Past emerging from present recording: reproductive health history reveals increase in prevalence of birth defects over time, and associations with exposure to weaponry in Gaza, Palestine and in Fallujah, Iraq.

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background

The legacy of contemporary wars is a long lasting, if not permanent, load for the health of people and for the environment through the long term toxicity of the weapon components and their extensive and indiscriminate use.

After exposure to weaponry in war areas various long term health impairments were reported: chronic illness, tumors, reproductive damages.

Reproductive damage

Our focus has been on birth defects and miscarriages

Experiential reports of increases in major structural birth defects and late miscarriages after US and Israeli attacks in Iraq, Afghanistan, Gaza-Palestine and Lebanon.

The link is the fact that US and Israel often use the same weaponry in these areas.

Major structural birth defects are an heterogeneous group of diseases that manifest at or around birth involving major structural alterations of body compartments.

Their origin is complex, for most of them the genetic determinants are unknown, or are multiple.

In general, they are sensitive to environmental cues and inducible by introduction in the environment of mutagenic or teratogenic substances.

Late miscarriages are often, though not always, associated with a malformed fetus.

The sudden introduction in the environment of new mutagens and teratogens results in a sudden rise in frequency of presentation of birth defects.

Chronic exposure to teratogens increases the probability of the manifestation of reproductive damage over time.

Candidate teratogens delivered by weapons long-lasting in the environment and cumulative effects in the body: Metals

Metals introduced as weaponry components are mutagens or epigenetic promoters of birth defects, interfering with germ cells and embryo differentiation, and acting as endocrine disruptors.

Metals are delivered by weapons in powders or nano-powders.

Metals are stable in the environment and are accumulated in time in the body over external concentration.

Both acute and chronic effects can be expected from toxic metals exposure.

Metal powders are the most likely weapon-remnant candidates to promote increase in birth defects in the progeny of people exposed at sexual maturation and during reproduction.

The final aim of our investigation is that of remediation and/or prevention, advice or services to the victims.

Steps for field work on the impact of metal contamination on reproductive health

Verify the extent of the damage to reproductive health.

Identify correlations for time and for exposure, and/or for contamination of parental couples with the occurrence of birth defect children.

Demonstrate if there is continuing assumption of toxic components of weaponry over time by the population that is reproducing.

Investigate the mechanisms of action of the toxicants.

What is known

Weaponry utilized in Gaza and Fallujah contains toxicant and teratogen metals.

Proof of fact was given that metals in weaponry used in Gaza 2006 and 2009 were delivered in wound tissues.

Proof of assumption by population after Cast Lead: weapon-derived metals were detected in children's hair in Gaza in 2010

Proof of their long lasting persistence in the environment: weapon-derived metals were detected in adults, newborn and children hair in Fallujah in 2010

Gaza, Palestine -2011
a war-remnants contaminated land

Keeping in mind that

- The consequence of exposure de novo to teratogens is a sudden increase in reproductive damage.

- In the absence of environmental remediation, environmentally stable contaminant(s) continue to act as inducers in time and accumulate in the body: their effects as teratogens result in persisting or increasingly high frequency of birth defects thereafter.

Verify the extent of the damage to reproductive health = detect changes in time

1-Compare with previous records

2-Conduct extensive epidemiologic enquiry

3-Identify "not-random" presentation of damages during the reproductive life of couples who stably reside in contaminated areas.

Lack of records is common in most places in the Middle East, and in all places where war or occupation has destroyed or undermined the health system.

In Gaza 2011

No reliable records of incidence of birth defects were taken at delivery, nor were they available from the past.

In 2011 at Al Shifa hospital, we registered at delivery the progeny of 4027 women

Among the 4027 women delivering in the period between May and October 2011, 78 have had previously a child with birth defects.

For these, we obtained the history of their reproductive life and the exposure to the attacks during Cast Lead.

We used a protocol for the registration of couples with children with birth defects, inclusive of international standards. The protocol also recorded:

- Detailed pedigrees (health, age and sequence) of progeny.

- intermarriage.

- Detailed record of collateral kin of first and second generation (relation, sex, number and health status)

- Late miscarriages

- Exposure at the time of the Cast Lead attacks and the persistence of parents in places of potential exposure to teratogens (historical residence since 2008)

This protocol allowed to identify pre-existence of birth defects in families and to study association of birth defect occurrence with exposure to Cast Lead.

It also allowed to describe the pattern of presentation in time of birth defects.

We studied a cohort of 58 couples with a normal newborn in 2011 and one (or more) progeny with birth defects anytime before.

The cohort had a total of 226 progeny and 1228 collateral kin.

