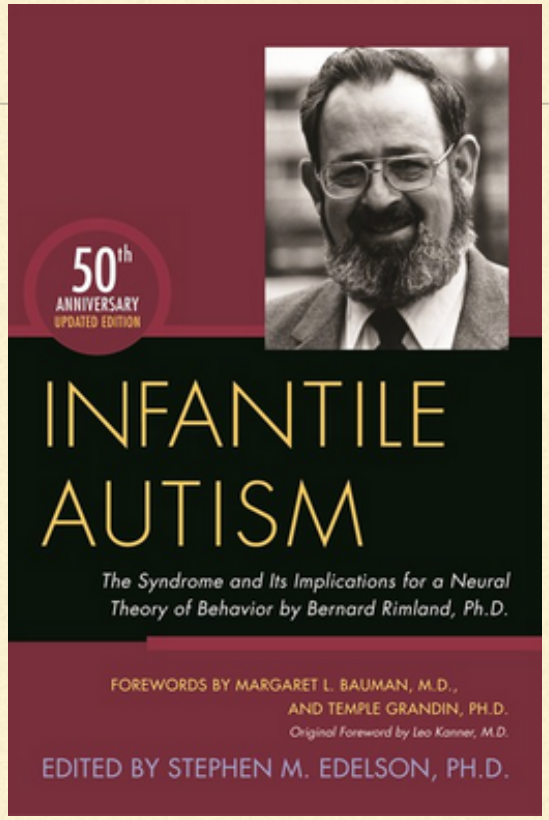
The Importance of Citizen Science in Autism Research

Jill Escher, MA, JD
@JillEscher

Escher Fund for Autism
Humans start as molecules

GermlineExposures.org

Citizen Science: Part of ASA's Heritage



ASA co-founder **Bernie Rimland**, Ph.D: Infantile Autism
The Syndrome and Its Implications for a Neural Theory of Behavior

Citizen science can change history.

I love formal science, but…

"Science" can err

Dogma, funding, conservatism can stifle innovation

Ivory tower syndrome

Technology empowers citizen science

We have data, too

Four paths of autism citizen science

- Hypothesis Hunting (causation, treatment)
- Philanthropy (you don’t need to be rich)
- Crowdsourcing
- Educating and Advocating

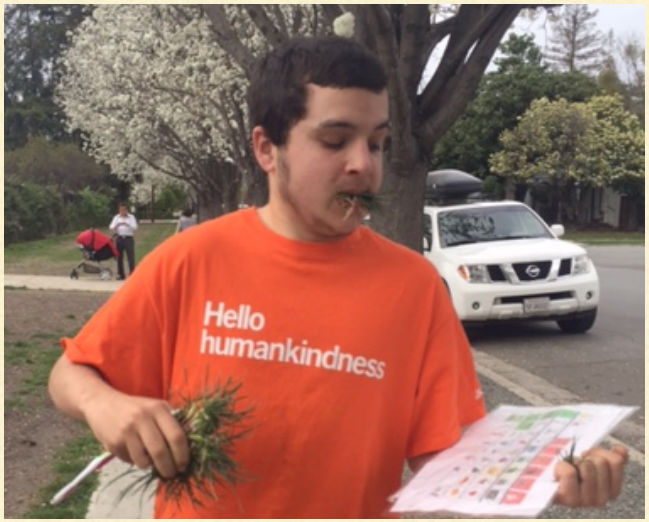
An accidental hypothesis hunter

I was born in 1965 in Los Angeles.

Three beautiful children from normal pregnancies.

No history of ASD, no other risk factors.

Yet **two kids nonverbal autistic.**



Son, 17

Daughter, 10

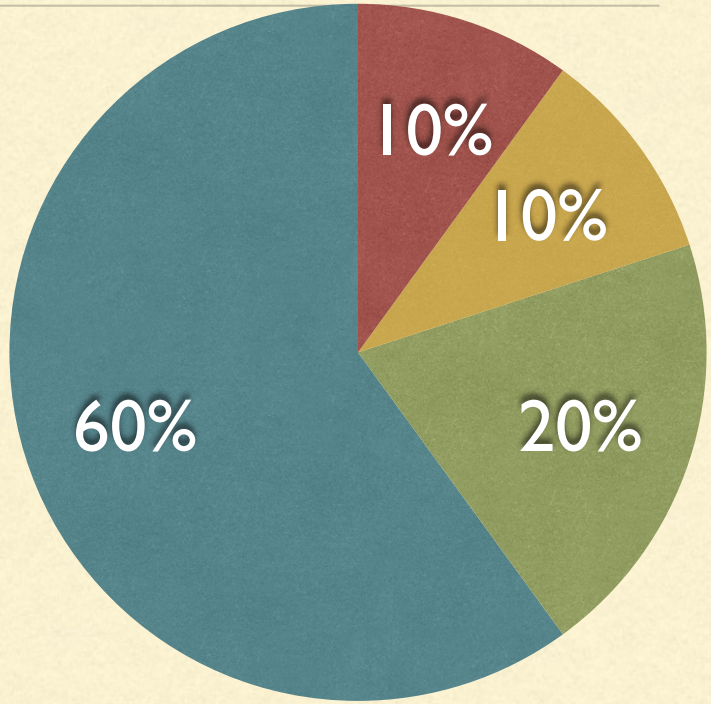
Why?
What happened?

