

DDT in human milk and mental capacities in children at school age: An additional view on PISA 2000*

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Abstract

OBJECTIVES: To investigate a possible lasting impact of dichlorodiphenyl trichloroethane (DDT) exposure in neonatal life on mental capacities in later life.

MATERIAL AND METHODS: Relationships were evaluated by correlation and regression analysis between total DDT concentrations in human breast milk in the years of birth (1984/1985) and measurements of mental capacities obtained in pupils of the PISA 2000 studies as well as percentages of backward children in Germany in 1994/95.

RESULTS: Comparing total DDT levels in human milk during the years of birth (1984/85) evaluable for eleven PISA countries with assessed mental capacities of 15-year-old pupils of PISA International, a significant inverse correlation was found ($p < 0.001$), even after adjustment for socioeconomic statuses ($p = 0.001$). Furthermore, a significant inverse correlation ($p < 0.001$) was also obtained between the total DDT concentrations in human milk in 1984/85 in ten foreign countries of three continents plus fourteen Federal States of Germany and the mental capacities of 15 year-old pupils of PISA International plus PISA National (Germany) 2000. Finally, a significant positive correlation was observed between total DDT contents in human milk in 1984/85 and the percentages of backward school children in 1994/95 in Federal States of Germany ($p < 0.001$).

CONCLUSIONS: These data – in association with additional experimental and epidemiological findings – suggest that DDT is a “neuroendocrine disrupter” as well as a “functional teratogen” leading to harmful effects on brain development and mental capacities in later life. Thus, a neuroendocrine prophylaxis during critical developmental periods in early life – as recommended by our group since many years – appears to be most important for primary preventive medicine but even for “preventive pedagogics”. The validity of these theses should be re-tested in future PISA studies.

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Abbreviations and Units:

PISA:	Programme for International Student Assessment
DDT:	dichlorodiphenyl trichloroethane
DDE:	dichlorodiphenyl dichloroethene
NEIS:	Neuro-Endocrine-Immune-System
NEIP:	Neuro-Endocrine-Immune-Prophylaxis
AUS:	Australia
CAN:	Canada
FIN:	Finland
GER:	Germany
ITA:	Italy
MEX:	Mexico
NOR:	Norway
POL:	Poland
SWE:	Sweden
UK:	United Kingdom
USA:	United States of America
BA:	Bavaria
BB:	Brandenburg
BW:	Baden Wuerttemberg
BR:	Bremen
HA:	Hamburg
HE:	Hesse
LS:	Lower-Saxony
MW:	Mecklenburg-Western Pomerania
NW:	North Rhine-Westphalia
SA:	Saxony-Anhalt
SAX:	Saxony
SH:	Schleswig-Holstein
SL:	Saarland
TH:	Thuringia
RP:	Rhineland-Palatinate

Introduction

DDT, which was worldwide used as pesticide, is a chlorinated phenyl derivative (dichlorodiphenyl trichloroethane). Some indications for negative long-term effects of chlorinated phenyl compounds on mental capacities were observed in animal experiments and studies in human beings (1,2).

In 1992, Eriksson et al. (3) reported that neonatal exposure to DDT clearly affected the muscarinic cholinergic receptors of the cerebral cortex in newborn mice, leading to permanent disturbances of the cholinergic system in the brain combined with disruption of learning capacity in adult life. Ten years before, we described that a significant decrease of acetylcholine in the brain, induced in newborn rats by maternal deprivation, gave rise to a significantly diminished emotionality, learning capacity, and memory capacity in later life (4). These permanent changes could be prevented by neonatal administration of an acetylcholinesterase inhibitor.