PBD

interviewer N	newborn sex	newborn date	Relation between parents	Residence	progeny previous BD in family	AGE years in summer 2011 1	2	3	4	5	6	7	8	9	10	11	12	13	14	type	EXPOSURE IN WAR
E148	F	2015-8-22	0	N Jabalia	Hydrocephalus			F	F NT			F	ms								B
E158	F	2015-8-23	0	GC Zaitoun	Congential heart diseasevsd					M		M CHD		F		F		M			not available
E244	M	2015-9-06	1	N Bet Hanoun	2x Osteoporosis							M		F				F	F OSTP	family°	B
E257	M	2015-9-07	0	GC al Shijaya	Congential heart disease Vsd			M CHD		F	M										*
E313	F	2015-9-13	1	GC al S.Redwan	Congential limb defects& asphyxia						F LIMB			M			F	F			NO
E320	F	2015-9-14	0	GC al Zaitoun	Congential heart disease vsd		M	F	M CHD												*
E332	M	2015-9-15	0	N Bet Lahya	Congenital hip dislocation		M CDH				M CDH		M CDH							family	*
F105	M	2015-5-20	0	GC al Shijaya	Celebral athrophy		M	M NT			F		F								not available
F137	F	2015-5-23	2	M Al Nosyrat	Hydrocephalus				M NT					M	F						not available
F156	F	2015-5-26	1	N Jabalia	Anencephaly		F		M NT			F									not available
F251	M	2015-6-07	1	N Bet Hanoun	Congenital heart disease	F CHD															*
F423	M	2015-6-19	1	GC Al Zaitoun	Celebral palsy		F NT	F NT	F NT	F		F			F					family	NO
F55	F	2015-5-14	1	GC al S.Redwan	Congenital cataract	M			Fcataract	F		M		F							not available
F584	M	2015-7-11	0	N Jabalia	Polycystic kidney			F KpoliC	F	2M dead											NO
F65	F	2015-5-15	0	GC Al Sabra	Congential heart disease		F CDH		F		M										not available
F68	M	2015-5-15	0	GC Al Tofah	Multiple	M M	M		M			F				M			M		not available
H1044	M	2015-8-16	2	N Bet Lahya	Brain Athrophy			F	M NT	F			F								*
H1049	M	2015-8-16	0	GC Al Reemal	Abdominal wall defect	M ABD															WP
H1116	F	2015-8-20	1	GC al Shijaya	Gastro intestinal					M	F GI		F				M	M	M		NO
H1161	F	2015-8-24	0	M _al Maghazi	Gastro intestinal		M GI		M	M											*
H1172	F	2015-8-25	1	GC al Shijaya	CLP				F			F		M CLP							*
H1291	F	2015-9-09	1	GC al Shijaya	3 x Multiple	F		M			F		M		F M			F		family	*
H1333		2015-9-15	1	M Al nosyrat	2x Polycystic kidney		F			M K POLI	M K POLI									family	NO
H1414	F	2015-9-25	0	N Jabalia	Hydrocephalus				M		M		M NT								WP
H211	M	2015-5-25	0	GC al Sabra	Polycystic kidney	M KpoliC															B
H212	M	2015-5-25	0	N Bet Hanoun	hydrocephalus					F		F				M	F+M				NO
H249	M	2015-5-29	0	GC al Sabra	Congential heart disease			M			F		M		F		M	ms	M CHD		B
H276	M	2015-5-31	0	N Bet Hanoun	Congential heart disease		M			M		F		M		M		F	M		WOUNDED
H279	F	2015-5-31	1	GC Al Reemal	Congenital lip dislocation			F CDH				M					F	ms			*
H535	F	2015-6-21	0	GC Al Tofah	Hydrocephalus		M NT		M	F	F										NO
H554	F	2015-6-22	0	GC Al Daraj	Congential heart disease		F		F CHD			M	F				F				NO
H597	M	2015-6-24	1	M Der El Ballah	Spina BifidaA				M NT		F			F							*
H637	F	2015-6-28	0	GC Al Jala'a	Hydrocephalus									M			M	M NT	M		B
H689	F	2015-6-28	0	GC al Zaitoun	Diaphragmatic Hernia			F		M GI		M	M								*
H849	F	2015-7-27	2	GC Al Tofah	Congential heart disease			F			M	M	M CHD								*
H859	M	2015-7-28	1	GC Al Saaf	Congenital derma	F PRE	F PRE	M	F DERMA												B
H907	F	2015-8-02	0	M Der El Ballah	Metal retardation								F						M		NO
H939	M	2015-8-04	1	N Bet Hanoun	Multiple	MULT															B
H949	F	2015-8-07	1	N Bet Hanoun	Congenital heart disease		F		M CHD		M		F								*
H973	F	2015-8-08	0	N Gabablia	Renal ageresis (absentlkidrey)		M K														*
M165	F	2015-8-21	1	GC Al Remal	unknow BD		F		F	M BD											not available
M239	F	2015-8-26	1	M Al Nosyrat	2 x Gastro Intestinal + Multiple	F GI		F GI		M M										family	NO
M318 P	M	2015-9-07	0	GC al Zaitoun	unknown BD		M RHdead		M	M BD		F RHdead			F+F						not available
M340	F	2015-9-08	2	N Bet Lahya	2 x mulyiple congential				M		F M		M		F		F M			family	not available
M350P	M	2015-9-11	2	GC al S.Redwan	Congential heart disease		F CHD	F			F		F	F	M						not available
M353P	M	2015-9-11	0	N Jabalia	unknown BD					F				F	M		M		F		not available
M365	F	2015-9-12	2	GC al Zaitoun	2 x unknown BD			M	M		M BD	M BD		M		F				family	not available
M286	M	2015-9-05	0	GC al Sabra	unknown BD			F+M		F			F		F ?BD			M	F		not available
M389	F	2015-9-13	1	GC Al Tofah	unknown BD			F	F		F BD	M									not available
M51	M	2015-8-11	0	N Bet Lahya	neural tube									F		M	F NT		F		not available
H8	M	2026-5-09	0	GC Al Remal	2 X Skeletal			F				F Foot	F			M SK	F			family	not available
H18	M	2026-5-09	1	GC Al shijaia	Brain atrophy		M NT	F													not available
E409	F	2015-9-22	0	GC Al Nazla	Spina Bifida					F NT	M			F	F			M			NO
E447	F	201-9-25	0	GC al Shijaya	Down Syndrome						M DOWN						F				NO
F48	M	2015-5-14	0	N Bet Lahya	2xCystic fibroids				M K		M K				F		F			family	*
H1064	F	2015-8-17	1	M Der El Ballah	Esophageal destruction	M GI	F														NO
H1496	F	2011.-10-4	1	N Jabalia	Polycystic Kidney		M K polyc		F				M	F							*
M499	M	2011.-10-4	1	GC Al Remal	unknown BD			M	F	F	M BD						M		F		not available
					Total born	10	21	22	26	21	22	18	17	15	12	7	15	9	11		
					with BD	7	9	6	12	7	10	3	3	2	2	2	2	2	2	69	
					with sporadic BD	6	7	4	10	5	5	1	2	1	1	0	1	1	1	45	
					with familair BD	1	2	2	2	2	5	2	1	1	1	2	1	1	1	24	

Colum 1 is case code number ; 2 sex of thedelivered normal child; 3 its date of birth,,; 4 parents are first cousins=1, second cousins=2, unrelated=0; residence of the couple; diagnosis extended for the first previous BD child; all next colums are the chronological list of children per couple with in red BD cases ms = miscarriage past 16 weeks and PRE for before term alive. ° an other child, older has same BD

*Occurrence of the birth defects was not related to intermarriage.