My kids' autism is a puzzle

Genetics?
About 10% of cases can be attributed to known genomic errors, 10% more forecast. But not found in my kids.

Environment?
Exogenous factors—ie, prematurity, certain drugs, maybe 20%. No environmental risk factors with my kids.

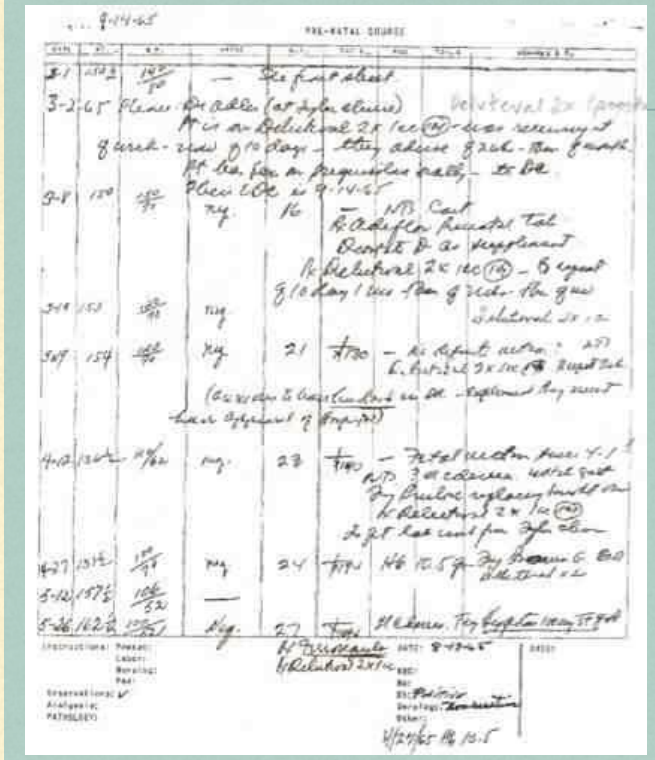
What else could it be?
At least 60% of ASD cases unexplained, but strong evidence of heritability. My kids fall in here: a puzzle.



What we know about causes of ASD

Then, a trio of bizarre discoveries

1.



In 2010, I obtained my mother's 1965 obstetric records. What did they mean?

2.

Prenatal Exposure to Synthetic Progestins and Estrogens: Effects on Human Development

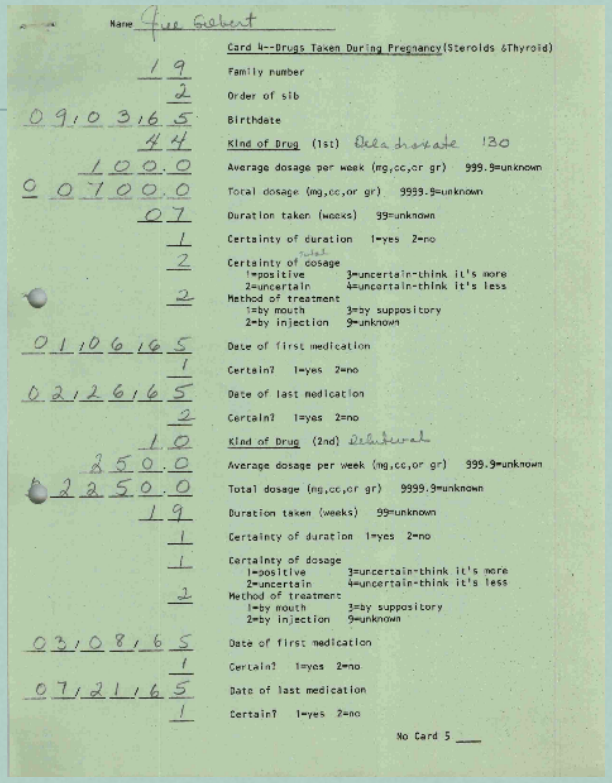
June Machover Reinisch, Ph.D.,[1] and William G. Karow, M.D.[2]

