

#### **EXECUTIVE SUMMARY**

In today's society people are choosing to have fewer children, and delaying having children at all into later, less fertile years. These two factors have driven fertility rates below replacement level in most of the world, but a crucial third factor gets little attention and is having a profound impact on fertility: toxicity. The economic and social ramifications will be severe.

# CHEMICAL TOXICITY AND THE BABY BUST

Unexpected threats to human fertility and, hence, chemical companies

Jeremy Grantham | February 2020

### "SUDDENLY, I'M NOT HALF THE MAN I USED TO BE."

Paul McCartney

A profound and largely unexpected phenomenon is occurring: we are choosing to have fewer children. The most significant drivers of this choice appear to be higher income and better education, especially for women. At the same time, we are choosing to postpone these fewer births into our later, less fertile years. Because of these two factors, fertility rates are below replacement level almost everywhere in the developed world and China. This development, despite its economic and social importance, is not yet receiving as much attention as it deserves, but now there is a new third factor that gets almost none: toxicity.

Human "fecundity" (the number of children you are <u>able</u> to have) is being affected by endocrine-disrupting chemicals, which interfere with hormones. This interference is growing at such a rapid rate that if left alone it is likely to leave us sterile in a few decades with only the rich able to easily afford the healthy lifestyles and the exotic medical help required to have babies.

One of the most measurable and most nerve-racking results of increased chemical damage is our very rapid decline in sperm quality and concentration, which appears to have fallen to one-third of its probable pre-industrial level. If we do not ban whole classes of chemicals in the next 10 years, we will face a crash in the number of new births. The effects of this will be felt to very different degrees by country: those countries that do not act will quickly fall behind in both births and general health. There are in fact indications that health and longevity in the U.S. are already being affected by high levels of toxicity. It is important both for society and the economy that this new information be correctly and quickly processed and that the back-up medical data, which is thin in parts, be supported by new and larger studies. Time is not on our side.

[For the immediate present I do feel a moral imperative to urge anyone pregnant to eat nothing but organic fruit and vegetables for the duration and men the same for six months prior. For more about this, please see the Appendix.]

### The Threat to all Life: from Insects to Humans

Our attention was drawn to this issue of rising human infertility via the dramatic loss of flying insects that has been registered in the last few years; a loss of up to 75% of the original populations of the pre-WWII era. A toxic stew of chemicals in the air, water, and soil is simply making our environment hostile to insect life. Almost all entomologists believe losses at this scale will have "catastrophic" consequences for the environment

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and ultimately for us. This can be seen as a second derivative chemical threat through insects to us. But now it appears we are vulnerable to a first derivative effect: the chemical stew is creating a world that is toxic not just to flying insects but to humans also, and very probably through cascading effects to a great majority of life forms.

# The Three Reasons for Reduced Fertility: Choice, Deferment, and now Toxicity

Given our current preferred lifestyles – at least given current economic conditions and social norms – families almost everywhere in the developed world (and in most developing countries also) are choosing to have smaller families. This effect – choice – caused by a variety of reasons that differ across countries, <u>is clearly the biggest driver</u> of lower birth rates.

In second place as a cause of reduced fertility is the now equally widespread tendency for women to be older when they have their first child. Since the natural fertility of women drops steadily with age and at a steadily accelerating rate after their midtwenties (and this applies also to men, although at a slower rate) – it is not surprising that this too would reduce the birthrate. In addition, the quality of both eggs and sperm falls with age so that the percentage of perfectly healthy babies also declines.

There are several recent books highlighting these two effects. One such book selling well is <a href="Empty Planet: The Shock of Global Population Decline">Empty Planet: The Shock of Global Population Decline</a>. Published in 2019, it outlines in great detail the very many reasons for the decline in birth rates yet does not even mention toxicity, so off the radar is this topic. The only buzz today, in fact, is in the world of well-educated 25- to 40-year-old women, between whom a growing number of apps on fertility-related topics, including exposure in everyday products to toxic chemicals, are now frequently exchanged.

But now toxicity intrudes as a third factor, and one that interacts particularly with the deferred age of pregnancy. A 16-year-old Nigerian girl (in Nigeria women typically start families when older than 16 but far younger than us) today has modestly more trouble becoming pregnant than 40 years ago, but she has the time to adjust and she can still produce the 5 children that is the current Nigerian average, despite toxicity and a falling sperm count. (Nigeria is one of the few developing countries for which we have good data; China is another. Both show rapid declines in sperm concentration and quality!)

