of children with autism and 97% with mental retardation, levels of at least one of these substances exceeded those of all control children.

A Croatian study[4] found individuals with autism had significantly lower concentrations of cortisol and significantly higher concentrations of the pituitary hormone adrenocorticotropin (ACTH). They reported,

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"The observed hormonal changes may indicate dysfunction of the hypothalamo-pituitary-adrenal axis in individuals with autism."

Other researchers have reported success treating autism with ACTH[5] and ACTH analogs[6].

L-Carnosine, a dipeptide, has enabled statistically significant improvements in autistic children.[7] Although the mechanism of action of L-carnosine is not well understood, it may enhance neurologic function, perhaps in the enterorhinal or temporal cortex.

A review by Kidd[8] reported that a variety of factors have been associated with treating autism including: Dietary restrictions, such as removal of milk and other casein dairy products, wheat and other gluten sources, sugar, chocolate, preservatives, and food coloring; Gastrointestinal treatment for controlling Candida and other parasites, and using probiotic bacteria and nutrients to correct dysbiosis and decrease gut permeability; Detoxification of mercury and other heavy metals by DMSA/DMPS chelation; and the consumption of long-chain omega-3 fatty acids. Kidd noted that current pharmaceuticals fail to benefit the primary symptoms and can have marked adverse effects.

"There are a lot of things to look at including endocrine disruptors. There clearly is something in our environment that is causing this. In the past, we spent far too much effort chasing genes. While that may be an important part, unfortunately there is little interest in environmental factors."
Rick Rollens, Co-founder of the Mind Institute.

Oxytocin Malfunction?

Other researchers have associated malfunctions in the opioid-based oxytocin hormone system with autism. Winslow et al noted that oxytocin knockout mice fail to recognize familiar mice after repeated social encounters, though olfactory and non-social memory functions appear to be intact.[9] Green et al suggest deficits in oxytocin processing may be important in the development of autism.[10]

Insel et al.[11, 12] hypothesize that an abnormality in oxytocin or vasopressin neurotransmission may account for several features of autism. They note recent gene targeting studies that alter expression of either the peptides or their receptors in the rodent brain partially support the autism hypothesis. They recommend the need for clinical studies using gene scanning, pharmacological and neurobiological approaches.

Sher[13] suggests the level of brain opioid activity is a contributing but not the determining factor in the pathogenesis of autistic disorder and that the development of autistic disorder is related to the interaction between the endogenous opioid system and various neurotransmitter systems in the brain.

Vaccines?

One widely circulated theory is that vaccines somehow play a role in causing or bringing on autism. Byrd said he has seen some evidence that seems to point to the measles, mumps and rubella vaccine, but it does not seem to account for the massive increase in autism cases. He discounts this theory because he has not seen any evidence of a stair step increase and then leveling off in the number of cases, after the introduction of this vaccine.

Rollens believes very strongly that vaccines play a role in autism. Rather than blaming a single vaccine, or the mercury-based preservative, he has suggested that the constant increase in the number of vaccines given to children is playing a role in the increase of autism. He said, "For those that argue that if it were just the vaccines it would level off, but we have not leveled off in the number of vaccines, we have just added more and more. He noted, "I don't think any of us feel as strongly as me about vaccinations."

Byrd wants to resolve the vaccine question. He noted that even though there is pretty good evidence