Seventy-one offspring of mothers administered combinations of synthetic progestins and estrogen for the maintenance of at-risk pregnancy were evaluated for their performance on IQ and personality tests. Siblings born of untreated pregnancies acted as controls. Hormone-exposed subjects were partitioned into three treatment subgroups dependent on the ratio of progestin to estrogen administered to their mothers during pregnancy. No difference in IQ was obtained among the three treatment subgroups even when scores were adjusted for sibling score and prenatal and perinatal complications. Responses to the personality questionnaire provided significant differences among the three groups. The group exposed to the progestin regime (progestin alone or in combination with very low doses of estrogen) and the estrogen regime (higher doses of estrogen than progestin) were most dissimilar. Progestin regime exposed subjects were characterized as more independent, sensitive, self-assured, individualistic, and self-sufficient. In contrast, the subjects exposed to the estrogen regime were more group oriented and group dependent. Analysis of difference scores generated by subtracting the score of an unexposed sibling from that of the exposed cosibling provided similar results. A general discussion is presented on the efficacy of hormone treatment for pregnancy maintenance, augmented fetal wastage of males, birth order and treatment, maternal knowledge of treatment and its possible postnatal effects on the offspring, and drug effects on the fetus.

KEY WORDS: synthetic progestin; estrogen; diethylstilbestrol; humans; personality; IQ; pregnancy maintenance; prenatal.

In 2011, I discovered I had been a subject in a study (Reinisch 1977) examining fetal effects of synthetic steroid hormone drugs.

3.



Name Sue Siebert

Card 4--Drugs Taken During Pregnancy (Steroids & Thyroid)

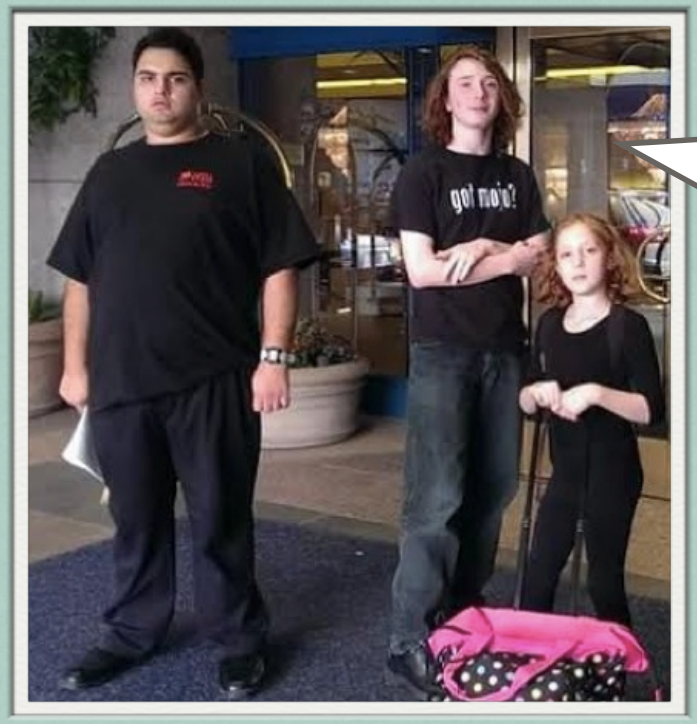
19	Family number
2	Order of sib
09.03.65	Birthdate
44	Kind of Drug (1st) Delalutin 130
100.0	Average dosage per week (mg,cc,or gr) 999.9=unknown
007100.0	Total dosage (mg,cc,or gr) 9999.9=unknown
07	Duration taken (weeks) 99=unknown
1	Certainty of duration 1=yes 2=no
2	Certainty of dosage 1=positive 2=uncertain 3=uncertain-think it's more 4=uncertain-think it's less
2	Method of treatment 1=by mouth 2=by injection 3=by suppository 9=unknown
01.06.65	Date of first medication
1	Certain? 1=yes 2=no
02.12.65	Date of last medication
2	Certain? 1=yes 2=no
10	Kind of Drug (2nd) Delalutin
250.0	Average dosage per week (mg,cc,or gr) 999.9=unknown
2250.0	Total dosage (mg,cc,or gr) 9999.9=unknown
19	Duration taken (weeks) 99=unknown
1	Certainty of duration 1=yes 2=no
1	Certainty of dosage 1=positive 2=uncertain 3=uncertain-think it's more 4=uncertain-think it's less
2	Method of treatment 1=by mouth 2=by injection 3=by suppository 9=unknown
03.08.65	Date of first medication
1	Certain? 1=yes 2=no
07.21.65	Date of last medication
1	Certain? 1=yes 2=no

No Card 5 ___

In 2013, I obtained records from the Kinsey Institute detailing my prenatal drug exposures.

