Research and Perspectives in Endocrine Interactions

Multi-System Endocrine Disruption

Bearbeitet von
Jean-Pierre Bourguignon, Bernard Jégou, Bernard Kerdelhué, Jorma Toppari, Yves Christen

2012 2011. Buch. XI, 175 S. Hardcover
ISBN 978 3 642 22774 5
Format (B x L): 15,5 x 23,5 cm
Gewicht: 450 g

Preface

In the field of endocrine disruption, the reproductive system has been a priority concern of scientists and environment/public health agencies for several decades, based on observations of fertility impairment in wildlife as well as in humans. In women, intrauterine exposure to diethylstilbestrol (DES) raised the issue of carcinogenicity as early as the 1970s. Although this synthetic compound has been banned for many years, there are still unclear matters of concern such as transgenerational epigenetic effects that provide rationale for monitoring the third generation descending from exposed pregnant women. Another lesson drawn from decades of research is the widened scope of the endpoints of repro-endocrine disruption. In the male, beyond germ cell line differentiation and semen quality, other targets involve testicular descent, epididymis, prostate and external genitalia. The list of potentially disrupting chemicals has also increased dramatically: not only are pesticides and insecticides – including chlordecone and polychlorobiphenyls (PCBs) – involved but also new classes of compounds are emerging, such as analgesics. In addition, chemicals linked to plastic manufacture, like phthalates, have been studied, resulting in convincing evidence of a causal role in the rodent model of testicular dysgenesis syndrome and increasing evidence of association with the occurrence of genital malformations in human males. Although phthalates are banned from some toys and cosmetics, they are still ubiquitous. Among pending questions, the evidence linking early exposure to phthalates and oligospermia/testicular cancer in human males deserves further study. Because phthalates are present in parenteral nutrition or perfusion material, the consequences of prolonged exposure in the critical sensitive period of neonatal life need to be addressed.

More recently, the hypothalamus and the brain have been shown to be possible targets of endocrine disrupting chemicals (EDCs), accounting for neuro-endocrine disruption. In the hypothalamus, the gonadotrophin releasing hormone neurons and afferent neurono-glial system are sensitive to EDCs, leading to disorders of sexual differentiation and maturation. Aromatase and kisspeptin-neurokinin B are likely key mediators of EDC effects. Other endpoints in the CNS possibly include neurogenesis, migration and synaptogenesis in brain cortex and hippocampus. Here, the thyroid hormone system is pivotal, due to its physiological role in early

CNS development. Although they have been banned, PCBs are still among the EDCs involved, due to their persistence in the environment. A still open question is whether stresses other than chemicals (e.g., psychosocial, nutritional, etc.) interact with the sensitivity to deleterious effects of EDCs. For example, does iodine deficiency or exposure to nitrates sensitize the brain to PCB effects?

Another emerging area of endocrine disruption is the central and peripheral control of energy balance. Among other findings, the occurrence of obesity and insulin resistance in adulthood after neonatal exposure to the potent synthetic estrogen DES has opened a new field, possibly substantiating a role for EDCs, including Bisphenol A (BPA), in the epidemics of obesity and type 2 diabetes. BPA accounts for particular epidemiologic and scientific challenges due to its ubiquity and non-linear dose-response curve. The metabo-endocrine endpoints involve adipocytes, pancreatic Beta cells and the intestinal epithelium, where cell proliferation as well as differentiation could be affected by EDCs.

These three areas – repro-endocrine, neuro-endocrine and metabo-endocrine disruption – share common features: ontogenetic disturbances result from particular fetal sensitivity to endocrine disruption with sexually dimorphic responses. Epigenetic mechanisms are likely pivotal.

It has been our privilege, thanks to the Fondation Ipsen, to convene in Paris (May 9, 2011) experts to exchange findings and opinions in the different areas of endocrine disruption summarized above. Questions raised about one system may find answers based on findings in another system, justifying a multi-system perspective in endocrine disruption that appears to be a whole-body burden and a challenge for the whole scientific community, including epidemiologists, toxicologists, geneticists and endocrinologists among others.

The editors wish to express their gratitude to Mrs Astrid de Gérard for the organization of the meeting and Mrs Mary Lynn Gage for her editorial assistance.

Jean-Pierre Bourguignon

http://www.springer.com/978-3-642-22774-5

Multi-System Endocrine Disruption

(Eds.)J.-P. Bourguignon; B. Jégou; B. Kerdelhué; J. Toppari; Y. Christen

2012, XI, 175 p. 24 illus., 15 in color., Hardcover
ISBN: 978-3-642-22774-5