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Autism On the Rise

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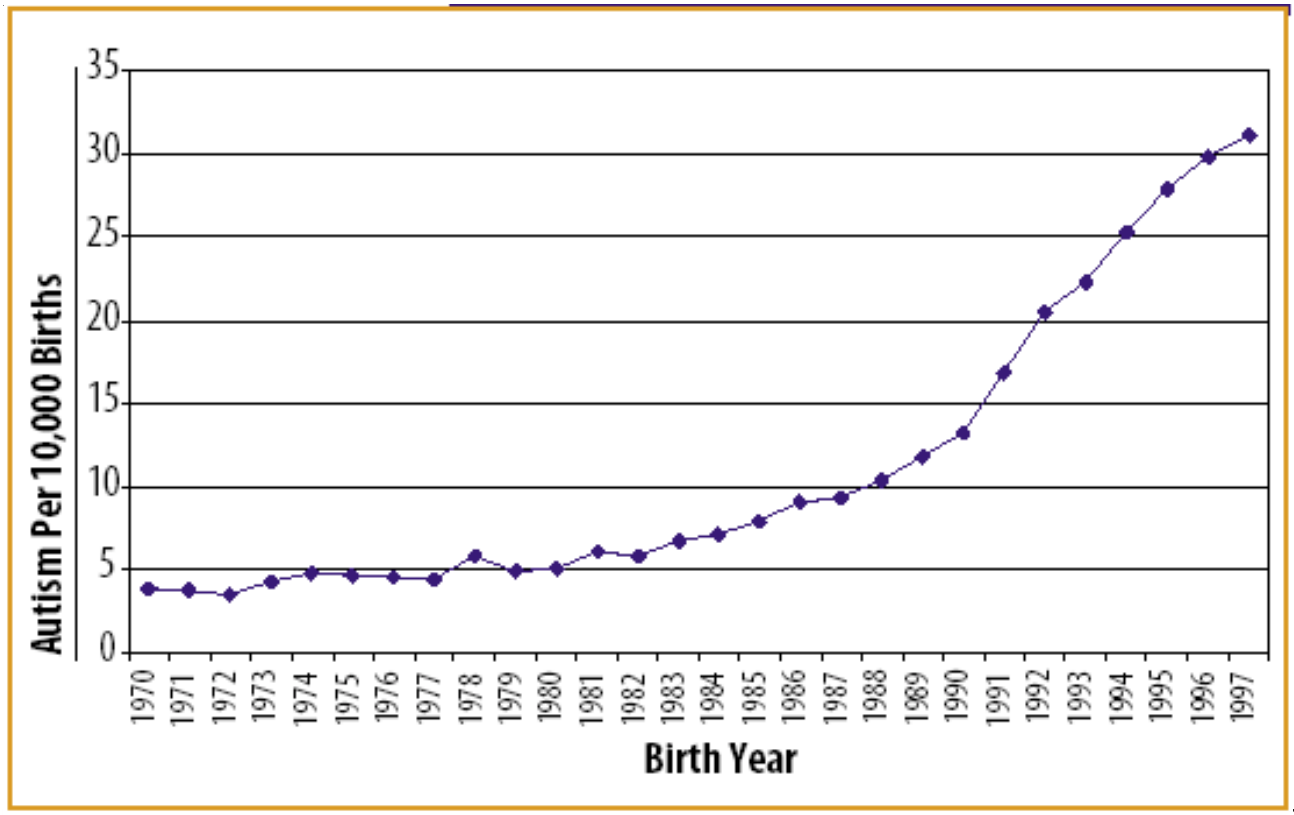

Figure 2. Uncorrected birth year prevalence rates of Autism from 1970 through 1997 from the 2002 population.

against vaccines being a cause of autism, many families firmly believe it played a role in their child developing autism He said, "It seems like we should definitely answer the question rather than leave it to debate." Byrd suggested that the best way to determine if vaccines do in fact play a role is to look at the recurrence of autism in families that do or do not vaccinate subsequent children. The rate of recurrence of autism in different children within the same family is about 1 in 20. The study would look at whether this changes with vaccinations.

Byrd said, "While there are good population studies, particularly on MMR and the thimerosal mercury containing preservative, the question still remains, and it gets in the way of moving the research about autism into the right direction and I think it is causing a level of fear that should be addressed so we can give families vaccinations without people being afraid of them."

One unanswered question is whether or not the age of the parents might play a role in causing these increases in autism. As Dr. Harry Fisch noted at the Yokohama conference last year, the rates of many diseases like Down's Syndrome and prostate cancer appear to be associated with a rise in the age of the parents at birth. Could the rising age of parents at birth play a role in these increases? However, Byrd doubts the raw data will be made publicly available as it contains detailed information on individuals and their families.

Conclusion

Outside of the emotional trauma of autism, it threatens a severe financial burden on society. The rate of autism has nearly doubled over the last decade in California, which could cost taxpayers nearly $16 billion a year in deferred care, based on Rollens' estimated costs. If these increases are representative of the growth of autism across the US, new cases of au-

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Autism On the Rise

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tism this year could cost American's $100 billion over their lives. And if the increase continues, American taxpayers could be burdened with an additional $200 billion a year in deferred care giving expenses by 2010.

If the worldwide prevalence of autism is rising as quickly as the studies in California and Georgia would suggest, it seems imperative that health agencies commit themselves to a substantial effort up front, in order to minimize the long term burdens of this epidemic. It would seem prudent to determine agents responsible for the changes in neurotrophins associated with autism.

Year	Cases	Annual costs
2002	20,000	$1,32 billion
2006	39,780	$2.625 billion
2010	77,984	$5.148 billion
2014	152,840	$10.32 billion
2018	299,580	$19.8 billion

Table 1: Projected growth of the costs of Autism in California based on recent trend and Rollen's estimated costs.

As Byrd noted, "It seems like the real work needs to be done as to figure out the causes of what autism is."