Bottom line: Unbeknownst to me, I had been prenatally exposed to a truckload of gene-tinkering drugs

Others shared this story: An example



We started as eggs when our mom was a fetus.

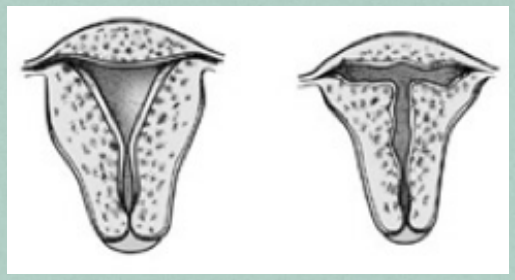
Joan Hutchens was also exposed prenatally to an "anti-miscarriage" hormone regimen in 1965.

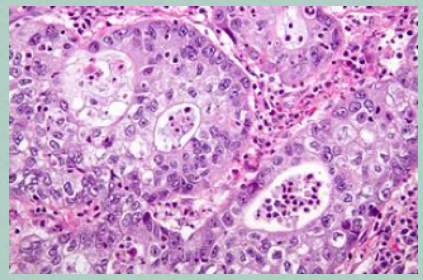
Three of her five children, above, have idiopathic autism.

No question that toxic pregnancy exposures can have devastating effects

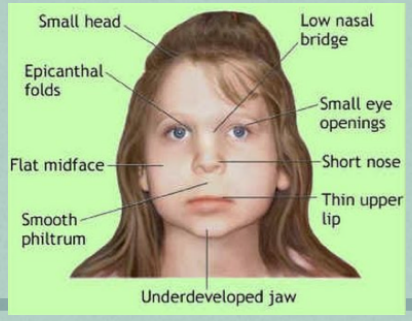
Thalidomide

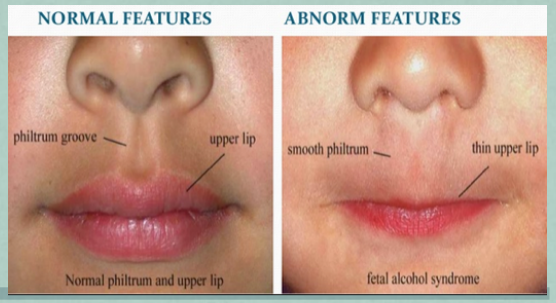
DES (Diethylstilbestrol)