In comparison to the Nigerian example a 36-year-old in France or the U.S. has a much greater problem becoming pregnant than 40 years ago and <u>on average</u> this group will have far fewer children than they would like. It is highly likely (although not yet completely nailed down) that the intersection of these two problems, toxicity and postponement, compounds the negative consequences; that is to say, that the total effect is likely substantially larger than the sum of the two separate effects.

### Recent Surprises in Fertility

The net effect of choice and postponement combined with the recent decade of "help" from toxicity has been an unexpected and accelerating decline in delivered fertility in developed countries, as well as the critically important China and India, with new annual cohorts of babies already declining in absolute numbers, not just growth rates.

The particular surprises for 2019 have been: 1) in Japan, whose 864,000 births were fewer than every year when its records began in 1899, when the population was about

40% of today's; 2) in the U.S., where the baby cohort was the absolute least for 32 years and the fertility rate an all-time low of 1.73 children per woman; 3) in China, whose baby cohort dropped to 14.6 million, the lowest in 70 years (ex the 1961 famine) and whose fertility rate – if they don't change the data – will be well below 1.6 children per woman; and 4) South Korea, where, shockingly, the fertility rate fell below 1.0! Probably for the first time anywhere in peacetime since the Bubonic Plague. Not a single developed country other than Israel (3.1 children per woman) is above the 2.1 replacement level, with some such as Italy at 1.3 and South Korea already reaching levels that could threaten economic and social stability due to unexpectedly low economic growth rates and much-increased retirement fund deficits.

## The Basic Data: the Decline in Sperm Concentration from 1973-2011

The definitive meta-study on the topic of decline in sperm count, by Levine, Swan et al.,<sup>2</sup> concluded (from the largest and most rigorous studies selected from over 7,500 abstracts) that sperm concentration in the developed world had fallen from 99 units<sup>3</sup> in 1973<sup>4</sup> to 47 in 2011. This is a compound rate of decline of 1.9% a year, a rate sure to threaten the viability of our species unless action is taken.

Prior to this paper there had been concerns about falling sperm counts for more than 40 years, but the various studies had individually been considered too local or too small and even the earlier meta-studies had been found unconvincing by a critical mass of influential academics. This study, though, removed almost all doubts, to a degree unusual in scientific circles.

Immediately after publication, the paper received considerable publicity in the press and had notable write-ups in the *Atlantic Monthly, Newsweek, GQ* (which is particularly good – a link is provided in the Appendix), and many other sources. Strangely, though, this publicity seemed to make little or no lasting impression for such an important and, we might say, personal topic. It seems as if we as a society are reluctant to process this very disturbing data. My financial audiences for example – The Financial Analysts Societies of New York and Boston (separately) – showed absolutely no awareness of toxicity problems. It feels as though I have woken up in 2050 with global average temperatures up almost 2° Celsius and no one has noticed that the climate has changed for the worse.

Exhibit 1 shows the key findings from Levine et al. together with my own extrapolations from this work. The type of statistical projection that my extensions to the data represent is routine in finance, where we are not trying to meet the rigorous and conservative requirements of a peer-reviewed paper but are trying to get the best estimate of an uncertain future. First, I took the data back to 1950 when the explosion of chemical use began. This was the age of ubiquitous DDT and the other very long-lived chemicals that gave us "Silent Spring." These were endocrine (hormonal) disruptors, already interfering with the fertility of humans and many other animals. I assumed a possibly very conservative compound rate of loss of 0.8% a year before 1973, compared to the 1.9% found in Levine et al. This took the number for 1945 to 120 units; a number that is roughly consistent with the very few studies of sperm count from that time. Also, pre-2000 studies from Finland, one of the healthiest countries in the world and therefore a good proxy for the pre-chemical era, show sperm concentrations of well over 120.

2 Levine et al. (2017). Temporal trends in sperm count: a systematic review and meta-regression analysis. *Human Reproduction Update*, Volume 23, Issue 6, November-December 2017, 646–659.

Millions of sperm per cubic milliliter of semen.

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There were not enough studies pre-1973 for academic purposes.

ourposes.

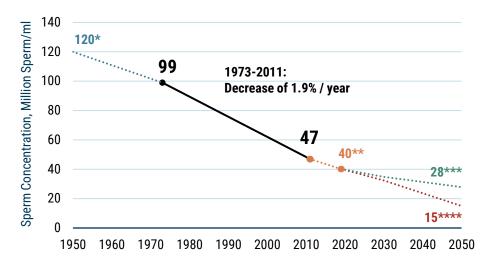
"Silent Spring," published in 1962 by Rachel Carlson, stimulated a surge of environmental concerns and governmental actions against toxic chemicals.