Decreased mental capacities were also observed in children who spent their first year of life in day-nurseries (5). In addition, decreased mental performance and psychical adaptability were demonstrated in pupils who were not breast-fed during their first months of life (6). Finally, we found in children who received no human milk but cowmilk formula abnormal blood concentrations of neutral amino acids which can affect neurotransmitter concentrations in the developing brain (7). Furthermore, we could demonstrate a significant increase in the prevalence of backward children in

Berlin between the mid 1950s and the late 1960s ($p < 0.001$), followed by a significant decrease afterwards (8). Interestingly, a similar time course was described for the production and application of DDT in Germany (9).

With regard to these observations, after publication of the International and National PISA-Studies in 2001 (10) and 2002 (11), respectively, we therefore tried to examine whether and how far perinatal DDT exposure estimated by maternal milk might be associated with mental capacities later in life.

Material and Methods

For evaluation of the general mental capacities of 15-year-old pupils the mean values of the scores for reading literacy, mathematical literacy, and scientific literacy were used for evaluable countries of worldwide PISA International (10) and for the Federal States of Germany of PISA National (11). In addition, percentages of backward children with decreased learning capability in 1994/95 were also taken into consideration for the Federal States of Germany, as published by the Conference of Ministers of Culture (12). For this calculation the Saarland (SL) had to be excluded as a statistic outsider because of its exceptionally high integrative pedagogic system (12). Berlin had also to be excluded here because of the different situations in East- and West-Berlin not allowing a reliable evaluation. Finally, Berlin and Hamburg had to be excluded in a combined evaluation of PISA 2000 data, since the mental capacities were not ascertained in enough pupils in these Townstates.

For calculation of total DDT contents in human milk during the years of birth (1984/85) for different countries worldwide, DDT levels in human milk compiled by Smith (13) were used for those 11 countries in which at least 100 human milk probes had been determined during and/or a few years before or after 1984/85. All data were extrapolated to the years 1984/85, i.e., the years of birth of PISA pupils. For Western countries with prohibition of DDT since the 1970s a population half-life time for DDT of 5 years (13) was used for extrapolation. For Germany, with regard to PISA International (10) the total DDT levels for the years 1984/85 were extrapolated by proportional combination of East- and West-Germany.

For calculation of total DDT concentrations in human milk in 1984/85 in the old Federal States of Germany the data of 1991–97 published by Vieth et al. were used for estimation of mean levels in 1993/94 (14, 15). These means were then multiplied with the factor 2.6, since the ratio of total DDT in human milk between 1984/85 and 1993/94 for the means of all old Federal States of Germany was found to be 2.6/1, approximately (15). For estimation of total DDT concentrations in human milk in 1984/85 in the new Federal States of Germany (former GDR) the data available for 1990–92 were used, published by Alder et al. (16). These means were multiplied with the factor 2 in order to estimate levels of 1984/85, since the ratio of total DDT in human

milk between 1984/85 and 1991 (mean of 1990–92) was found to be approximately 2/1 for all new Federal States of Germany (16, 17). Hence, from a whole-population based point of view the half-concentration times of DDT were somewhat longer in whole Germany (East + West) than in other countries (13). However, this is conceivable by the fact, that DDT application in East-Germany was first strongly reduced and then completely prohibited only in the mid 1980s, while in West-Germany it was prohibited already in the 1970s. Moreover, foodstuffs with different total DDT contaminations were considerably exchanged between East- and West-Germany, especially after the reunification.

For statistical evaluations, relations between variables were first analyzed by Spearman's rank correlation test. DDT levels were not normally distributed and were therefore normalized by log-transformation. For analysis of relationships, univariate linear regression analysis was then performed, followed by multiple linear regression analysis with adjustment for socioeconomic status data provided by PISA International (10). For all evaluations, $p < 0.01$ was considered significant. All statistical tests were accomplished using the SPSS for Windows version 10.0 statistical software package (SPSS, Munich, Germany).

Results

As demonstrated in **Fig. 1**, a significant inverse relationship was found between the logarithms of total DDT concentrations in human breast milk during the years of birth in 1984/85 of pupils in eleven different countries worldwide with sufficient DDT determinations according to the criteria described above (13) and the mental capacities at 15 years of age in school children in these countries according to PISA 2000 (10), even after adjustment for the socioeconomic status.