*For 10 of the 58 couples there was a clear genetic background for the defect.

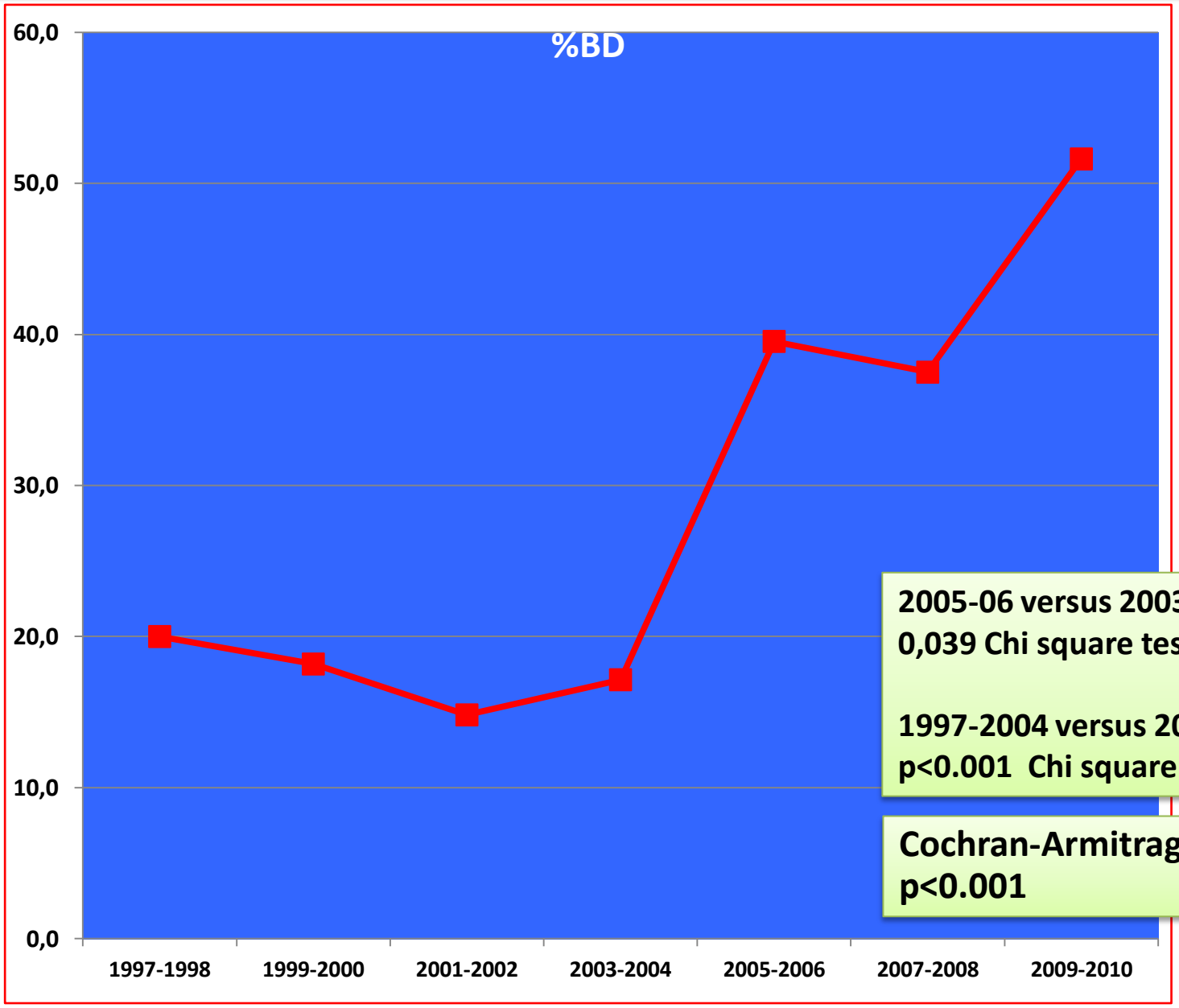
*No familiarity could be shown for the other 48 couples or from analysis of the collateral kin (n=1228).

*When recurrence of birth defects occurred, in two thirds of cases it involved different primary organ and kind of birth defect.

Together, these circumstances suggest that the birth defects in the cohort occurred mostly as novel events (sporadic), and these, in absence of novel inducers, should occur with equal chances in time.