The more precise assumption was starting at 0.2% in 1950 and rising to 1.5% by 1972, averaging 0.8% a year.

Nouminen et al. (1993). Semen quality of Finnish men. The BMJ, Volume 306, June 1993, 1579.
Vierula et al. (1996). High and unchanged sperm counts of Finnish men. International Journal of Andrology, 19, Feb 1996, 11-17.

#### EXHIBIT 1: SPERM CONCENTRATION IN THE WESTERN WORLD

Actual Data For 1973-2011; Projected Backwards And Forwards



Source: Hagai Levine, Niels Jørgensen, Shanna Swan, et al. (2017). Temporal trends in sperm concentration: a systematic review and meta-analysis. Human Reproduction Update, 23(6), 646-659

Second, I extrapolated the observed 1.9% a year drop from 1973 to 2011 out through 2019. Bearing in mind a public comment by Levine that the rate of decline of 1.9% a year appeared to be "if anything" accelerating, this rate of extrapolation could also be deemed to be conservative. This takes the sperm concentration to 40 this year, or one-third of the "original!" I strongly suspect that truly pristine, pre-chemical environments would reveal a base rate higher than 120. Perhaps a study done in some corner of New Guinea or some isolated Pacific Island might make the point. (Though finding research volunteers may be difficult!)

### Sperm Concentration and Consequences for Fecundity

Discussion<sup>8</sup> with Swan and others suggests that we homo sapiens are so overengineered that the reduction in sperm concentration from pre-chemical original levels of 120 or more to about 50 in 2010 left our effective fertility rate substantially unaffected. We had been given a biological pass as it were: with the normal distribution based around 50, only a small percentage of the public, around 5%, needed medical help in getting pregnant due to lack of sperm count. But in just the last 10 years, as we have dropped from 50 to 40, we now see up to 20% of young couples having trouble with becoming pregnant to the point where medical help or advice is needed. By 30 units, which at current rates of decline of 1.9% would be reached in a mere 15 years, it seems that the median couple will need help. And by 20 units, which at 1.9%, without allowance for any possible acceleration, would be reached in only 37 years, only 15% or 20% of couples will not need help. This decline is nearly certain to continue until action is taken to ban all or at least most of the chemicals that reduce our fertility.

<sup>\*1950-1973:</sup> Assuming decrease of 0.8% / year

<sup>\*\*2011-2019:</sup> Assuming continued decrease of 1.9% / year continues

<sup>\*\*\*2019-2050:</sup> Assuming 'improvement' to 0.8% decline / year

<sup>\*\*\*\*2019-2050:</sup> Assuming continued 1.9% / year

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It is a strange choice that we in America should put a lower priority on our sperm count and our fertility than on corporate profits, but it appears to be the one we are making!

### Importance of Chemical Damage in Utero

Reading between the lines as a well-informed amateur, it seems that half the chemical damage a person born today would receive, in a lifetime lived under current conditions, is done in 9 months in utero and the other half by a thousand small cuts over the next 80 years of life. (Some academics say that if focused only on fertility this ratio still understates the percentage of damage done in utero.) A developing fetus seems uniquely vulnerable to chemicals (and particulate matter<sup>9</sup>) at dose levels much smaller than had previously been thought dangerous.

### The Problems of Measuring and Controlling Chemical Damage

Asking the question as to precisely which chemicals cause the reduction in fertility in general and the sperm count in particular reveals some extreme problems. We have created a toxic stew of very many dangerous chemicals. None of them have ever been tested by the EPA together with other chemicals, although we know from academic work that in combination their danger levels can rise very materially. A great majority of chemicals have in fact never been tested at all, even on their own. (Existing testing facilities can cover about 100 chemicals a year out of a current universe of over 140,000 globally<sup>10</sup> with an annual increase of up to 2,000!)<sup>11</sup> Further, banned chemicals can be replaced – and often are – by very similar chemicals that avoid the ban but, by being very close cousins, are highly probably also toxic. Further compounding this issue in the U.S. is that the benefit of doubt is given to the intellectual capital of the major chemical companies. In the U.S. we must prove that a particular chemical in the stew causes this or that precise outcome, a hurdle so high that left unchanged we would be sterile before it could be routinely cleared. The best evidence we can usually hope for currently in the U.S. is strong circumstantial evidence – very strong correlation between chemical use and bad outcomes.

