2-m.amp. shock in response to a warning auditory stimulus, individual trials being separated by 6-min. intervals. The criterion of completed conditioning was a correct response to the conditioning stimulus of not less than 9 out of 10 times on two consecutive days. The animals were then used for assay and the number of mistakes plotted against the dose-level. N-Acetyl-5-methoxytryptamine caused no behavioural disturbance at dose-levels of 0·2 mM/kgm. At dose-levels between 0·1 and 0·3 mM/kgm. 5-methoxygramine caused a somewhat greater degree of disturbance than did gramine. At 0·1 mM/kgm., 5-methoxytryptamine, bufotenine and serotonin all gave similar results, though in the case of the latter compound the paresis of the hind legs which developed introduced a physical handicap which modified the interpretation of this result. The most active compound of the series proved to be 5-methoxy-N : N-dimethyltryptamine, which caused 10 mistakes out of 10 trials at a dose-level of 0·05 mM/kgm. This was three times more effective than bufotenine, which has been reported to be psychotomimetic in man[6] and to affect the performance of trained rats[7]. At dose-levels exceeding 0·1 mM/kgm. the animals given 5-methoxy-N : N-dimethyltryptamine developed rhythmic beating of the forepaws, which tallied closely with the description given by Fabing and Hawkins[6] for the effects of bufotenine in rats which we have, however, not observed. 5-Methoxytryptamine also proved quite potent and in the same range as bufotenine. Finally, 5-methoxygramine appeared to cause more mistakes than did gramine itself.

Thus the ability of gramine, serotonin and bufotenine to cause behavioural mistakes was increased by O-methylation; and whereas N : N-dimethylation of 5-methoxytryptamine increases its potency, N-acetylation inactivated it.

It can therefore be concluded that O-methylation of hydroxyindoles is not an inactivation mechanism as is the O-methylation of catecholamines. The O-methylation of hydroxyindoles, however, changes their activity in the three assay procedures used in the following ways: oxytocic activity is still exhibited though slightly decreased; the vasopressor activity of serotonin is decreased but that of bufotenine is increased; ability to cause behavioural mistakes is increased. In addition, although O-methylation and N-acetylation are both necessary for the frog skin lightening activity of melatonin[2], it is the N-acetyl group which renders melatonin inactive towards smooth muscle, blood pressure and behaviour.

We wish to thank Dr. P. A. Khairallah for his help and Mrs. G. H. Britton for her generous financial support.

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HÆMATOLOGY

A Possible Specificity of Albumin Auto-antibodies

Anti-I was the name given by Wiener *et al.*[1] in 1956 to a cold antibody found in the serum of a patient suffering from cold antibody hæmolytic anæmia. Further investigations into the I group system were made by Jenkins *et al.*[2], Tippett *et al.*[3], Weiner *et al.*[4] and Marsh[5]. These workers showed that cold auto-antibodies (previously called non-specific cold agglutinins) had I specificity and that occasional powerful examples of these antibodies may be found as auto-agglutinins in cases of cold antibody hæmolytic anæmia. The I antigen has an almost universal distribution, Wiener *et al.* finding only five i people from 22,000 blood donors, while Jenkins *et al.* failed to find an example of the i phenotype after testing 17,000 donors. Marsh afterwards described examples of cold auto-antibodies having i specificity and showed that normal infants at birth possessed the i phenotype, which changed within 18 months of birth to I. He concluded that the rare i phenotype in adults arose from the absence of a genetically determined factor essential for the proper development of I. The majority of cold auto-antibodies therefore appear to have I specificity, a minority may be anti-i.

In 1956, Weiner *et al.*[6] described some examples of a rare auto-agglutinin active against all cells, but only when they were suspended in bovine albumin. These auto-agglutinins were inactive by anti-globulin or enzyme techniques and could not be absorbed by saline-suspended red cells. We have encountered two examples of the albumin auto-agglutinin described by these workers and were able to test them for I or i specificity.

Both sera were active against the patient's own cells and also all cells of a large genotyped panel, but only when albumin suspended red cells were used. One serum contained an additional trace of anti-D which was successfully removed by absorption with saline-washed rhesus-positive red cells.

The sera were tested against the red cells of two examples of the i_1 phenotype, one i_2 and four cord blood samples, with appropriate adult controls. The tests were all positive with about the same strength of reaction. Repeated tests with one of the sera in titration (using AB serum as a diluent) showed that the i_1 and i_2 cells scored the same as the adult controls; the cord samples were slightly weaker.

It is apparent from these results that while cold auto-antibodies have I or i specificity, albumin auto-agglutinins are not aimed at antigens within the Ii system.

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