The massive rise in cases of autism would suggest an environmental factor. If this is the case, it is imperative that health agencies uncover these now, rather than settling into what could amount to a multi-trillion dollar burden in the future.

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Sidebar: Background on Autism and Mind Institute Findings

Autism is a lifelong neurological disorder that primarily strikes males. Communication and social interactions are severely impaired for persons with autism. Unable to learn from the natural environment as most children do, the child with autism generally shows little interest in the world or people around him. Although some children with autism develop normal and even advanced skills, most exhibit a wide range of behavioral problems. The treatments for autism are largely behavioral, and can take 20-40 hours per week of one on one interaction. But it is not always successful, and it is hard to tell from the beginning which groups of kids are most likely to benefit.

Concerned about the increase in the number of persons with ASD, the California Legislature and Governor in 1998 created and funded the Medical Investigation of Neurodevelopmental Disorders (M.I.N.D.) Institute at the University of California, Davis Medical Center, and funded a study looking at the growth of autism.

Specific findings of the study indicate:

1. The cumulative prevalence of autism in California increased from 7.5 per 10,000 for the sample 1983-85 birth cohort to 20.2 per 10,000 for the 1993-95 birth cohort, an increase of 269 percent. A separate study conducted by the US Center for Disease Control in Georgia found the prevalence of autism there to be 34 per 10,000. (Yeargin-Allsopp, et al, 2003).

2. Families immigrating into the state for services were not a factor affecting prevalence in California.

3. Any shift in the interpretation of diagnostic criteria could not explain the increased prevalence.

4. The regional centers had achieved high levels of diagnostic accuracy, i.e., 89 percent of the children with autism selected for the study were accurately diagnosed by regional centers. Interestingly, the study also concluded that 18 to 19 percent of persons in the study diagnosed with mental retardation and without full syndrome autism met DSM IV criteria for autism. The study supported the interpretation that the increased prevalence of autism in California is a valid phenomenon and is driven by factors beyond improved identification and diagnosis.

CA Adds DEHP to Reprotox list

California has added DEHP as a reproductive toxicant to the list of chemicals that must be labeled on products sold in the state. Companies who sell products with DEHP in them could be fined up to $2500/day per instance, unless the levels are low enough to be "safe." The California OEHHP based their decision on FDA[1] and NIOSH[2] reports. The EU has banned the use of DEHP in cosmetics and children's chew toys, and there are efforts underway to limit its use in medical devices and other products.

DEHP - di (2-ethylhexyl) phthalate - is used to add flexibility and durability to blood storage bags, hospital tubing and gloves. It is also used in vinyl flooring, coated fabrics, paper, and cosmetics.

While DEHP has been listed as a carcinogen since California's Proposition 65 was originally enacted in 1988, labeling was not necessary due to a lawsuit (Baxter Healthcare Corporation vs. Joan Denton). Baxter is a major manufacturer of medical devices such as IV tubing. Baxter's lawsuit did not contest the 1988 listing of DEHP as a carcinogen. Instead, it contested the "safe harbor number" OEHHA had adopted for DEHP. The safe harbor number identifies a level of exposure to DEHP that requires a Proposition 65 warning. Sacramento Superior Court Judge Talmadge Jones issued a ruling in October 2002 that a preponderance of the evidence indicates that the biological processes that caused cancer in laboratory mice and rats as a result of DEHP exposure do not apply to humans. Therefore, under the judge's ruling, DEHP remains on the Proposition 65 list as a carcinogen, but there is no warning requirement for it as a carcinogen.

Allan Hirsch, Deputy Director, External and Legislative Affairs with the California Office of Environmental Health Hazard Assessment said, "OEHHA has appealed the ruling, and obviously we are hopeful the ruling will be reversed on appeal."

He added, "This case has no bearing whatsoever on DEHP's listing as causing reproductive toxicity. That listing is an entirely separate process. Our decision to list DEHP for repro effects was based solely on the NIOSH and FDA documents, and had nothing to do with the lawsuit. The warning requirement for DEHP as a chemical causing reproductive toxicity will take effect in October 2004, regardless of what happens to the lawsuit. We are free to develop a safe harbor number for DEHP for repro effects, regardless of the outcome of the lawsuit. (There is no legal requirement for us to develop a safe harbor number for it, and we have not decided if or when we would do so.) In the absence of an OEHHA safe harbor number, a business sued for failing to provide a Prop 65 warning would still be free to argue in court that the exposure was too low to cause repro effects as defined by Prop 65, but the burden of proof would be on the business to demonstrate that. Again, the lawsuit only involves Prop 65 warnings of DEHP as a carcinogen, and has no bearing on the legal obligations of any business, as of Oct. 2004, to provide Prop 65 warnings regarding DEHP's repro effects."