But they do not

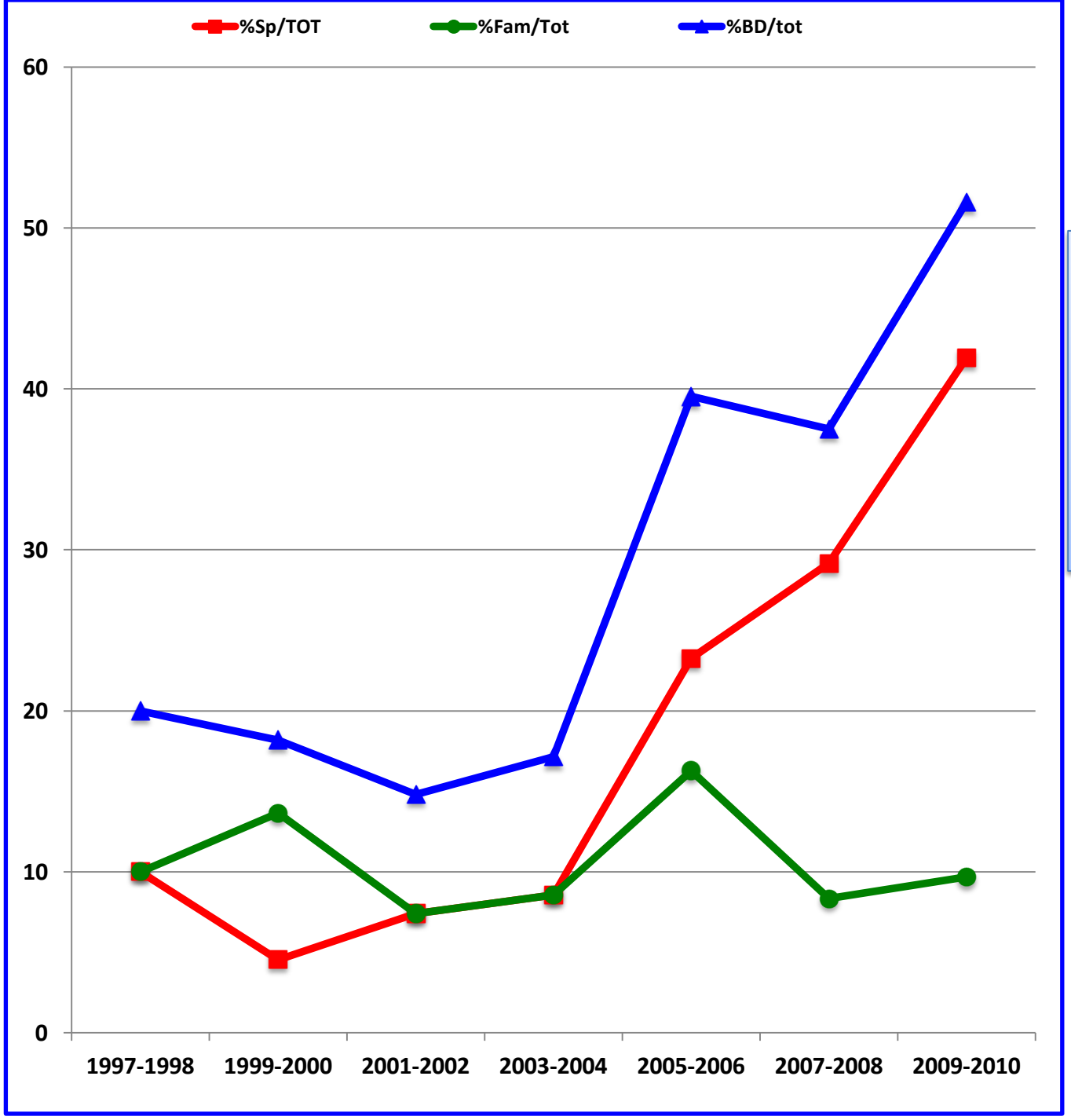
% of BD children in the progeny of 58 couples, grouped in two-year windows by birth date



2005-06 versus 2003-2004- p= 0,039 Chi square test

1997-2004 versus 2005-2010- p<0.001 Chi square test

Cochran-Armitrage trend test p<0.001

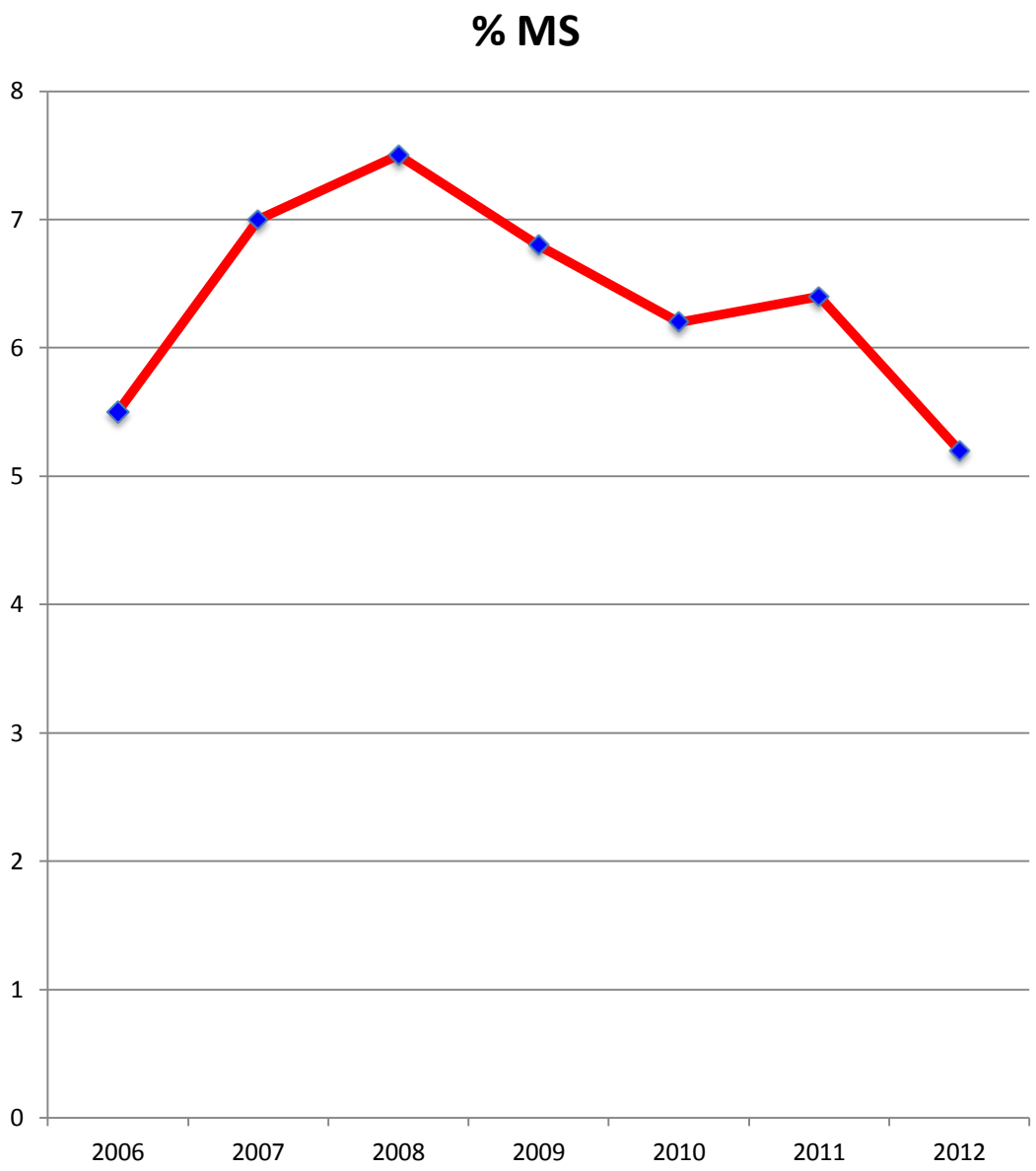


% of Birth defects on total born

For Sporadic BD
Cochran-Armitrage trend test p<0.001

For familiar BD
Cochran-Armitrage trend test p=0.59

Miscarriages



Percentage of miscarriages among more than 35.000 women per time point assisted by UNWRA for prenatal care among the refugee population.