In contrast, the E.U. takes the position that once scientists have raised a strong doubt about the safety of a chemical, or group of chemicals, then they, the chemical producers, should prove their innocence. It is a strange choice that we in America should put a lower priority on our sperm count and our fertility than on corporate profits, but it appears to be the one we are making! Compounding this problem today we live under a Presidency where public protection receives a rapidly decreasing priority and environmental regulations are being removed, even though we in the U.S. start from an already low base where many chemicals that are banned in Europe are ruled as safe here. Cosmetics, for example, which contain up to 10,000 chemicals in the U.S. and are substantially unregulated, have a particularly dangerous number of endocrine disruptors. Yet, only a handful of chemicals used in cosmetics have ever been banned here compared to over 1,300 banned in Europe and 500 or so banned in Canada. Similarly, neonicotinoids – the most used insecticides, which have been proven lethal to flying insects in general and honey bees in particular, and are also very likely to be dangerous in extremely small doses in utero - have largely been banned in the E.U. but left untouched in the U.S.

### Damage to Fecundity from Pesticides, Cosmetics, and Phthalates

Two small but effective studies from Harvard and Mass General in 2015 and 2017 showed that for women the levels of pesticides on fruits and vegetables were highly correlated with reduced live births – a 40% reduction from top quartile to bottom. Men

Zhang et al. (2019). Air pollution-induced missed abortion risk for pregnancies. *Nature Sustainability*, 2, 1011-1017. [A very recent study of the effects of pollution in China, with a sample size of over 250,000 women, concluded that small particulate matter, of the type that comes from burning coal and diesel oil, had surprisingly severely affected babies in utero and caused a substantial increase in silent or early stage miscarriages. It is likely that much increased general mortality from particulate matter will be reported in the next year or two.]

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European Chemicals Agency.

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U.S. Department of Health.

who consumed fruits and vegetables with lower levels of pesticides had double the sperm count as men consuming food with higher levels of toxicity! Larger confirmatory studies are badly needed, but it turns out that research funding in this critical field is curiously lacking. (A summary of these two studies can be found in Part 2 of the Appendix.)

Reading between the lines, these and other results indicate a strong possibility that the aggressive, active chemicals in pesticides, designed as they are to kill, are likely to be a large fraction of the chemical threat during pregnancy. Active chemicals in shampoos and soaps, face creams including sunscreen, and fragrances anywhere in any product seem likely to be another substantial percentage of the threat to pregnant women as do the ubiquitous class of chemicals known as phthalates. These are used in most plastics and are also common in cosmetics, ubiquity that is nearly impossible to avoid even for a day. Phthalates are proven endocrine disruptors and are therefore damaging to healthy reproduction. (One recent study<sup>12</sup> on the topic of phthalates found that they are so universally distributed that almost all study subjects tested positive for six or seven or more of the nine types of phthalates!)

The data on damage to sperm count quality and quantity is the most comprehensively measured of all fertility inputs. But the damage to fecundity is complex and broadbased and goes far beyond reduced sperm count. This is reflected, for example, in the increase in the rate of miscarriages at over 1% a year<sup>13</sup> from 1970 to 2000, a rate that appears to have continued through to the present. It is also reflected in the reduced number of live births caused by ingestion of pesticides as previously mentioned.

### Transgenerational Effects Lead to Compounding Damage

We now know that children born to chemically exposed mothers and fathers have chromosome damage that will often be passed on to their children in turn and, possibly, their grandchildren, a transgenerational effect not even considered possible 30 years ago. Thus, as these children with acquired chromosome damage go through their first 30 years accumulating their own incremental damage, this should in turn worsen the outcomes for their children. That is to say damage should be compounding, not settling down to a stable level reflecting a stable level of chemical toxicity. And that is exactly what Levine and Swan found. From 1973 to 2011, the loss of sperm count was indeed compounding at 1.9% a year with some indications that the rate of loss might even be accelerating. It was clearly faster in the 20 years after 1995 than it had been in the prior 20 years.

The damaged children, as the back-up data shows, are not just affected in their reduced fertility. The male children are on average less male in almost every way than in the past, and both male and female children are less robust going forward: they are more likely to have heart disease, cancer, and other afflictions, especially autoimmune problems. This damage is carried through their entire lives, ensuring that on average their life expectancies have also been reduced. And worst of all, many of these increased vulnerabilities are in turn passed down to their children. Progress is being made against the great majority of medical conditions but Exhibits 2 and 3 show some of the medical problems that are increasing – some very rapidly. Most of them are very likely to be related to increased chemical exposure that, along with other damage, has compromised immune systems. But, horrific as some of this damage from chemicals is, damage to fecundity is the fastest moving and most consequential effect of toxicity. If allowed to continue – which today looks likely – it will result not only in a rapidly declining birth rate, which may be a mixed blessing for considerations such as climate damage and resource limitations, but will also lower health quality in general and reduce the life expectancy of whole populations, which will be an unmixed curse.