Moreover, as demonstrated in **Fig. 2** a significant inverse relation was also observed between the logarithms of total DDT concentrations in human milk of ten foreign countries *plus* fourteen Federal States of Germany during the years of birth in 1984/85 and the mental capacities of pupils in these countries and Federal States at 15 years of age, i.e. in 2000 (10, 11).

Finally, in **Fig. 3** it is shown that a significant positive correlation does exist between the logarithms of total DDT contents in human breast milk probes in fourteen Federal States of Germany in 1984/85 and the percentages of backward children in 1994/95, visiting special schools because of decreased learning capability.

Discussion

In this study population based levels of DDT in human breast milk during the years of birth of pupils evaluated in the worldwide PISA 2000 studies were found to be inversely correlated to the mental capacities in children at school age. These observations speak for a dose-dependent deleterious impact of perinatal DDT exposure on mental health and mental fitness throughout later life.

Since the 1970s neurotransmitters as well as classical hormones and cytokines were recognized by our group to be important organizers of the brain and the Neuro-Endocrine-Immune-System (NEIS). Obviously, these chemical messengers are capable to epigenetically "program" fundamental processes of life by irreversible interactions with the genome during critical pre- and early postnatal differentiation periods (18, 19, 20). In view of extensive animal experiments as well as epidemiological and clinical studies, mental disorders and important diseases of reproduction, metabolism, information processing and immune responsiveness –

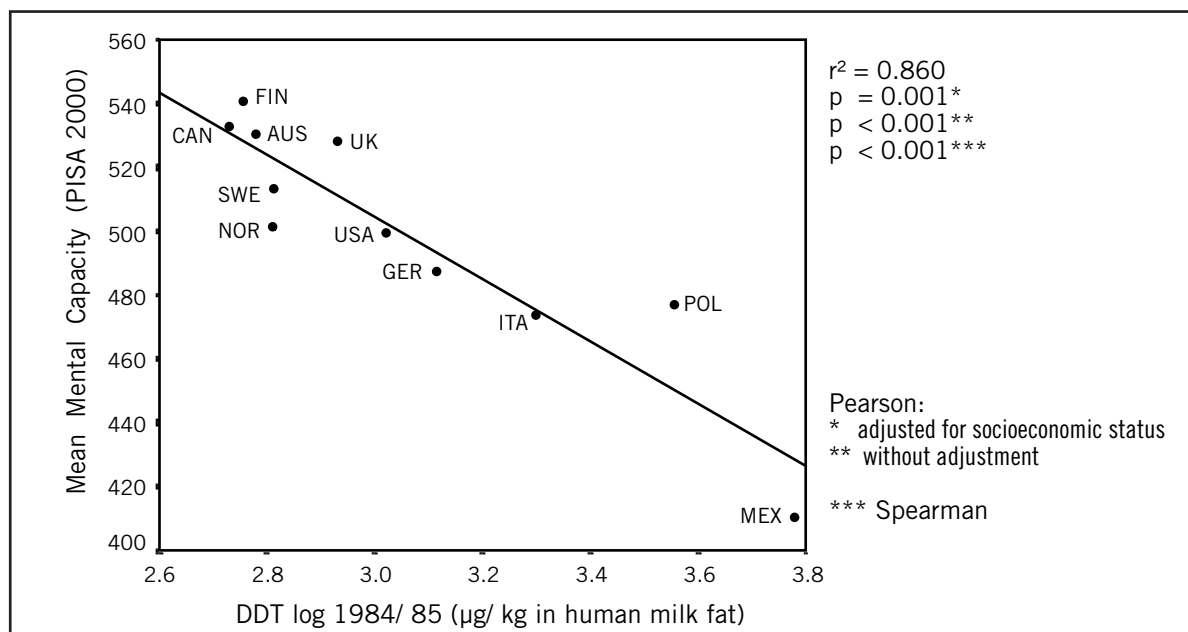


Fig. 1. Linear regression plots for DDT concentrations in human breast milk (log-transformed) in the years of birth (1984/85) vs mean mental capacities in school children according to PISA International 2000 (10).