"Our decision to list DEHP for repro effects was based solely on the NIOSH and FDA documents."
—Allan Hirsch, Deputy Director, External and Legislative Affairs with the California Office of Environmental Health Hazard Assessment

The State of California's action in listing di(2-ethylhexyl) phthalate (DEHP) as a reproductive toxicant under the provisions of Proposition 65 is not supported by the scientific evidence, according to the American Chemistry Council's Phthalate Esters Panel.

"This action is unnecessary and inappropriate on three counts," said Marian Stanley, manager of the Phthalate Esters Panel of the American Chemistry Council. "First, the premise for the ruling is flawed. The regulatory reports from the Food and Drug Administration and the National Institute for Occupational Safety and Health, on which the action is said to be based, did not set out to determine if DEHP causes reproductive toxicity in humans, nor did either report conclude that it does. Second, in over 50 years of its use, to the Panel's knowledge, there has been no reliable evidence demonstrating that DEHP has caused

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DEHP on Reprotox list

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reproductive toxicity in humans. Third, there is recent research involving animals and humans suggesting that there would be no adverse reproductive effects expected in humans, even from relatively high exposures."

Recent data collected by the Centers for Disease Control and Prevention (CDC), when converted to actual exposure levels, show the average DEHP exposure in humans is more than 30 times lower than safety levels set by the Environmental Protection Agency (EPA). Federal regulators have expressed concern that critically ill newborn males who undergo intensive, life-saving medical procedures may be exposed to levels of DEHP that exceed the conservative federal safety levels based on rodent studies. However, a recent follow-up study of a few of these children found normal reproductive development.

"The regulatory reports from the Food and Drug Administration and the National Institute for Occupational Safety and Health, on which the action is said to be based, did not set out to determine if DEHP causes reproductive toxicity in humans, nor did either report conclude that it does."
—Marian Stanley, manager of the Phthalate Esters Panel of the American Chemistry Council.

Gerald McEwen, VP of Science at the Cosmetics Toiletry and Fragrance association said, "There is very little DEHP at all and the labeling is only required if the exposure exceeds the amount that is allowed for the particular chemical. The levels that someone would be exposed to are practically nothing, because this is a plastisizer, so you would have only the minor amounts that are in there from the incomplete plasticizing of the polymers that are in the product. Most gets converted into some other form before it is applied, or immediately during the process. Bounty hunters can bring lawsuits that do not have any merit, and it is up to the company to show that their exposure does not exceed what the safe exposure is."

Others are applauding this decision. "The Office of Environmental Health Hazard Assessment (OEHHA) has made the right decision to officially list DEHP as a reproductive toxicant," said Charlotte Brody, RN, executive director of Health Care Without Harm. "Now manufacturers have a choice, they can either make products without Prop 65 reproductive toxins or other dangerous chemicals, or they can notify health care providers that their products contain DEHP and may pose reproductive hazards." "Animal studies considered relevant to humans link DEHP exposure to defects of male reproductive organs, such as the testicles," said Ted Schettler, MD, a practicing physician in Boston and science director of the Science and Environmental Health Network. "Ample scientific evidence shows that certain patients, particularly pregnant women and developing boys, should be protected from DEHP."

The Proposition 65 listing follows on the heels of warnings from the Food and Drug Administration, National Toxicology Program, and Health Canada that DEHP may cause birth defects and other reproductive harm. FDA has warned health care providers that they should protect certain vulnerable patients from DEHP and has said DEHP-free alternatives should be used for some medical treatments, particularly in Neonatal Intensive Care Units (NICUs). "Health care providers all over the country have begun to raise concerns about DEHP exposures and have initiated efforts to investigate and eliminate DEHP in their facilities," Brody said. California hospitals have been leaders in this effort. Kaiser Permanente, Miller Children's Hospital in Long Beach, Lucile Packard Children's Hospital at Stanford University, and John Muir Medical Center in Walnut Creek are phasing out PVC medical devices from NICUs.

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EU REACH Launched

The European Union has proposed a controversial chemical safety law. Industry said the law could harm the $US 618 billion chemical market, while environmental groups believe the new law does not go far enough. The bill puts new burdens on chemical companies to prove that chemicals already in use since before 1981 are safe. Industry estimates the new legislation could cost about $US 6.07 billion over the next decade. The REACH proposal is expected to be finalized in late 2005 and to be phased in over the following decade.

In a press conference, EU Environment Commissioner Margot Wallstrom said, "Today, more than 100,000 chemicals can be marketed (sold) without testing. We need a balanced approach. Modern society needs chemicals, but we want to know we can handle the risks of those chemicals."

