

Health in a Bottle

SEARCHING FOR THE DRUGS THAT HELP

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Some drugs are used for the diagnosis of disease states rather than as therapeutic agents. A good example of such a drug, used in the diagnosis of a rare clinical disorder, is metyrapone, marketed by CIBA Pharmaceutical Company, whose trademark is Metopirone, in January, 1962. The pituitary gland is a small structure connected to the base of the brain. Its anterior (front) lobe manufactures several hormones that travel at intervals in the blood to various other endocrine (hormonal) glands, which are stimulated to secrete the hormones they manufacture into the bloodstream. Sometimes the pituitary gland loses its ability, at least partially, to produce its hormones, thus causing a state of partial hypopituitarism or limited pituitary reserve. One of the hormones secreted by the

(3)

pituitary gland is ACTH (AdrenoCorticoTropic Hormone). This substance stimulates the cortex (outer portion) of the adrenal glands (one is perched atop each kidney) to manufacture, among other compounds, cortisol (hydrocortisone), an important hormone. As the level of cortisol rises in the blood, the secretion of ACTH is inhibited. When the blood level of cortisol is low, the secretion of ACTH is stimulated. This is a good example of an automatic biologic feedback mechanism.

ACTH really causes the formation of precursors of cortisol, and the drug, metyrapone, blocks the final synthesis of cortisol from these precursors. When it is given to normal people, it causes a large continuous secretion of ACTH because the level of cortisol in the blood naturally is very low. The precursors of cortisol are excreted in the urine and can be determined chemically. If the pituitary gland is normal and is secreting ACTH, the level of these substances increases when metyrapone is given to the patient. If, on the other hand, the patient's gland is underactive (partial hypopituitarism) the administration of the drug does not cause an increase in the urinary level of cortisol precursors.