TECHNICAL PAPERS

The Antirheumatic Effect of Sodium Gentisate

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The mechanisms involved in the activity of rheumatic diseases are as unknown as is the rationale of the antirheumatic action of salicylate. Salicylate administration has been shown to inhibit the spreading effect of hyaluronidase (*1*). *In vitro,* however, salicylate inhibits hyaluronidase in very high concentrations only, whereas the biological oxidation product of salicylate, gentisic acid, does so *in vitro* in concentrations of a few μg/ml (*3*). The inactivation of the enzyme is apparently irreversible and is believed to be due to a condensation of the semiquinone with the enzyme protein.

Since increased hyaluronidase activity has been suspected as a possible cause of the breakdown of interfibrillar cement in rheumatic diseases (*2*), the antirheumatic action of Na gentisate (supplied by Hoffmann-LaRoche, Inc., Nutley, New Jersey) has been investigated in a small number of patients. The results have been sufficiently uniform to warrant the present report. Gentisate has the same antirheumatic effect as salicylate without some of its disadvantages. In 5 patients with acute rheumatic fever, the administration of Na gentisate in doses comparable to those customarily employed for salicylate has been followed by disappearance of pain, swelling, and heat in the joints, by the fall of temperature to normal, and by fall in sedimentation rate. In one patient, withdrawal of gentisate after 3 days of administration was followed within 44 hrs by a return of acute joint symptoms, which again responded promptly to renewed administration of gentisate. The joint pain of 7 patients with rheumatoid arthritis has responded similarly to gentisate as to equivalent amounts of salicylate. In one patient, the salicylate was not tolerated because of the co-existence of a chronic duodenal ulcer, whereas gentisate caused no gastric irritation. Four patients with persistently active rheumatic fever—so-called "chronic rheumatic fever"—have responded similarly to gentisate and salicylate.

No untoward effects have been observed in the patients given as much as 10 gm/day, save in one patient who, on 8 gm/day, developed some epigastric distress which subsided immediately on withdrawal of the gentisate. No significant increase in prothrombin time, no tinnitus or aural symptoms have developed. No sign of methemoglobinemia or of liver damage has been observed. It seems significant that the increase in urinary glucuronic acid excretion observed with salicylate ingestion (*4*) does not occur with gentisate.

Only about one-quarter of the gentisate ingested was recovered in the urine as gentisic acid. So far we have been unable to detect gentisic acid in the blood, using a color method by which 5 γ/cc of hydroquinone in the urine can be detected. It appears that gentisate is rapidly oxidized in the body.

In summary, sodium gentisate appears to exert antirheumatic activity equal to, or greater than, that of salicylate. It is suggested that the antirheumatic action of salicylate is due to its oxidation product, gentisate. A detailed report of this work will be published shortly.

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References

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Does Glutamic Acid Have Any Effect on Learning?

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Recent studies of the role of glutamic acid in learning and intellectual capacities have presented a picture of conflicting findings. Following a clinical report (*6*) that the feeding of excess glutamic acid to epileptic children seemed to improve their 'mental alertness,' Zimmerman and Ross (*9*) did a controlled study on the learning ability of albino rats of the Sherman strain. They found that feeding either proline or glutamic acid in 200-mg doses in excess of a basic chick Growena diet resulted in a superior performance of these animals on a Warner-Warden, 8-cul, single alternation maze. Later, Albert and Warden (*2*) reported that excess glutamic acid had beneficial effects on the performance of rats in a complex reasoning problem. Furthermore, extension of this work to humans in studies of feebleminded children has suggested that excess glutamic acid intake can increase the IQ as measured by standard intelligence tests (*1, 7, 8*). Since the earlier animal studies, however, two reports have appeared which failed to demonstrate any effects of glutamic acid on the rate of learning or in the reasoning ability of the albino rat. Marx (*5*) found no difference between glutamic-fed and control animals in the learning of a Stone multiple-T water maze. Hamilton and Maher (*3*) reported that glutamic acid feeding did not result