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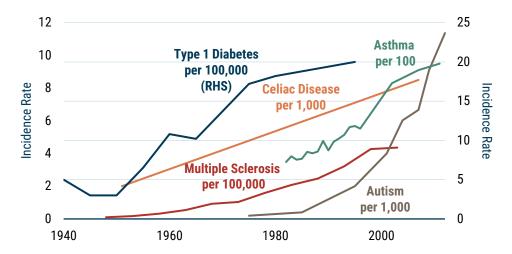
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Meeker et al. (2009). Phthalates and other additives in plastics: human exposure and associated health outcomes. Philosophical transactions of the Royal Society of London. Series B, Biological sciences, 364(1526), 2097–2113.

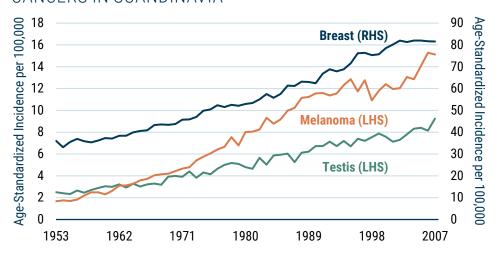
Lang et al. (2012). Trends in self-reported spontaneous abortions: 1970-2000. *Demography*, Aug 2012; 49(3): 989-1009.

EXHIBIT 2: INCIDENCE OF AUTOIMMUNE DISORDERS IN WESTERN WORLD



Source: Boström et al. 2012, Rubio-Tapia et al. 2009, Autism Speaks, National Center for Health Statistics, Gale 2002

# EXHIBIT 3: AGE-STANDARDIZED INCIDENCE RATE OF CANCERS IN SCANDINAVIA\*



As of December 2007 | Source: World Health Organization International Agency for Research on Cancer \*Average of Denmark, Finland, and Norway. (Countries chosen for having longest available data.)

### Country-Centric Nature of Fecundity-Related Toxicity

Although there is some toxicity carried over national borders by wind and water, this issue is very largely a country by country matter and there is, unlike with the climate crisis, no free rider effect: only those countries that respond by limiting toxicity will benefit. If Finland, say, bans all potentially fertility-affecting chemicals in the next 20 years it will get a visible, nearly immediate, improvement in health and life expectancy as well as fertility; if the U.S. government, by contrast, sides with the manufacturers of toxic chemicals, it will not. If the U.S. moves the slowest, then its health and fertility outcomes will be the worst. A whiff of justice at least!

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A report in November 2019 from JAMA (The Journal of the American Medical Association)<sup>14</sup> shows in detail how U.S. life expectancy for the 25-65 age group has declined for three consecutive years (2015, 2016, 2017), a completely unprecedented event here or anywhere else in the developed world in modern times. Incremental opioid addiction has been the largest factor in this decline in recent years, and several other negative factors like increased suicides will also be playing a role. But at least the current data is compatible with a rising component of damage from toxicity: the U.S. has the worst numbers in the developed world for life expectancy and the U.S. is also by far the most profligate country in chemical use. It uses the most per capita and has the least regulation. For example, the U.S. allows 85 pesticides - accounting for a quarter of the total use – that are outlawed or being phased out in the E.U., China, or Brazil. In contrast, only four chemicals are banned here and not in those countries! Also indicative is that California, the only state in the U.S. to avoid this decline in life expectancy, has one of the best (or least bad) records in chemical use safety.<sup>15</sup>

### Shanna Swan's New Book and Future Recognition of this Issue

Shanna Swan, a lead author of the meta-study discussed in this paper and a leader in analyzing fertility and fecundity, has written Count Down, a book aimed at the general public. The book, which has been accepted by Scribner for publication, is due to come out in late 2020. If it makes a great impact, and certainly the timing could not be better given the data, we believe this topic could gather steam at a rate few issues ever achieve. We appear to be playing Russian Roulette with our species and few people seem aware of this problem. Most of the few that are aware don't seem to care enough, or at least are for now incapable of projecting their concerns effectively enough to grab the attention of the general public and, hence, politicians. But we have seen in Europe over the last few years how rapidly public awareness about plastic pollution has increased, and this fertility issue is far, far more significant.