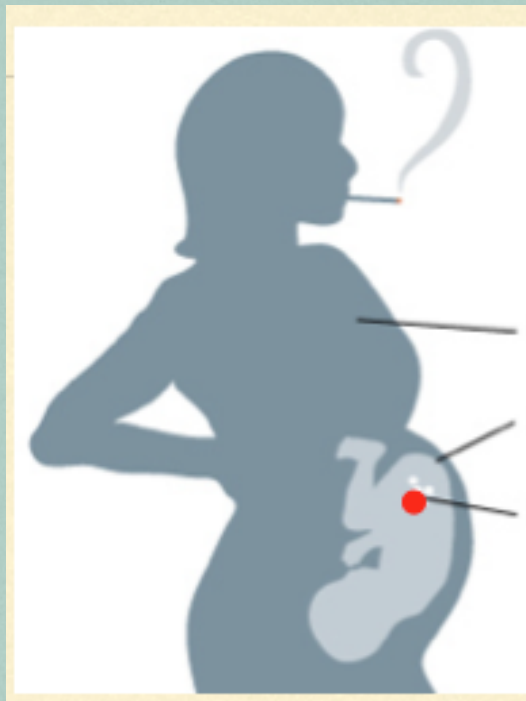


Fetal Alcohol Syndrome





BUT there's more … pregnancy exposures may also affect grandchildren



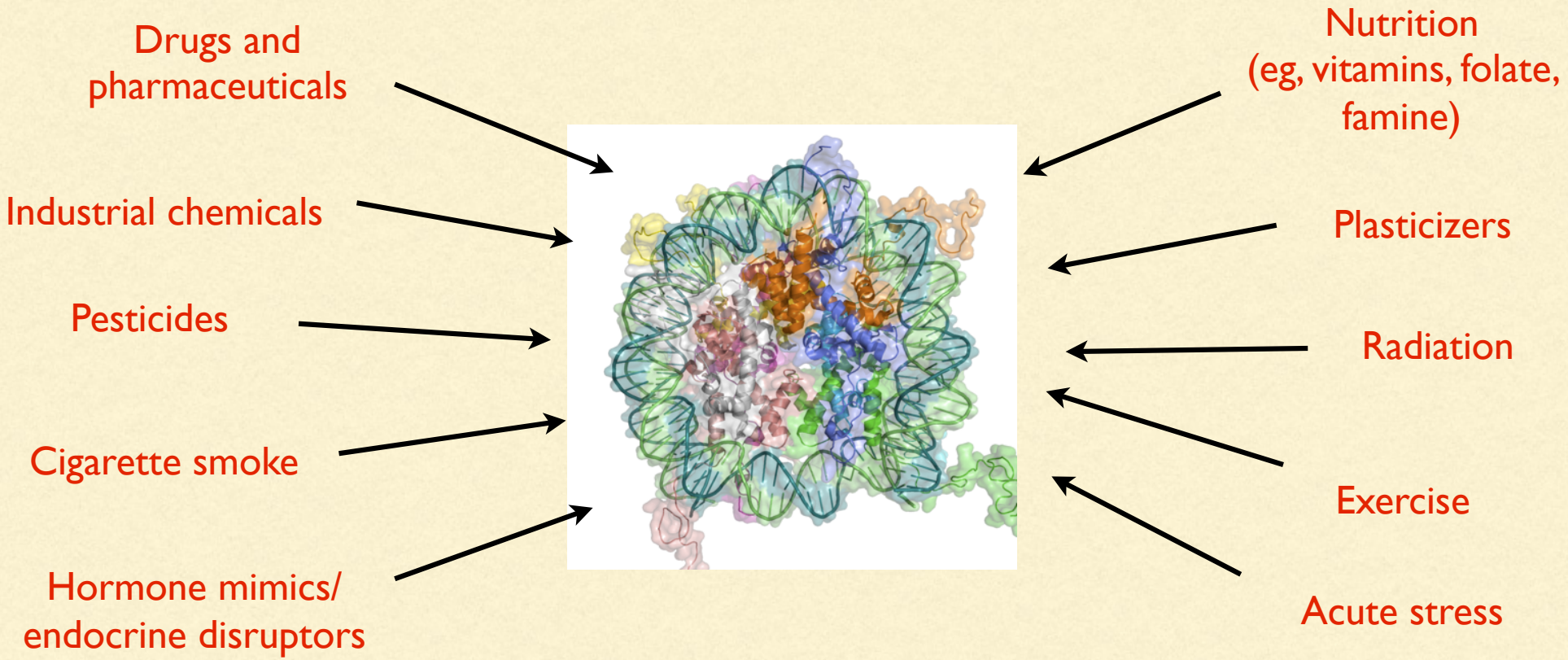
F0 = Mother
F1 = Fetus
F2 = Germ cells / grandchildren

Via the vulnerable fetal germ cells

Germline mutation or epi-mutation

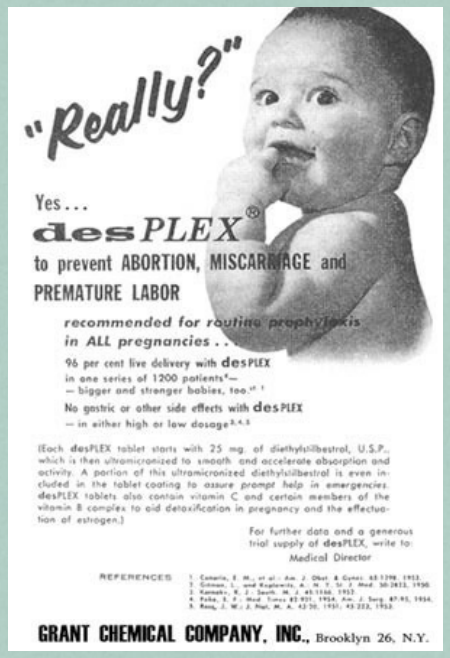
Mutation: Change in DNA sequence.

Epigenetics: “Heritable changes in gene expression caused by mechanisms other than alterations to underlying DNA sequence.”

