

## **2. Action mechanisms of endocrine disruptors**

### **(1) Definition**

There is continuing international scientific debate over the definition of endocrine disruptors because the interactions of these chemicals with the endocrine system are not well known. At the 50<sup>th</sup> World Health Assembly in 1997, resolution WHA 50.13<sup>\*1</sup> was adopted. This resolution stipulated that the Director-General of the WHO should take the necessary steps to reinforce WHO leadership in undertaking risk assessment of endocrine disruptors, and in promoting research on the health effects of exposure to these chemicals.<sup>\*1</sup>

The term “endocrine disruptor” refers to any kind of chemical which disrupts the aforementioned endocrine system. The term “disruption” refers to damaging effects on the reproduction and development of humans and wildlife that may ultimately threaten the “continuation of species.” In practice, it has not yet been determined which substances should come under this category, and various attempts at categorization are under way. At present, the working definition is the one given below, focusing on the phenomena that bring about “ ~ changes in endocrine environment which have damaging effects on reproduction and development at various organism levels.”

- What is an “endocrine disruptor”?

“An endocrine disruptor is an exogenous substance or mixture that alters function(s) of the endocrine system and causes adverse health effects in an intact organism, or its progeny, or (sub)populations.” [The International Programme on Chemical Safety (IPCS)/the World Health Organization (WHO)]<sup>\*2</sup>

However, the Smithsonian Workshop of February 1997 defined an endocrine disruptor as “ ~ an exogenous agent which interferes with the synthesis, secretion, transport, binding, action, or elimination of natural hormones in the body which are responsible for the maintenance of homeostasis, reproduction, development or behavior.” This definition emphasized the importance of considering the functional characteristics of endocrine mechanisms in understanding these chemicals.

### **(2) Action mechanisms**

Generally, endocrine disruptors are natural products or synthesized chemicals which mimic, reinforce, or inhibit the actions of hormones. There are various assumptions about the action mechanisms of these chemicals in the body. Several possibilities, given below, have been suggested regarding actions on hormone receptors.

1. Inhibition of the interaction between hormones and receptors

A chemical may modify the binding of a hormone with its receptor, thereby affecting normal cellular functions involving the hormone.

2. Function as false hormones

A chemical similar to a hormone in structure may interact directly with the hormone receptor, thereby causing unnecessary and abnormal cellular functions.

3. Alteration of the development of receptors and their functions

A chemical may activate or suppress the development of a cell receptor and alter the normal hormonal activities.

4. Alteration of functions by interactions with hormones

A chemical may interact with a hormone and alter the message issued by the hormone, thereby altering cellular functions.

5. Abnormalities or deficiencies due to impairment of hormone production

A chemical may damage the production of a hormone, in particular one which regulates steroid metabolism, thereby causing hormone abnormalities or deficiencies.

The actions of endocrine disruptors are known to involve several possible factors, including (a) the same chemical may have different effects on different organs, (b) the same chemical may have different effects at different stages in development, including the fetal period, (c) chemicals may be affected by the individual organism's environment, nutrition, age, or other effects, (d) chemicals may interact with other factors, such as other chemicals that may be present (e.g., additive effects and synergistic effects), and (e) the same chemical may cause different responses in different species.

In this way, these chemicals are assumed to affect various processes involving endocrine functions and their mechanisms; in fact, such phenomena have been reported. As the actions of hormones in the body are very diverse, endocrine

disruptors may cause commensurately extensive disorders. Therefore, the definition given at the Smithsonian Workshop (mentioned above) should be also considered. Based on our present understanding is the suggestion that these chemicals may affect not only the endocrine system but also higher-order systems, such as the nervous and immune systems.