ON THE PATHOLOGICAL ACTION OF ARSENICALS UPON THE ADRENALS

By Wade H. Brown and Louise Pearce

ROCKEFELLER INSTITUTE FOR MEDICAL RESEARCH, NEW YORK
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The fact that arsenicals of diverse chemical constitution exert a pronounced pathological action upon the adrenals has not been generally recognized. The importance of this adrenotropic action was first impressed upon us while carrying out the routine biological tests of compounds of arsenic in our chemotherapeutic studies. Observations on more than sixty compounds including such substances as arsenious acid, arsenic acid, sodium cacodylate, atoxyl, arsacetin, arsenophenylglycine, salvarsan, and neosalvarsan have shown that, without exception, toxic doses of all of these arsenicals produce definite lesions of the adrenals.

The adrenotropic action of all compounds of arsenic is not equally great or identical in character but the lesions produced by a given compound in a given animal species are quite constant and in some instances are the dominant pathological manifestations of the toxic action of the compounds. The essential features of this action concern vascular changes in the adrenal, alterations in the lipoid content, cellular degeneration, and the effect upon the chromaffin.

In general, arsenical intoxication in the guinea pig produces an acute enlargement of the adrenals with some congestion and hemorrhage. The lipoid granules, normally demonstrable in the outer half of the cortex with Herxheimer's Scharlach R., first appear as larger droplets. Later, the demonstrable lipoids increase in amount and are spread over the entire adrenal cortex. This stage of lipoid increase is succeeded by one of diminution which with some compounds progresses almost to exhaustion.

The cells of both the cortex and the medulla show a variety of degenerative changes and even necrosis; colloid degeneration of the medulla is particularly striking. While the cortex is slightly infiltrated with leucocytes the accumulation of both leucocytes and polyblasts in the medulla is especially marked with such substances as arsenophenylglycine.

Regeneration of cortical cells by mitosis is very active after forty-eight hours and mitotic figures are occasionally seen in the cells of the medulla.

The effect of arsenicals upon the chromaffin is of especial interest. Some compounds seem to exercise but slight influences upon the chro-
maffin content of the adrenals while others, such as sodium cacodylate, salvarsan, and neosalvarsan, cause a rapid and marked decrease in this substance, as judged by the color of the medullary cells after fixation in Müller's fluid.

From these observations it appears that the adrenotropic action of arsenicals is one of the most constant and important features of arsenical intoxication and we suggest that therapeutic doses of some arsenicals may be found to produce definite stimulation of the adrenal glands.

VARIATIONS IN THE CHARACTER AND DISTRIBUTION OF THE RENAL LESIONS PRODUCED BY COMPOUNDS OF ARSENIC

By Louise Pearce and Wade H. Brown
ROCKEFELDER INSTITUTE FOR MEDICAL RESEARCH, NEW YORK
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The chemical agents employed in the production of experimental nephritis are usually divided into two classes, those producing tubular lesions and those producing vascular lesions, to the latter group of which the compounds of arsenic have been assigned. From a study of the renal lesions produced by a large number of arsenicals, however, we have been led to question the validity of such a classification and to view the pathogenic action of such substances from the standpoint of their chemical constitution as well as their arsenic content.

The classical hemorrhagic kidney of arsenuous acid is by no means constant for all compounds of arsenic. Grossly, the kidneys of dogs given lethal doses of such substances as arsenuous acid, salvarsan, neosalvarsan, galyl, arsenophenylglycine, atoxyl, and arsacetin are separable into two extreme groups, the red and the pale kidneys, with transitional types in which the predominating changes ally them more closely with the one group or the other. In the group of red kidneys, congestion and hemorrhage are the dominant features of the arsenical action, while in the pale kidneys, the dominant lesion is tubular.

Upon closer analysis of the gross and microscopic changes we can make a further differentiation of the action of compounds that produce kidneys of the one or the other of these types. For example, arsenuous acid, salvarsan, neosalvarsan, and galyl all produce red kidneys, but the congestion and hemorrhage produced by arsenuous acid is diffuse in character with but slight tubular necrosis, while the vascular injury of salvarsan, neosalvarsan, and galyl is more pronounced in the cortex and the boundary zone and is accompanied by much more marked