$p<0.001$ between 2006 and 2008

Courtesy of Dr. M.Abu Kader, Unwra

In summary:

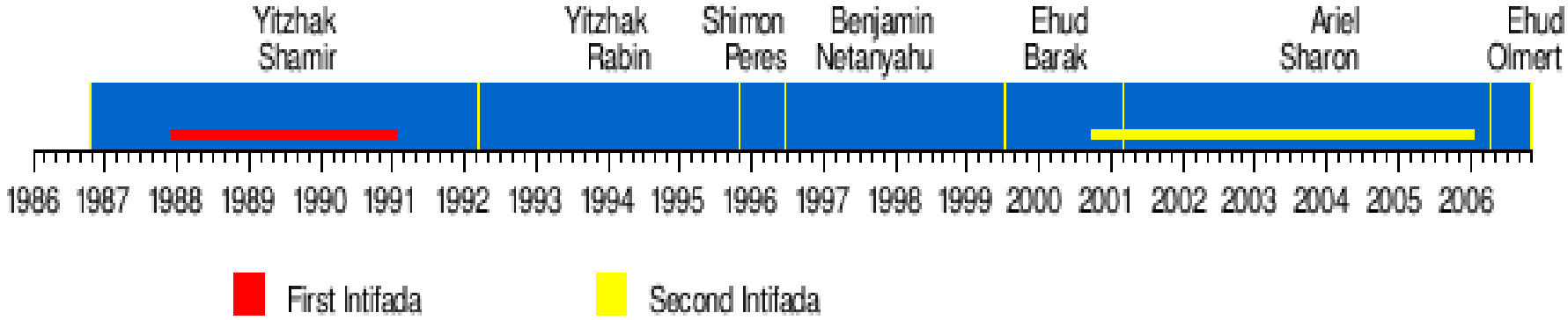
In Gaza there are abrupt changes in the reproductive health, with a rise in the presentation of miscarriages and birth defects.

They start before Cast Lead.

Many attacks were recorded before Cast Lead during the second Intifada.

Many of the ammunitions and weapons used before 2006 are also described to contain teratogen metals.

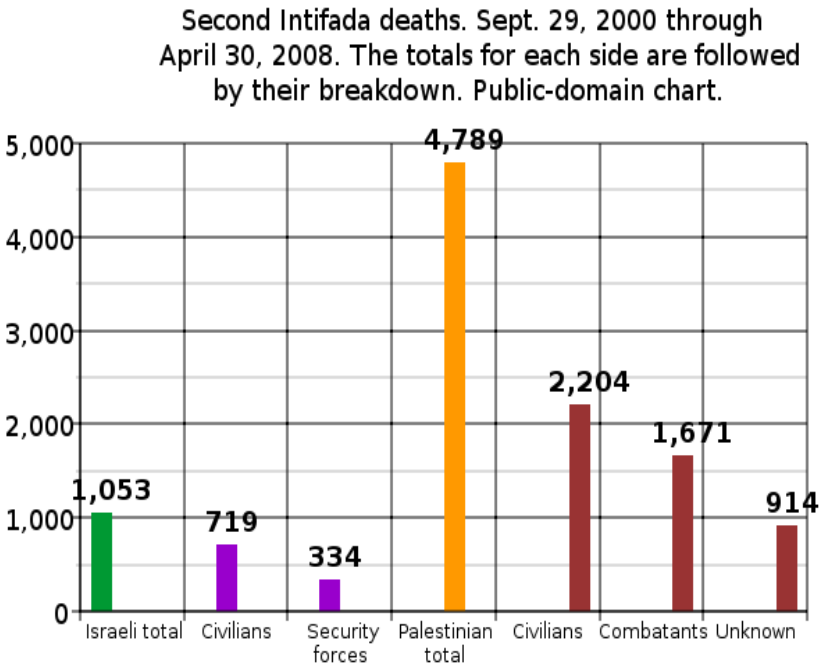
Weapons utilized in 2006 were analyzed and shown to include teratogen metals.



- the second Intifada in Gaza implied use by IOF of live ammunitions, shaped cone Heat ammunitions, air attacks by missiles started in 2001, and use of gases (CN, CS, OC) was documented.

- in 2005 destruction of the Gaza power station by bombing.

- in 2006 attacks with bombs with penetrator head and new weapons without fragments, which were shown to contain teratogen metals.



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On May 18, 2001, Israel **for the first time since 1967 used warplanes** to attack targets in the territories. Prior to that, airstrikes had been carried out with helicopter gunships. -Amnesty International's report on the first year of the Intifada.. ". In particular, the IDF have used US-supplied helicopter ...

2004

May- IDF launched a series of **armored raids** mainly on Rafah and refugee camps in Gaza
May 11 and 12, Palestinian militants destroyed two IDF M-113 APCs
May 18- the IDF launched **Operation Rainbow**

September 29-October 19, **2004** **Operation Days of Penitence**...**Thanks, ground troups and Israeli rocket strikes**. The U.S. government issues a statement urging Israel not to use excessive force during its current offensive into the Gaza Strip. (BBC)
The Israeli military begins an operation to create a 9 km (5.6 mi) "buffer zone" within the northernGaza Strip.
United Nations Secretary-General Kofi Annan requests that Israel halt its current military operations in the Gaza Strip
Israeli **unmanned drone aircraft** **fired a missile** towards the Al Ajramy street in Jabalia camp.
Israeli tank fired artillery at homes

- **2004 september-october**
- An Israeli **tank fired artillery** at homes in the Al Maslakh neighborhood of Jabalia camp
- Israeli military sources said were.. killed by a **missile fired from a helicopter**
- two Palestinian children were killed when the **Israeli military shelled** a crowd near the Jabaliya refugee camp.
- Israel says that **an Israeli helicopter gunship** fired
- Israeli **tanks fired shell** towards Abu Hasira neighborhood, near Jabalia …and in the town of Beit Lahia
- Israeli drone launched a **missile** hit close to the UNRWA Women's Center and towards Al Harthani Secondary School in Beit Lahia.