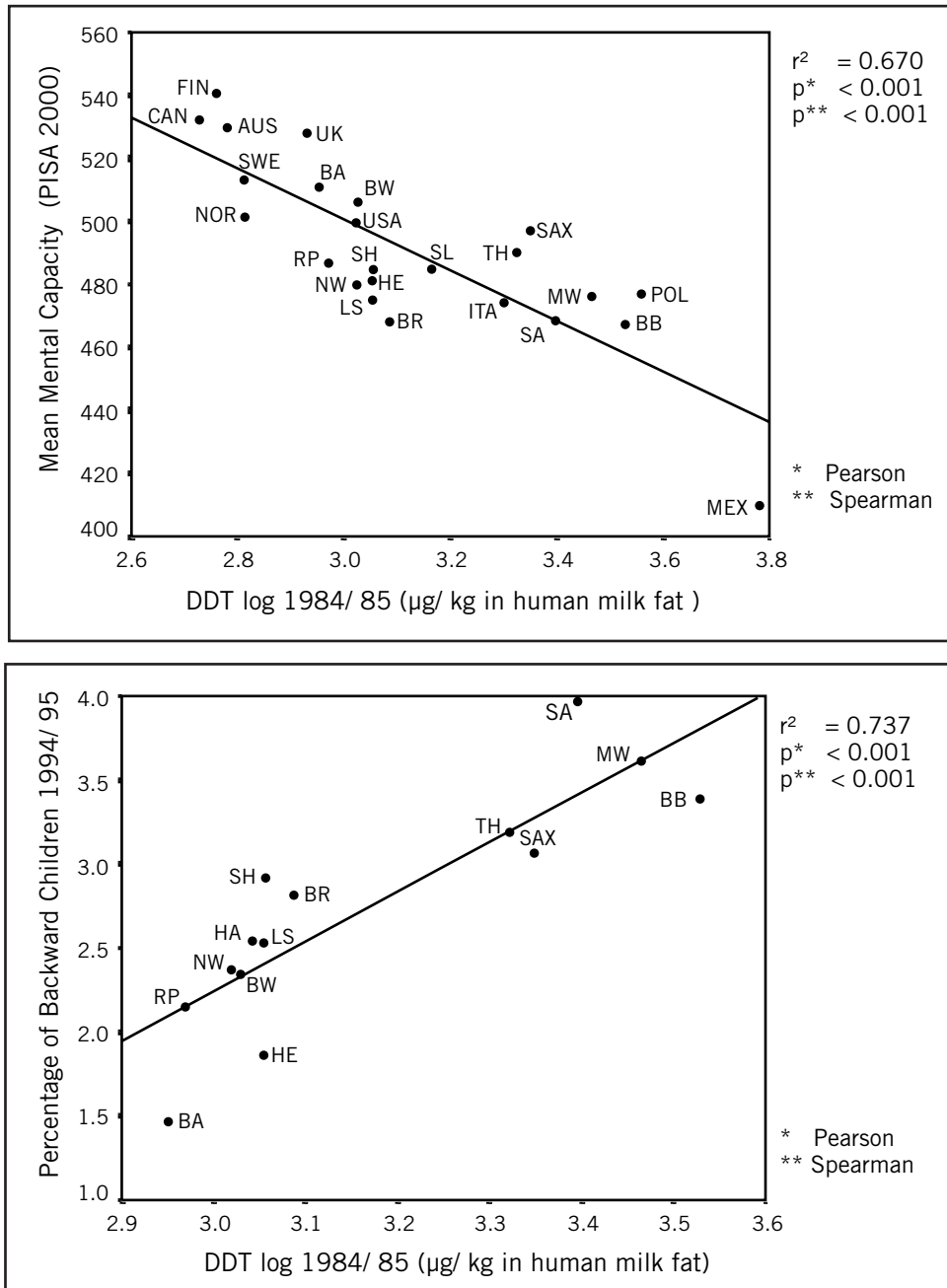


Fig. 2. Linear regression plots for DDT concentrations in human breast milk (log-transformed) in the years of birth (1984/85) vs mean mental capacities in school children according to PISA International (10) plus PISA National (Germany) 2000 (11).

Fig. 3. Linear regression plots for DDT concentrations in human breast milk (log-transformed) in the years of birth (1984/85) vs percentages of backward school children in 1994/95 in fourteen Federal States of Germany.

called so far as being idiopathic, essential, cryptogenic, primary or genuine – were thereby recognized to be inducible by teratogenic effects resulting from abnormal levels of neurotransmitters, hormones and/or cytokines and may therefore be preventable, at least in part, by improving the external and/or internal environment during critical organization periods of the organism. Therefore, the “*Functional Teratology*” was founded as the science of teratogenetically induced persisting malfunctions (19, 20). In other words, “*Structural Teratology*” or teratomorphology as the science of macroscopic malformations was supplemented by “*Functional Teratology*”, e.g. teratophysiology, teratoneuropsychology and teratoimmunology.

The findings described in this investigation suggest that DDT may be co-responsible for the development of reduced mental capacities and increased frequencies of backward school children. Therefore, DDT appears to be an important “functional teratogen” for the development of mental disorders, possibly mediated by persistent disturbances of the cholinergic system (3). Noteworthy, in a further preliminary evaluation we have meanwhile found in East-Berlin significantly more cases of cryptorchidism in backward children (9 out of 61 boys) as compared to control boys (8 out of 315; $p < 0.001$). On the other hand, from this investigation DDT and its metabolite DDE seem to be perinatal inducers of increased risk of developing cryptorchidism

(several fold increase after introduction of DDT and several fold decrease after prohibition; $p < 0.001$). It should be mentioned, however, that total DDT concentrations in human milk are not only an indirect indicator of the exposure of the offspring to DDT in early postnatal life but also in prenatal life.