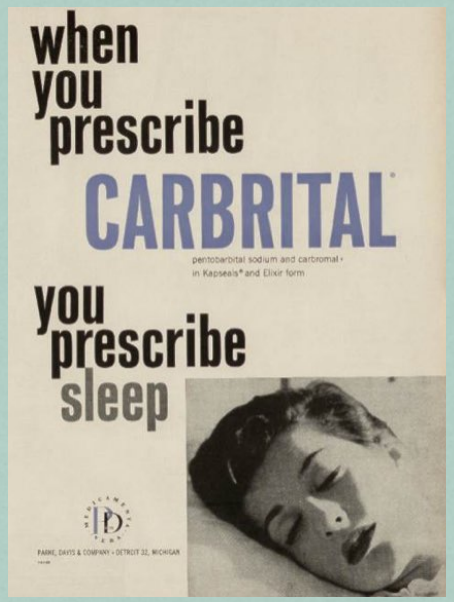


The medicated pregnancy was pretty much a vast human experiment

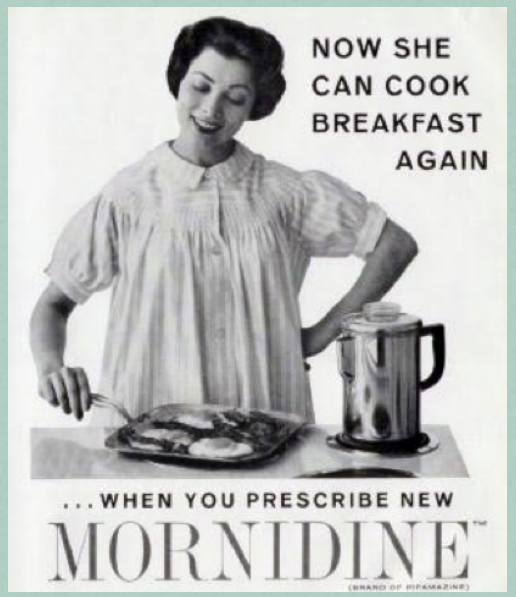
Synthetic hormones



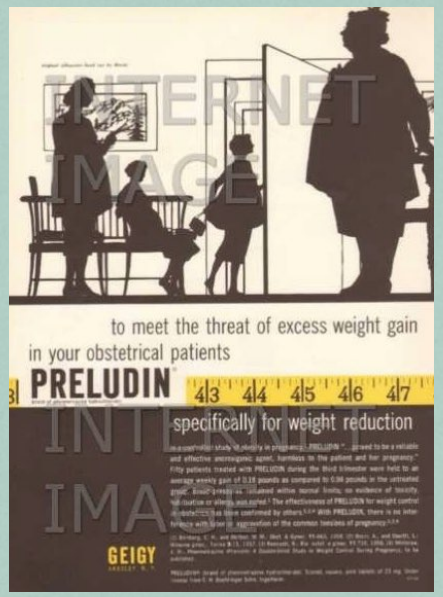
Sedatives, barbiturates



Anti-nausea drugs



Amphetamines



The fetus and its proto- sperm/egg were of little concern.

(Other postwar exposures, too)

Pesticides (eg, DDT)

Agent Orange (dioxin)

Plasticizers
(eg, BPA, phthalates)

Flame retardants
(eg, PBDEs)