In the conference, Wallstrom noted compromise was reached on some of the most contentious parts of the bill. She said, "I don't think it will turn the whole chemicals industry on its head... It's come down to a reasonable cost to be able to label products 'user safe.'"

Under the new legislation, chemical makers will be required to register the properties of existing chemicals in a centralized database. They have until 2016 to register approximately 30,000 chemicals currently in use. High production chemicals, or those with cancer causing, reprotoxic, or bioaccumulative effects will be required to undergo a risk assessment. Those considered the most dangerous will require authorization for their use.

Changes made to the original bill include a 2/3 reduction in the data requirements, reduced restriction on industrial usage, and the exclusion of polymers from regulation.

Q&A with RJ Witorsch on BPA Report

E/E Letter interviewed Dr. RJ Witorsch regarding some of his work on BPA in general, and also looking at the recent BPA report published in E/E 174.

E/E Letter: What are your thoughts on the recent E/E Letter BPA survey?

Witorsch: Your report appeared quite comprehensive, thorough, and objective.

Congratulations on a job well done.

E/E Letter: Considering the comparative differences between humans and rodents, is there any value to using rodents to do assays of endocrine active compounds? Is it possible with rodents, that the endpoints might not be relevant to humans, but that they could give us a sense of the relative potency of endocrine active compounds? Are there any other animal models, on which it would be feasible to assess potential human effects of endocrine active compounds? In your paper you mention baboons, but I imagine the cost of doing any significant study with them might be prohibitory. Are there other primate species that might be economical to do these kinds of assessments on?

Witorsch: These questions can be handled together. Much of what we know about endocrine physiology has come from work in rodents. Accordingly, I would be last person to state that data obtained in mice and rats are of little use for the assessment of endocrine active compounds. As a matter of fact, assays such as the rat uterotrophic assay are crucial for determining the potency of unknown compounds relative to a standard (e.g., estradiol) or definitively characterizing agonist and/or antagonist activity of ligands for hormone receptors. Furthermore, rodent models are being used to determine which agents act via alpha or beta isoforms of ER. However, there may be certain situations where species differences warrant caution in interpretation of findings. Endocrine effects during gestation is one of these situations. As I indicate in my paper, there are critical differences between humans and murines in the levels of estrogen attained, the specific estrogens being secreted, the organ relationships involved in androgen production and it's aromatization, and the hormonal control of pregnancy. These differences matter, particularly if one attempts

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Witorsch on BPA

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to interpret their findings in terms of public health issues.

On the other hand, this does not mean that murines should be excluded as a model to study fetotoxic effects. As I indicate in the paper, murines and humans are closer to one another in the early stages of pregnancy (fertilization, implantation, and placenta formation) than humans are to variety of other mammalian species. Furthermore, it is my understanding that murines have been an extremely useful model for studying the effects of such fetotoxicants as tobacco, alcohol, excess glucocorticoids or stress in-utero.

As far as I know, primates are unique among mammals with regard to the endocrine control of pregnancy (e.g., luteal-placental shift during first trimester, adrenal-placental pathway with regard to estrogen production, and levels of estrogens attained). Accordingly, in certain situations, there may be no other alternative but to use a primate (which I assume would be very expensive).

E/E Letter: If BPA does act through non-nuclear receptors, as some have suggested, would that add any weight to the relevance of rodent models to human risk assessment?

Witorsch: BPA is not unique with regard to possibly acting through non-nuclear receptors. It has also been suggested that estradiol and SERMs act through membrane bound receptor mechanisms (e.g., electrolyte channels) under certain conditions. Therefore, I don't think a BPA non-nuclear receptor mechanism would make it particularly unique as an endocrine disruptor or have any impact with regard to the human - rodent dichotomy.

E/E Letter What is your assessment of the relevance of some of the in-vitro studies suggesting effects such as

A. Interference with normal gene expression @ .23 ppb (Quesada, 2002);

B. Increases a process in prostate cancer cells that renders them less responsive to the standard hormone treatment used to force prostatic adenocarcinomas into remission @ .23 ppb (Wetherill, 2002)

C. Breast cancer promotional effects @ 2 ppb (Krishnan, 1993)

D. Affects thyroid transcription @ .0069 ppb (.03 nM)(Moriyama, 2001)

Witorsch: In general, I think in vitro studies have value but should always be viewed with caution when it comes to real-world situations (such as whole animal physiology and toxicology). As a matter of fact, most of my work over the last decade (on glucocorticoid-prolactin interactions, apoptosis, and glucocorticoid-mediated endocrine disruption) has employed cultured cells. In vitro studies have value in providing insights with regard to such phenomena as hormone and xenobiotic interactions with endocrine receptors, post-receptor signaling, and discerning sub-threshold (e.g., "hormetic") effects. However, cell culture is different from the whole animal situation and, therefore, should be interpreted with caution. Cultured cells are often derived from cancers or are genetically modified by transfection, do not experience hemodynamic changes (e.g., blood flow or pressure changes), are incubated in chemically defined medium as opposed to real blood, and lack normal levels of plasma proteins that may restrict xenobiotics interaction with the cell.