### The Tendency of the Medical Establishment to Understate the Problem

One of the reasons that the rising impact of chemical toxicity has been underestimated is that the medical establishment treats lower sperm counts and reduced fecundity as quite ordinary and no cause for alarm. In fact, health clinics and other members of the medical establishment talk today as if 20 units is still in the "normal" range and by implication presents no problem. This appearance of normalcy works against a rapid recognition of this rising problem with fecundity. But, academics in this field tell me the number used to define "normal" 20 or 30 years ago was 50 units (which although clearly no longer "normal" by earlier standards is at least unlikely to materially alter the likelihood of unaided pregnancy). At the new "normal" of 20 units, a majority of couples will need help, a very strange definition of "normal," even if the fertility clinics of the world represent that they can still largely offset that damage through their medical skills. A problem with that argument, though, is that IVF is expensive, at about \$35,000 for the normally needed three procedures in the U.S. and about one-third of that in the European Union. It is also invasive and unpleasant and, worst of all, probabilistic. After spending your money and going through a long and unpleasant process you will only have about a 30% chance of success. Our species does not process probabilities well at the best of times so we should not be surprised that, today, about 85% of those in the U.S. who are told they are infertile and could use IVF refuse the treatment. Many more abandon treatment after one or two failed rounds (failure here is almost universally

Mortality Rates in the United States, 1959-2017. JAMA 2019; 322(20):1996-2016, November 26, 2019.

Nathan Donley, "The USA lags behind other agricultural nations in banning harmful pesticides," Environmental Health 18, June 2019, Article 44.

Woolf and Schoomaker. (2019). Life Expectancy and



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#### Disclaimer

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said to be particularly painful psychologically) even though, counterintuitively, successive rounds of IVF have increasing chances of success per attempt.

### Future Work on Fertility

There are obvious paradoxes on population that have not been discussed: it is strange to worry about a growing global population and a baby bust at the same time! There are also economic consequences of a baby bust that could be discussed from the implications for the baby food market at the micro level to the long-range implications for GDP growth from a declining work force at the macro level. These paradoxes and consequences will be discussed in part two in coming months.

### **Underestimated Investment Risks in Chemical Companies**

A year and a half ago, in my paper 16 "The Race of our Lives (Revisited)" I mentioned that many investors were considering divestment from fossil fuel companies. I recommended that those investors should also consider the underestimated risks in chemical companies. The case here was that chemically-induced health problems were more personal and potentially frightening than the slower moving and psychologically more distant effects of climate change. As it turned out – a complete coincidence – Monsanto was successfully sued a few weeks after my paper was published and now, just 18 months later, three successful suits (many thousands of claims are still outstanding) have caused Monsanto's parent company Bayer to lose market capital, relative to other chemical companies, approximately equal to the entire price – over \$60 billion – that Bayer paid for Monsanto just two years earlier! This loss of value was entirely caused by a relatively marginal cancer, non-Hodgkin's lymphoma.

In comparison, the rapidly growing damage to fertility is an immediate threat to the survival of our species that must be counteracted in the next handful of years (and surely will be?). It is almost certain to become a major investment issue soon, ending with the banning of broad classes of chemicals, which constitute a major fraction of earnings for some chemical companies. It is clear to me that several chemical companies represent high levels of risk in this area, risks that are currently underestimated. The ethical and social behavior of some chemical companies as they lobby to defend substantially all their products, thought by independent scientists to be dangerous, should perhaps also raise questions. But the bottom line is this: either endocrine disrupting chemicals will go out of business or we will!



"Publicly, we're still saying there are no side effects."

# APPENDIX: PART 1

Following are comments by Hagai Levine, the lead author of the original meta-study on temporal trends in sperm count referenced in this paper. Please note that this is the original text and grammatical or usage errors have been left unchanged.

# Are humans at the verge of extinction? The implications of declining sperm counts.

Hagai Levine, School of Public Health, Hadassah Medical Center and Hebrew University, Jerusalem, Israel; <a href="mailto:hagai.levine@gmail.com">hagai.levine@gmail.com</a>

The old Hebrew "Zera" stands for both sperm and for root.

Let's begin with my roots. My grandmother, Hana Levine, is now 92 years old. She told me that when she was pregnant with my father (1952), a friend came from USA and offered her to take a good drug to prevent miscarriage. Being a public health nurse, my grandmother decided not to take this drug. This was not the case for millions of women who took Diethylstilbestrol (DES) between 1948-1971. Their children and grandchildren suffered from higher chances of cancer, infertility and miscarriages. DES led to a paradigm shift – we now have clear evidence that certain drugs/chemicals can disrupt proper development, especially of the reproductive systems. We also realized that the timing, not only the dose, makes the poison. Meaning, that during critical periods, even extremely low doses can cause damage for generations, especially through disruption of hormonal processes.