- **2005** June 28 **Operation Summer Rains**
- In the early hours Israeli **tanks, APCs and troops** entered the Gaza strip just hours after the **air force had taken out two main bridges and the only powerstation** in the strip, effectively shutting down electricity and water.
- On November 26, 2006, a truce was implemented
- IDF stressed the safety of their troops, using such heavily armored equipment as the **Merkava heavy tank and armored personnel carriers, and carried out airstrikes with various military aircraft including F-16s, drone aircraft and helicopter gunships**

Correlation of exposure to Cast Lead events with reproductive health in Gaza

We have previously presented evidence of correlation between birth defects in 2011 and exposure to white phosphorus shelling in 2009.

We also showed that WP shells contain teratogen metals

Birth defects presentation in 2011 and exposure to White Phosphorus during Cast Lead:

-couples with newborn with birth defect

27% exposed

-couples with normal children

1.7% exposed

Difference between exposure for parents of BD children *vs*. those of normal children is highly significant, $p < 0.001$.

Presence of the ammunition and their use in the residential places of families were confirmed on UN mine action maps

Not only exposure to White Phosphorus

After 2009 a large part of the reproducing population had been exposed to weaponry.

We registered:

61% of the couples with a newborn with birth defects in 2011 were exposed during Cast Lead to various weaponry.

67% of couples in the cohort of 58 couples with previous birth defect were also exposed during Cast Lead.

Given that metals delivered by weapons persist in the environment, and all the couples had stable residence, their continued exposure is likely and similarly for the residents of the same areas.

The recent and persisting diffuse exposure of the population to weaponry before, during and after Cast Lead, is likely to determine a further rise in birth defects in the future.

Conclusions from the study in Gaza

There is an increase of birth defects starting in 2005, possibly associated with military attacks during the second Intifada and the first fielding of novel metal augmented weaponry.

In 2010, and after further attacks with the same and similar weaponry, a positive trend was detected in the rise of frequency of BD, and is shown association of BD presentation with exposure to WP.

The trend is due to increase in sporadic BD, while familiar BD are steady over time.

Data of metal load in the hair of children collected at birth in 2011 are being elaborated presently and they will give further insight into the issue of contamination of affected individuals.

We need to continue registration at birth with the protocol implemented already, and is necessary to start studying molecular changes in affected individuals

In Fallujah, Iraq- 2010

No records of prevalence of birth defects were taken at the time, nor they were available from the past.

There was also no possibility, given the local situation, to conduct a “proper” epidemiological investigation

Assumption

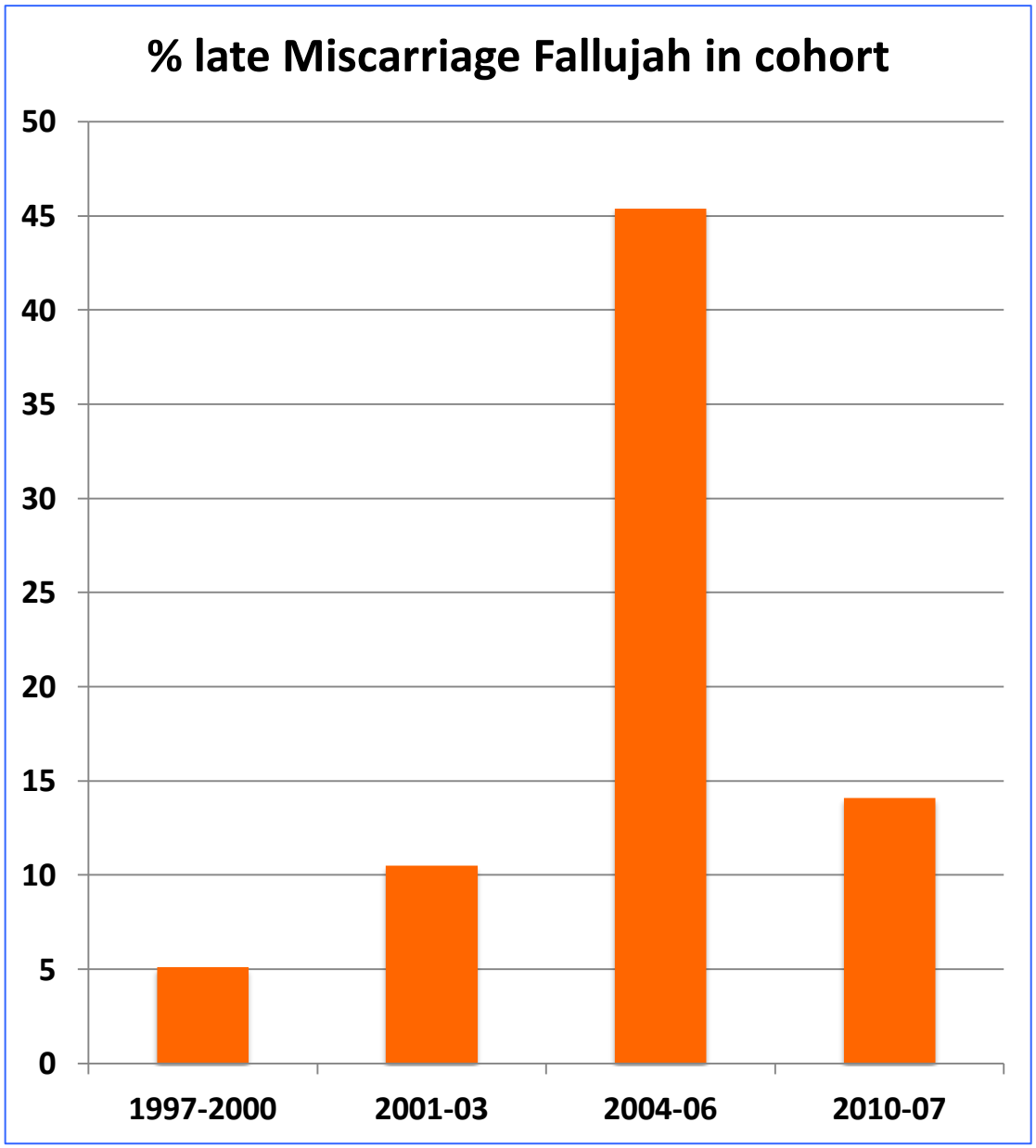
If the incidence of birth defects increased in time since 2004 up to 2010, as denounced by doctors, the potential environmental effectors associated with weapons used in the 2004-05 major attacks should be persistent and detectable to the present.