PCBs

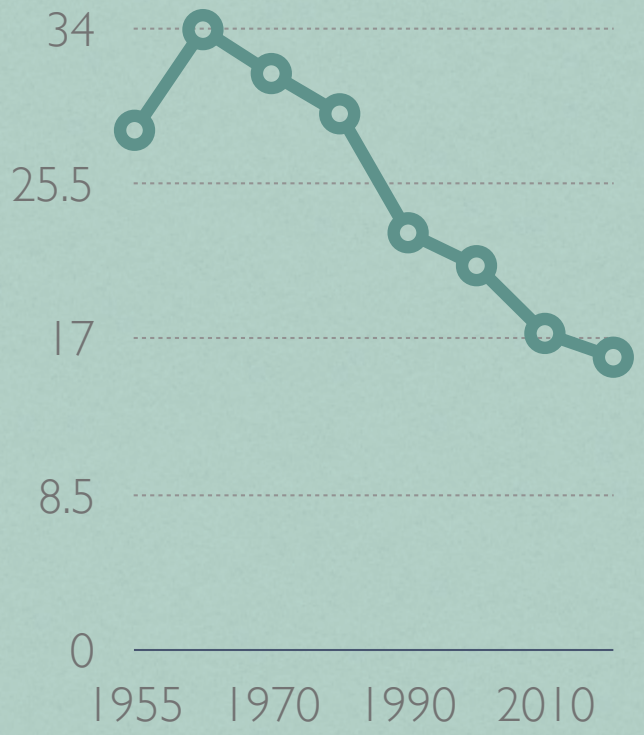
Air pollution

Radiation

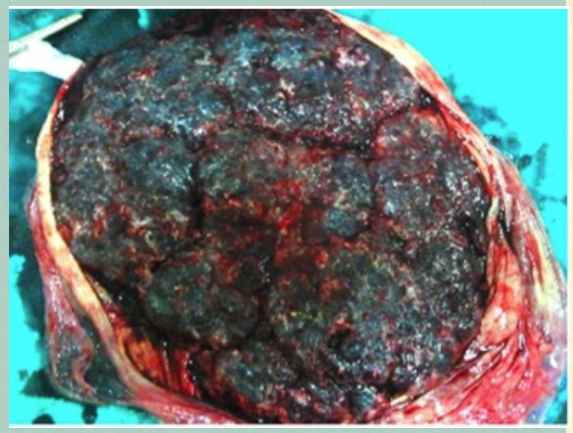
But the mother of all pregnancy exposures was smoking

Doctors sometimes recommended it as an appetite suppressant

Smoking prevalence among US females



Cigarette smoke = toxic, mutagenic and epimutagenic components



Do we feel the consequences today?

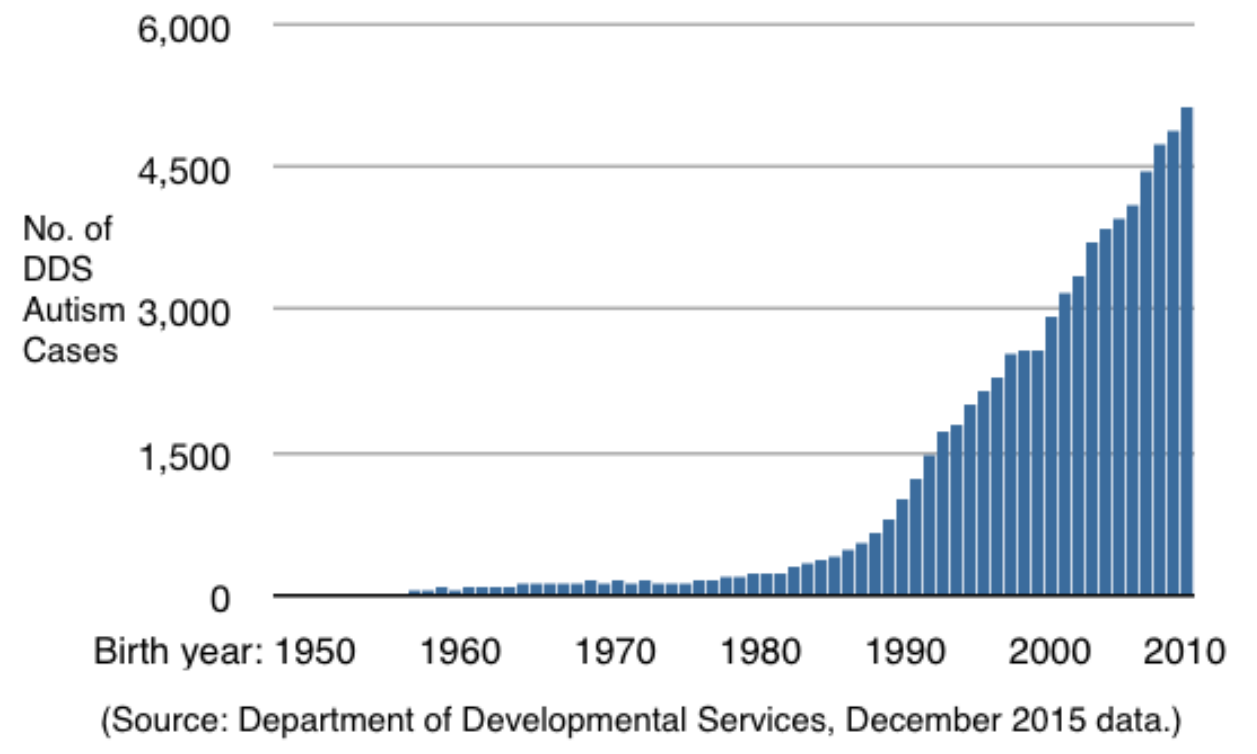
For example, heavy grandmaternal smoking is common in grandchild ASD

Families had no history of autism. Sampling of the grandchildren.

Yes, these are anecdotes but they may raise important questions about potential germline mutagenesis or epimutagenesis.