In our opinion, it is reasonable to suggest that millions of human beings may be mentally, emotionally and/or physically handicapped or disabled through developmental disorders and/or even diseases that could be essentially prevented by a Neuroendocrine Prophylaxis or Neuro-Endocrine-Immune Prophylaxis (NEIP). In this context, 10 recommendations were given for the prevention or correction of abnormal levels of systemic hormones, neurotransmitters and cytokines during brain development, e.g., by prevention of pollution with teratogenic environmental chemicals (21, 22).

Nowadays, different school-systems and pre-school-systems, of course in interaction with the families, are generally considered to be responsible for very different mental capacities and school outcomes in various countries and federal states. In our opinion, however, these systems offer predominantly different learning possibilities, whereas the natural, chemical, and psychosocial environments during critical differentiation periods of the brain predetermine most of all life-long learning *capabilities*, which are mediated and perinatally "programmed" by neurotransmitters, hormones and cytokines.

Due to this theory, mental capacities can be expected to be improvable for the future in many countries and federal states by reduction of DDT levels and concentrations of other teratogenic pollutants as well as by prevention, e.g., of malnutrition, stress, alcohol, nicotine, and drug abuse and/or psychosocial deprivation during pre- and early postnatal organization periods of the brain, when stem cells are developing *in vivo* to billions of highly differentiated neurons. Therefore, considering the presented data a NEIP by preventing or correcting abnormal levels of neurotransmitters, hormones, and/or cytokines appears to be not only an innovative measure for primary preventive medicine (22) but also for "primary preventive pedagogics" with an apparently great importance for the future of human societies.

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