In 2010 we began a project to detect metal contamination at present time in the hair of newborn and infants with birth defects and their parents.

56 couples were enlisted as “first comers” with a birth defect child in maternity and pediatric of Fallujah General Hospital, by Dr Alaani and Dr Tafash, during 6 months in 2010.

33 couples had a birth defect newborn child in 2010,

23 couples had an infant or child with birth defect.



Transient and significant increase in miscarriages in the years 2004-2006

The changes in frequency of presentation in time suggests the introduction of inducers in the environment.

The change in the frequency of presentation in time of MS in 56 families has significance $p<0.0003$ by Chi square test for trend

PEDIGREES

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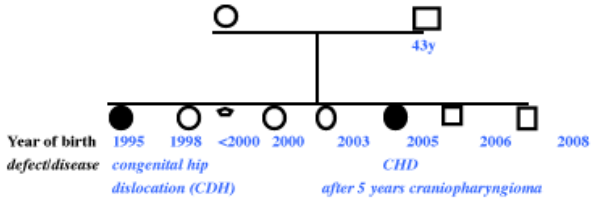

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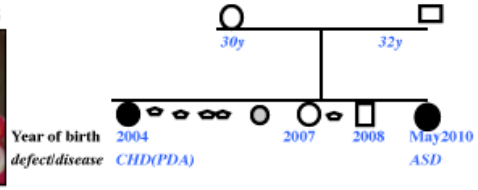

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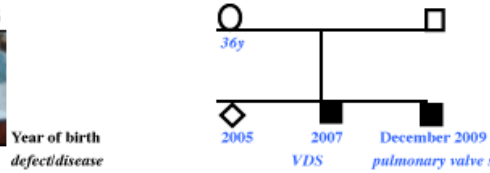

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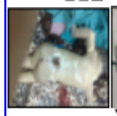

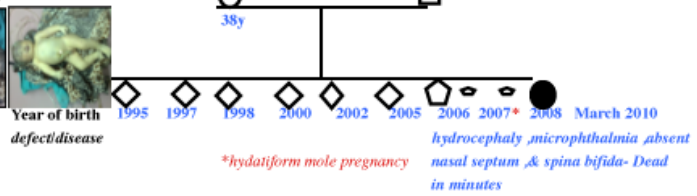

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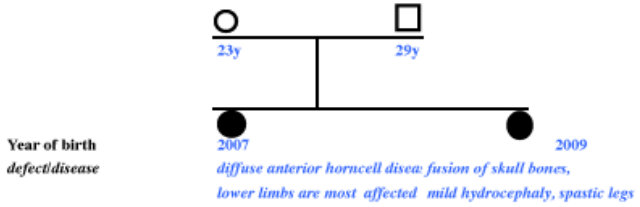
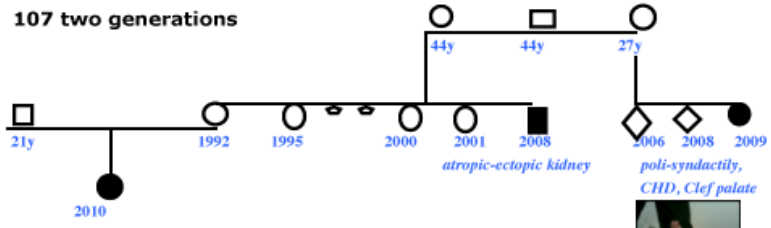


107 two generations



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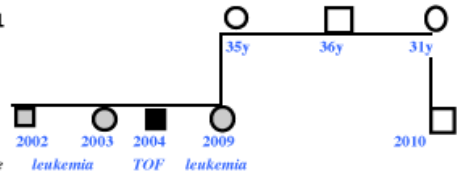

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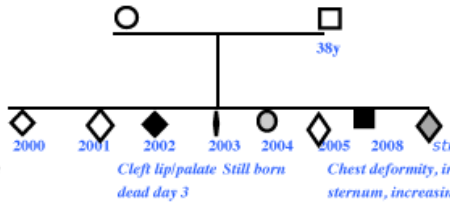

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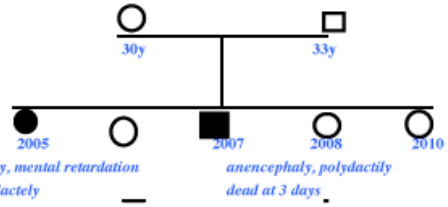