Forty years after my father's birth, Carlsen et al published their seminal paper, claiming that there is a decline in sperm concentration, at least in Europe and USA. Their article was not well accepted and was heavily criticized.

In 2017, we published a systematic review and meta-analysis on trends in human sperm counts. We found a significant decline in sperm counts between 1973 and 2011, driven by a 50-60% decline among men unselected by fertility from Western countries. Imagine any other biologic parameter, like IQ or hemoglobin decreasing by 50% over 40 years. In the study, we did our best to minimize limitations and indeed our study was well accepted by the scientific community. There is now widespread consensus that sperm count is indeed declining. This is a wake-up for humanity. Something in our modern environment or lifestyle is very wrong. Although we don't know the direct causes, endocrine disruption by chemicals of the male reproductive system during development is a clear suspect to investigate.

What will happen in the future? Will sperm count reach zero? Is there a chance that this decline would lead to extinction of the human species? Given the extinction of multiple species, often associated with man-made environmental disruption, this is certainly possible. We should bear in mind that together with sperm count decline, we see an increase in congenital malformations of the male reproductive system, decrease in testosterone and increase in testicular germ cell tumors as well decreased fertility and increases in miscarriage rates. In addition, low sperm count has been found to predict earlier death and increased morbidity from multiple causes.

Our efforts should be, not primarily on predicting the future, but on shaping it. Despite interest from the media, no one has seriously addressed the challenge posed by this public health problem. The immediate need is a concentrated effort to understand the complex causes of human sperm count decline and its implications. Most importantly, we need to identify the concrete steps needed on both the global and local level, to target to the root causes of the decline, reverse this trend and secure our future.

We must act now. With the implications of sperm disruption for future generations these changes may well be irreversible. When the extinction of the human species is at stake can we really take the risk?

# APPENDIX: PART 2

#### Summary of Two Important Studies on Pesticide Damage

Two of the best studies available on this topic have been done by a Harvard-run unit at the Mass General fertility center in Boston. In one, 325 women who were having trouble getting pregnant signed up for help and were asked to self-report on the amount of fruits and vegetables they ate each day.<sup>17</sup> These items were then rated according to the USDA data on pesticide residues, from strawberries and cherries (terrible) to avocados (not so bad). Using the amounts eaten and the corresponding pesticide ratings, the women were grouped based on the estimated quantity of pesticides they had each consumed. At the end of the program, the best (or least bad) quartile, or about 80 women, had 65% successful live births, the next two quartiles progressively fewer, and the bottom quartile only 39%! That such a rough survey would produce such a big difference seems remarkable and disturbing. Others will be less impressed because of the small sample. For me, this study begs for an answer as to what might have happened had the best group eaten nothing but organic food. (Also, unfortunate, the babies from this study were not examined, for everything we have learned suggests that the rankings for inherited damage would have shown a similar steep drop by quartile.)

This study above, published in October 2017, was preceded in 2015 by a similar small but careful study<sup>18</sup> by some of the same authors. They measured the sperm count of 189 young men, screened to avoid smokers and the severely obese, who also self-reported on their consumption of fruits and vegetables – similarly rated on pesticide residue – for six months. Results showed that the large positive effects on sperm count from eating more fruits and vegetables disappeared completely when the food had high levels of pesticides. The important comparison, though, is that the quarter who ate the best (or least bad) fruits and vegetables had twice the sperm count of the bottom quartile, who ate the most toxic mix! Both projects are very small and badly need larger backup studies but are remarkably consistent in their results. These studies are in the following bibliography.

Chiu et al., "Association Between Pesticide Residue Intake from Consumption of Fruits and Vegetables and Pregnancy Outcomes Among Women Undergoing Infertility Treatment with Assisted Reproductive Technology," *JAMA Intern Med.* 2018, 178(1):17–26.

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Chiu et al., "Intake of Fruits and Vegetables with Low to-Moderate Pesticide Residues Is Positively Associated with Semen-Quality Parameters among Young Healthy Men," Journal of Nutrition, May 2016, 146(5):1084-92.