Therefore, they may be of value for identifying potential toxicants or endocrine disruptors but I think such studies may be of limited value in terms of risk assessment, particularly for low dose exposures.

E/E Letter: Any final comments?

Witorsch: My major concerns about the low dose in utero effect of BPA are the lack of consistency in it's demonstration from one laboratory to the next and, as I attempted to elaborate in my paper, it's relevance to human pregnancy. If the putative effects of BPA in mice are real, they are very modest (e.g., 30% increase in prostatic weight), are usually within the normal range and, thus, of dubious clinical significance. To imply that a slight increase in prostatic weight or body weight associated with in utero BPA exposure is evidence that the substance is a risk factor for prostate cancer or obesity is in my opinion premature and scientifically irresponsible.

Greenpeace Phthalate Campaign

Greenpeace UK has launched an anti-chemicals campaign in Europe, alleging that chemicals such as Disney pajamas, perfumes, shampoos, and plastic goods contain allegedly "dangerous chemicals" such as phthalates and nonylphenol. In a press release, the group noted, "Shockingly, Disney-branded pajamas available at The Disney Store and other big retailers were amongst the worst offenders. We were astounded to learn that a brand aimed at children could sell products which could damage their health."

The pajamas affected are:

Buzz Lightyear pajamas for boys;

Piglet pajamas;

Tigger pajamas with caption '100% Cheeky'

The group demanded that the Disney company "recall and withdraw from sale" all the affected pajamas, along with "any product containing persistent, bioaccumulative or toxic chemicals".

As a result of the campaign, some Disney stores, along with Debenhams and Mothercare, who have also been stocking Disney pajamas, have now stopped selling the disputed garments. However, Asda and Woolworths have not yet withdrawn them

Marian Stanley manager of the Phthalate Esters Panel of the American Chemistry Council, noted about the Greenpeace campaign, "The allegations about phthalates made by the Greenpeace United Kingdom campaign are not consistent with the findings of U.S. and European regulatory bodies. The European Union's final risk assessment on DINP found no concern about the use of DINP in any current application, including such sensitive end uses as children's items. In early 2003, the U.S. Consumer Product Safety Commission (CPSC) completed a very extensive study on the safety of DINP and vinyl in children's toys and other items for children. The CPSC study concluded that there is "no demonstrated health risk " to children from DINP-containing vinyl items – not even to infants who mouth toys softened with DINP. The CPSC also found that dermal penetration of DINP from vinyl items is minimal and would not pose a health risk at expected exposure levels. Suggesting that phthalates used in the decorative logo on Winnie the Pooh pajamas pose a health risk to children from phthalates is just simply not justified in view of the conclusions of these respected international regulatory authorities."

Reference: http://www.greenpeace.org.uk/MultimediaFiles/Live/FullReport/6043.pdf

Jim Solyst on Precautionary Principle

A recent issue of the Rachel News #178 headlined "Corporate Campaign Against Precaution" contained a rather extensive essay concerning the use of the precautionary principle (or lack there of). The newsletter alleges that the precautionary principle is now under sustained corporate attack through an effort to attempt to align corporate and environmental goals. In particular it criticizes mediation attempts by the Keystone Group between corporations and environmental groups like the Environmental Working Group, Environmental Defense, the World Wildlife Fund (WWF), and Defenders of Wildlife.

In response to some of these concerns, Jim Solyst with the American Chemistry Council, noted, "The major obstacle to discussing precaution is the lack of a common definition, there are at least 19 different definitions of the precautionary approach or precautionary principle. For example, the ACC supports the language included in Principle 19 of the Rio Declaration and the J'Burg WSSD language, which essentially re states the Rio language. But even the Rio and WSSD language does not constitute a definition.

The attached article does not offer a definition, my sense is that the authors would support the Wingsrpead definition, which ACC believes is extreme. By the way, I am one of the "corporate speakers" who spoke "Recently in California." I would guess that items 1-4 are taken from my presentation, obviously the author has taken some liberties with my remarks but essentially our view is that the current U.S. regulatory and judicial system is precautionary. You should take a look at Chapter 3 Emerging Risks (page 51) of the 2003 OMB Report to Congress on the Costs and Benefits of Regulations. This chapter focuses on precaution. It is on the OMB OIRA web site."