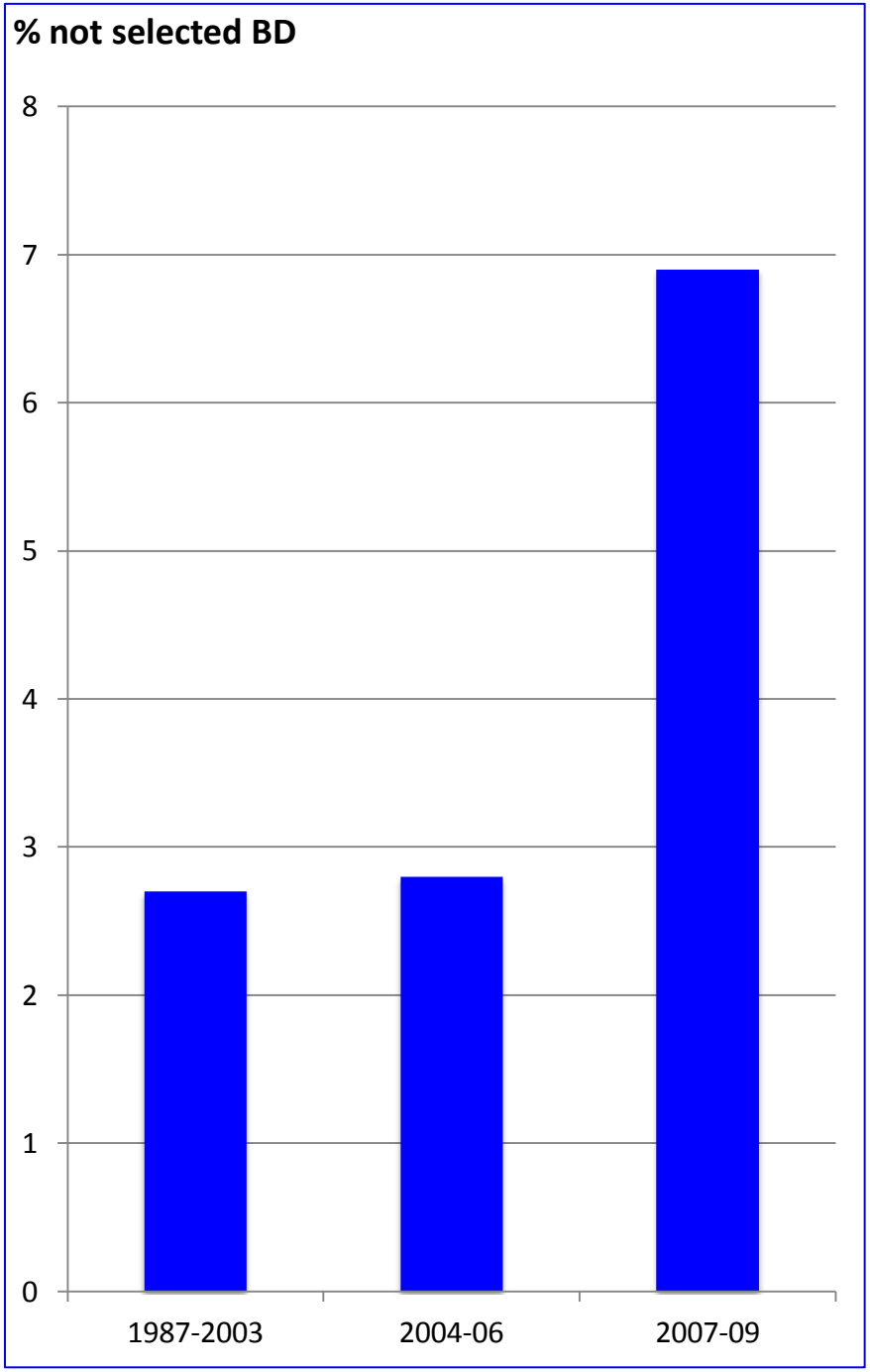
empty healthy	male
filled in black- birth defect	female
filled in grey dead	unknown sex
	twins
	still born
	miscarriage

Legend

Reproductive history of families with birth defects:

A) Families with newborn child with birth defect registered in 2010.

B) Families with birth defect patients returned for controls, children were born before 2010.



Distribution in time of BD that were not selected for in the cohort, shows their presentation in time.

Within the limits of small numbers, the increase in time of birth defects would be expected if effectors were suddenly introduced in the environment.

In summary, in Fallujah

The increase in the presentation rate of miscarriages and birth defects occurred after 2004.

Families were exposed to war-related events (83%), had stable residence (96%), BD presentation was unrelated to intermarriage.

In 2010, parents and their children still accumulated uranium from the environment at medium-high levels in their hair.

Other toxicants (Hg, Pb) are found occasionally in high levels in the children's hair.

In conclusion

We present a novel method to study the past of reproductive life based on studies of detailed pedigrees in a relatively small cohort of actively reproducing people

Information to reconstruct the history of reproductive health can be obtained **reliably**.

In addition, the information can often be controlled independently.

Accurately dated pedigree collection identifies the time of change in prevalence of miscarriages and birth defects in the past and describes its pattern in time.

Historical residence and exposure data allow to correlate these changes with war events.

Analytical studies in couples with birth defects give proof of contamination of the victims and indicate correlation of assumption of metals with birth defect occurrence.

The study of a relatively small cohort makes possible findings about the reproductive health changes that are often impossible in war or post war or occupied countries, and reduces the genetic heterogeneity of the sample.

The method can also be applied to the study of other environmental sensitive diseases, or to consequences of other major environmental changes with the potential to affect health.

Useful when there is urgency and is impossible to carry on longer population surveys due to the local conditions, or to the limited resources of skills and personnel

like when

registers were destroyed by
catastrophe, war, or are unreliable
and
signs of abrupt changes in presentation of diseases occur

but also

To rescue unavailable information of previous events when starting anew a register

Final remarks

It is not enough to obtain only numbers of prevalence or incidence of birth defects in the countries after war and aggressions.

For the people, the doctors and the scientists, it is important that we obtain, in each case, knowledge of correlation with exposures and timing of events.

The use of our protocol allows to obtain the history of the presentation of birth defects, to learn the familiarity of the disease, to correlate it with aggression, and to plan for the analytical and research work, in reality.

Thus, the approach adopted by WHO in Iraq is not sufficient. Their decision not to investigate correlations and causes is not justified.

Once the time is identified when a novel teratogen agent started to affect the reproductive life, specific toxicological inquiries can be better directed and issues of bonification and of public health addressed more efficiently.

Mechanistic events should be investigated at the molecular level, which possibly will give cues for remediation, prevention, counseling.

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Dedicated to

Resistant Palestinian child

Literature on metals in weaponry and implications for birth defects

GAZA

*Metals in craters since 2006 and in WP ammunitions in Gaza- *Newweapons 2010*

*Proof of fact of metals in weapon's wounds in Gaza- *Skaik et al 2010*

*Metals in Gaza children's hair after Cast lead- *Newweapons 2010*

IRAQ

*Metals in Iraqi newborn, children and adults hair-*Manduca 2011*

*DU in Bassora, Iraq, *local Government, UN*

*Sporadic presentation of birth defects in 4 polygamous families in Falujah, *Alaani et al 2011*

*Reports of enriched U contamination in hair of parents with child with birth defect in Falujah- *Alaani et al 2012*

*Pilot study about increase in birth defects in Falujah, Al*aani et al 2012*