We still have few answers about the main drivers of ASD surge

Calif. Department of Developmental Services
Autism Cases by Birth Year 1943-2010



Citizen science can help

Jill's Citizen Science Hypothesis

Part of the rise in autism of the 1980s-2000s can be attributed to sperm and egg errors caused by certain pregnancy exposures of the 1950s-1970s, including:

- Smoking
- Artificial hormones
- General anesthesia

I think autism families are a largely untapped goldmine of ideas for research. What are <u>your</u> ideas?

2: Be a Philanthropist

$$ you raise can seed innovative research and you can help inform the study purpose and design.

- Step 1: Create a donor-advised fund
- Step 2: Create a “Request for Proposals”

3: Crowdsource

Simons SPARK project

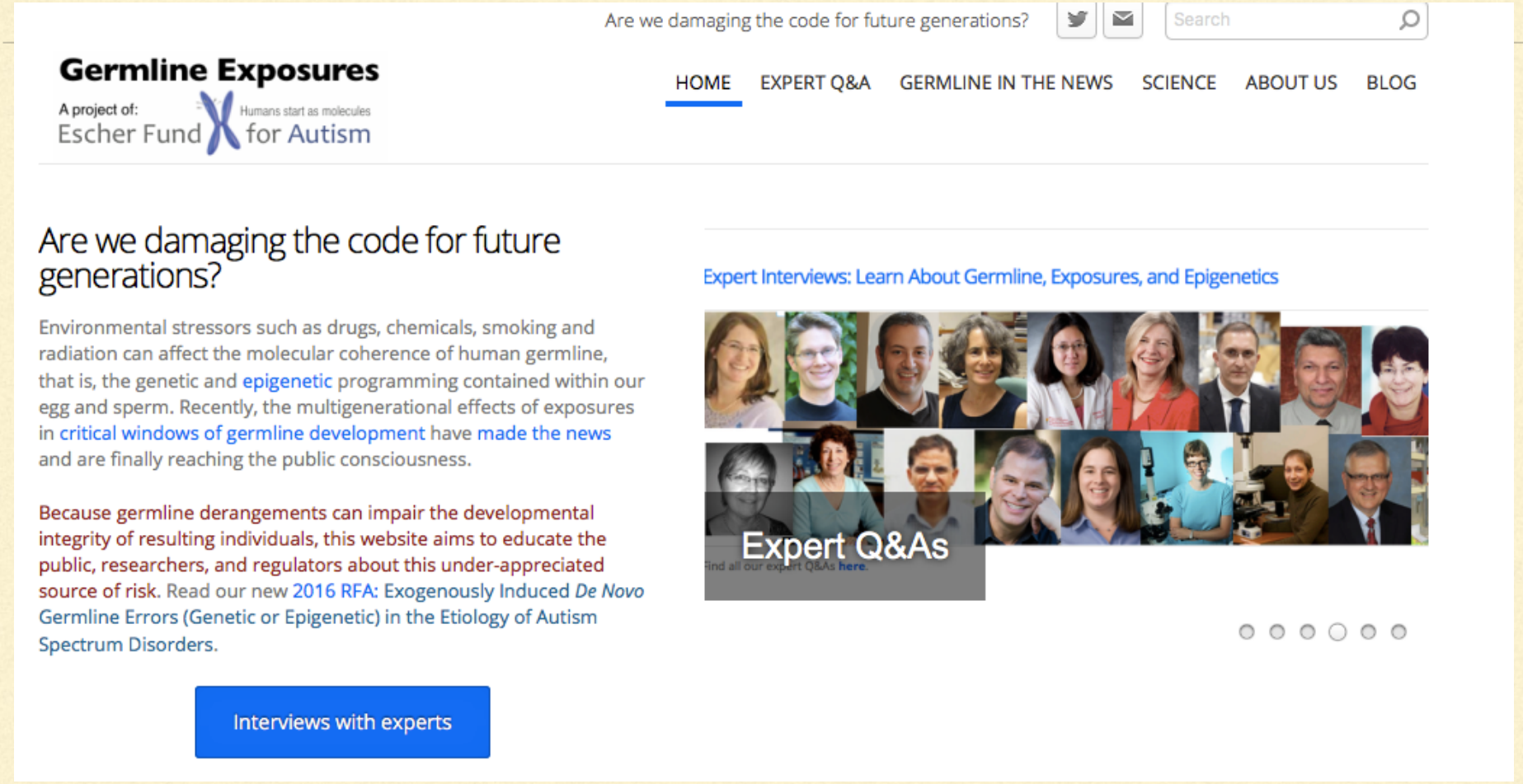
SPARK
Igniting autism research
Improving lives

Crowdsourcing data via mobile app (eg, Stanford project)

4: Educate and Advocate

- Organize a conference
- Build a website
- Write a report

Build a science education website



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