EPA Decides Against Regulating Dioxin in Sewage

While considerable research has highlighted concerns about dioxin such as carcinogenicity and reproductive effects, the EPA has decided against regulating its use in sewage sludge applied as fertilizer on US crops. Apparently, while the EPA has been making stringent efforts to reduce its emission into the air, a similar concern does not exist with regards to food crops, or the effects of dioxin laced sludges on the environment. Dioxin is produced by the combustion of chlorine containing chemicals including plastics, salts, and trees in the forest.

After studying the issue for five years, the EPA said in a statement it determined "that dioxins from this source do not pose a significant risk to human health or the environment." It noted that the highest risk of this policy would be to farmers who consume their own crops and meat products throughout their lifetime.

An EPA analysis claims that only 0.003 new case of cancer per farm family could be expected each year, or only 0.22 new case per family over a span of 70 years. In a press release, it stated, "The risk to people in the general population of new cancer cases resulting from sewage sludge containing dioxin is even smaller due to lower exposures to dioxin in land-applied sewage sludge than the highly exposed farm family which EPA modeled."

Furthermore, the agency argues that regulation is unnecessary since its data has suggested that the dioxin levels in treated sewage sludge are on the decline. A 2001 survey found reduced dioxin levels in sewage sludge since its last survey in 1988.

GMO Leakage Not ED Concern – yet

Considerable debate has emerged over the regulation of genetically engineered crops used for medical production, particularly owing to concerns that these organisms could leak into the environment resulting in the widespread contaminations of the medicines into the wild. The USDA has logged numerous complaints about companies' inadequate safeguards to keep some of these GMOs out of the environment.

A few years ago Epicyte launched a research project to develop a plant capable of making a male birth-control pill. While the research was fascinating, it raised considerable concerns about the possibility of uncontrolled GMO contamination sterilizing men by accident. However, Debbie Robertson, an Epicyte spokeswoman, noted, "The production of an antibody against sperm in plants was a research project implemented by Epicyte several years ago. The project was discontinued."

Schlumpf on Sunscreens

Dr. Margaret Schlumpf has done a variety of research suggesting that sunscreens could have estrogenic and androgenic effects. E/E Letter asked her about the significance of some of these findings and her ongoing research. Her recent report "UV filters with antagonistic action at androgen receptors in the MDA-kb2 cell transcriptional- activation assay has suggested that some of the chemicals used in sunscreens could have anti-androgenic effects. Her previous work on "In Vitro and in Vivo Estrogenicity of UV Screens." has suggested that some of the chemicals used in sunscreens could have estrogenic effects.

E/E Letter: How do the levels of concentration you measured, compare to the type of dose a person might receive from wearing UV-filtered sunscreens?

Schlumpf: We are using low doses in order assess developmental toxicity (= chronic studies) of UV filters. The current LOAEL of 4MBC is 7mg/kg.bw/d

ADI is LOAEL/ UF (uncertainty factors) = interspecies 10x; intraspecies 10x; and use of LOAEL instead of NOAEL 10x (USEPA, UNEP/IPCS) ADI = 7mg/kg/ 1000 = 0.007mg/kg/d 4MBC

Calculation of margin of safety(MOS) = NOAEL/systemic exposure dose

Systemic exposure dose is given (industry) : 0.23mg/kg for 4-MBC

So Margin of safety is: NOAEL / SED = 7mg/

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0.23 = 30 (using LOAEL instead of NOAEL as we do not have LOAEL yet, LOAEL would of course be lower)

Margin of safety is recommended to be > 100

E/E Letter: Were any of the levels you indicated effects within the range of exposure that someone might receive from wearing sunscreen products?

Schlumpf: We do not have exact data on human exposure. They should be done

E/E Letter: Are you currently involved in, or do you know others involved in looking at chronic exposure levels, that might be in line with the dose a person might receive from wearing sunscreens?

Schlumpf: We are in the European 5th Framework CREDO/EURISKED Cluster on hormone active chemicals. There the substances are studied by additional groups.

E/E Letter: Are you aware of any research looking at the fate of these chemicals, once they get into the blood stream? In particular, do any of these chemicals make it past the placenta into the developing uterus? Also how quickly do these chemicals break down once inside a body, or do they bioaccumulate, particularly in fatty tissue or breast milk?

Schlumpf: Some of them have been analyzed in human milk.