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#### **BIBLIOGRAPHY**

The following are listed in order of the suggested reading sequence. The first item is Part 1 of the Appendix. The full text of the meta-study, which has been discussed in part in the body of this paper, can be accessed via the link in the second item. Items three and four are highly recommended.

- 1. Comments by lead author H. Levine.
- Original meta-study, "Temporal Trends in Sperm Count...": <a href="https://academic.oup.com/humupd/article/23/6/646/4035689">https://academic.oup.com/humupd/article/23/6/646/4035689</a>
- 3. GQ, "Sperm Count Zero": <a href="https://www.gq.com/story/sperm-count-zero">https://www.gq.com/story/sperm-count-zero</a>
- 4. Two Studies on Pesticides and Fertility: <a href="https://jamanetwork.com/journals/jamainternalmedicine/article-abstract/2659557">https://jamanetwork.com/journals/jamainternalmedicine/article-abstract/2659557</a> <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4841922/pdf/jn226563.pdf">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4841922/pdf/jn226563.pdf</a>
- 5. *Atlantic Monthly,* "Sperm Counts Continue to Fall": <a href="https://www.theatlantic.com/family/archive/2018/10/sperm-counts-continue-to-fall/572794/">https://www.theatlantic.com/family/archive/2018/10/sperm-counts-continue-to-fall/572794/</a>
- 6. Vox, "Sperm Counts are Falling": <a href="https://www.vox.com/science-and-health/2018/9/17/17841518/low-sperm-count-semen-male-fertility">https://www.vox.com/science-and-health/2018/9/17/17841518/low-sperm-count-semen-male-fertility</a>
- 7. *Nature Scientific Reports*, "Effects of DEHP and PCB153 on Sperm Quality": <a href="https://www.nature.com/articles/s41598-019-39913-9">https://www.nature.com/articles/s41598-019-39913-9</a>
- 8. *American Journal of Epidemiology,* "Good Semen Quality and Life Expectancy": <a href="https://academic.oup.com/aje/article/170/5/559/102217">https://academic.oup.com/aje/article/170/5/559/102217</a>
- 9. Environmental Research, "Reduction in Pesticide Metabolites after a Week-Long Organic Diet": <a href="https://linkinghub.elsevier.com/retrieve/pii/S0013-9351(14)00067-X">https://linkinghub.elsevier.com/retrieve/pii/S0013-9351(14)00067-X</a>
- 10. Fertility and Sterility, "Increased Risk of Chronic Medical Conditions in Infertile Men": <a href="https://www.fertstert.org/article/S0015-0282(15)02087-7/fulltext">https://www.fertstert.org/article/S0015-0282(15)02087-7/fulltext</a>
- The Journal of Clinical Endocrinology & Metabolism, "A Population-Level Decline in Serum Testosterone Levels in American Men": <a href="https://academic.oup.com/jcem/article/92/1/196/2598434">https://academic.oup.com/jcem/article/92/1/196/2598434</a>
- 12. Human Reproduction, "The Mediterranean Diet and IVF Success Rate": <a href="https://academic.oup.com/humrep/article/33/3/494/4828066">https://academic.oup.com/humrep/article/33/3/494/4828066</a>
- 13. *The BMJ*, "Evidence For Decreasing Quality of Semen During Past 50 Years": <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1883354/pdf/bmj00091-0019.pdf">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1883354/pdf/bmj00091-0019.pdf</a>
- 14. *Nature Scientific Reports*, "Environmental Chemicals Impact Dog Semen Quality", <a href="https://www.nature.com/articles/srep31281">https://www.nature.com/articles/srep31281</a>
- 15. International Journal of Andrology, "Disruption of Reproductive Development in Male Rats Following In Utero Exposure to Phthalates": <a href="https://onlinelibrary.wiley.">https://onlinelibrary.wiley.</a>

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- 16. Environmental Health Perspectives, "Prenatal Phthalate Exposures and Anogenital Distance": <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4286276/pdf/ehp.1408163.pdf">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4286276/pdf/ehp.1408163.pdf</a>
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- 18. Environmental Health Perspectives, "Decrease in AGD among Male Infants with Prenatal Phthalate Exposure": <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1280349/pdf/ehp0113-001056.pdf">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1280349/pdf/ehp0113-001056.pdf</a>
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  PMC2874619/pdf/nihms-158991.pdf
- 21. *The Journal of Clinical Endocrinology and Metabolism*, "Endocrine Disruption of Androgenic Activity by Perfluoroalkyl Substances": <a href="https://academic.oup.com/jcem/article/104/4/1259/5158211">https://academic.oup.com/jcem/article/104/4/1259/5158211</a>