Reference: Hany J. and Nagel R. 1997 Nachweis von Uv Filtersubstanzen in Muttermilch. Deutsche Lebensmittel Rundschau 91:341 - 345

E/E Letter: What kind of sunscreens do you wear, or would recommend?

Schlumpf: I am using sunscreens with TiO and ZnO (pigments).

Reference:

Risheng Ma, Bea Cotton, Walter Lichtensteiger, and Margret Schlumpf. UV Filters with Antagonistic Action at Androgen Receptors in the MDA-kb2 Cell Transcriptional-Activation Assay

Toxicol. Sci. 2003 74: 43-50.

http://toxsci.oupjournals.org/cgi/content/abstract/74/1/43?etoc

Word of Mouse

http://www.epa.gov/superfund/programs/lead/products.htm#guidance
Superfund Lead-Contaminated Residential Sites Handbook (August 2003)
Description: This Handbook provides comprehensive reference for project managers addressing lead-contaminated residential sites. The handbook lays out only the minimum considerations and is intended to promote national consistency in characterizing and cleaning up lead-contaminated residential sites. Contents of the handbook include various aspects of the remediation process, from initial research on the nature and extent of site contamination, through cleanup level selection, prevention of recontamination, community involvement and health education programs. This Handbook is not policy or guidance, and users are encouraged to refer to appropriate agency guidance and/or policy.

http://www.bequalm.org/about.htm
The Biological Effects Quality Assurance in Monitoring Programmes (BEQUALM) provides up to date information on all aspects of BEQUALM, from its beginnings as an EU funded research program through development of the self-funded scheme to the launch of the scheme with the QA/QC work programs for the coming year and beyond. It is designed for individuals and organizations involved in statutory monitoring for biological effects in the marine environment and regulatory laboratories wishing to obtain external QA/QC for the techniques used.

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http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=22436
The National Children's Study (NCS): The Impact Of Environment On Children's Health And Development
The National Children's Study is a longitudinal cohort study designed to "investigate basic mechanisms of developmental disorders and environmental factors, both risk and protective, that influence health and developmental processes." The National Children's Study is an interagency effort sponsored by the Department of Health and Human Services (DHHS) and EPA. The National Institute of Child Health and Human Development (NICHD) is the lead organization. The National Institute of Environmental Health Sciences (NICHD), the Centers for Disease Control and Prevention (CDC), and EPA are working jointly with NICHD to plan and conduct the study.

E/E Lit Scan

BPA removal

Yoon Y, Westerhoff P, Snyder SA, Esparza M. HPLC-fluorescence detection and adsorption of bisphenol A, 17beta-estradiol, and 17alpha-ethynyl estradiol on powdered activated carbon. Water Res. 2003 Aug;37(14):3530-7.

The adsorption of three estrogenic compounds (bisphenol A (BPA), 17beta-estradiol (E2), and 17alpha-ethynyl estradiol (EE2)) on several powdered activated carbons (PAC) was investigated. PAC screening studies (six PAC brands) indicated all three compounds were removed by PAC, but the percentage removal ranged from 31% to >99% based upon PAC type/dosage and presence/absence of natural organic matter. The order of removal was highest for E2, followed by EE2 and BPA. This study confirms that PAC treatment is feasible for >99% removal of three estrogenic compounds from raw drinking waters that may be at risk for containing such compounds, at least at initial concentration of 500 ng/l and higher.

Hu JY, Yuan T, Ong SL, Song LF, Ng WJ. Identification and quantification of bisphenol A by gas chromatography and mass spectrometry in a lab-scale dual membrane system. J Environ Monit. 2003 Feb;5(1):141-4.

In this study, a lab-scale microfiltration (MF) and reverse osmosis (RO) based water reclamation system was set up to monitor and evaluate the removal of bisphenol A (BPA). A satisfactory removal of BPA was readily obtained by RO and BPA was abated to an undetectable level in the product water. The results of this study demonstrated that membrane technology could be effectively used for BPA removal.

BPA and NPE Anti-androgenic Effects:

See, HJ, S Chattopadhyay, E-Y Gong, RS Ahn, and K Lee. 2003. Antiandrogenic Effects of Bisphenol A and Nonylphenol on the Function of Androgen Receptor. Toxicological Sciences. 75(September):40-46. (Online June 12, 2003, 10.1093/toxsci/kfg150.)

http://toxsci.oupjournals.org/cgi/content/abstract/75/1/40

The researchers found that BPA and nonylphenol adversely effect the androgen receptor by blocking androgen binding, interfering with the movement of an androgen receptor to the cell nucleus, and slowing down genetic communication, using an invitro yeast assay system. Androgen receptor binding was inhibited by 30% at 5 nanomoles NP and by 40% at 50 nanomoles BPA.