Allergic Reactions to Dipasic

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Dipasic,* formerly called GEWO 339, is a para-aminosalicylic (PAS) salt of isonicotinic hydrazine (INH). Its structure is thought to be:

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\begin{align*}
\text{NH} & - \text{C} - \text{NH}_2 - \text{O} - \text{C} - \text{OH} \\
& \text{O} - \text{C} - \text{NH}_2
\end{align*}
\]

Each Dipasic tablet contains 47.2 mgm. of INH and 52 mgm. of PAS in chemical combination. This substance was first investigated pharmacologically and bacteriologically by Smith and Wiederkehr¹ who found, by \textit{in vitro} testing, that various dilutions of tubercle bacilli, resistant to streptomycin and INH, were sensitive to GEWO 339; and they claimed further that its effectiveness \textit{in vivo} exceeded that of a physical mixture of INH and PAS. In addition, it has been found that, under certain conditions, Dipasic may split to form free PAS and INH.² ³

Aufdermaur and Brodhage⁴ found that Dipasic restricted lymphogenous and hematogenous spread of the tubercle bacilli in guinea pigs and that it accelerated the healing process. The latter author⁵ suggested that the salt probably possessed a bacteriostatic effect of its own.

The clinical trials of Dipasic in patients with pulmonary tuberculosis showed favorable responses of varying degrees and revealed the presence of no allergic manifestation necessitating cessation of therapy with this drug.⁶ ⁷

Of 17 patients included in a bacteriologic and clinical trial of Dipasic, three have experienced allergic responses to Dipasic. The severity of these reactions has required the discontinuance of Dipasic. Because only mild or transient reactions were noted by other workers using Dipasic, it was thought advisable to call attention to these reactions in patients who had such previous sensitivity. Each of the three patients were previously sensitive to para-aminosalicylic acid.

\textit{Case 1, No. 5114:} W. M., a 72 year old man, was first admitted to Kings County Hospital Medical Center on June 30, 1954 when the diagnosis of bilateral caseopneumonic pulmonary tuberculosis was made on the basis of x-ray manifestations and positive sputa. He was started on streptomycin ½ gm. twice weekly, PAS 4 gm. twice daily, and INH 100 mgm. twice daily, beginning in August 1954. PAS was discontinued because on the ninth of August 1954 he developed erythematous, confluent plaques which were severely pruritic and confined mainly to his trunk. He responded well to the discontinuation of PAS and the administration of chlortrimeton 4 mgm. four times daily. The patient was discharged to the chest clinic in March 1955 on PAS, streptomycin and INH. Another pruritic dermatitis which developed in June 1955 necessitated discontinuing PAS.

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* Dipasic supplied through the courtesy of the Panray Corporation, New York City.
Because of recent positive gastric contents, increased cough and decreased appetite, he was placed on Dipasic 600 mgm. daily on May 11, 1956. After two days of Dipasic he developed generalized pruritus which progressed to a generalized rash with conjunctivitis. By June 22, 1956 these signs and symptoms had all but disappeared after stopping the Dipasic and treatment with benadryl 50 mgm. four times daily.

Case 2, No. 58901: J. L., a 71 year old unemployed man, was admitted to the Second Division Pulmonary Disease Service at Kings County Hospital on the 21st of December, 1955, having been referred by his family physician because of persistently positive sputum and bilateral caseocavitary pulmonary tuberculosis despite some clinical improvement and therapy consisting of INH and daily streptomycin. Ten days after admission he developed generalized pruritus which was not relieved by the mere addition to his regimen of pyribenzamine by mouth, or the intramuscular administration of benadryl.

Eventually all medications had to be stopped because of severe dermatitis which was thought to be due to streptomycin, PAS, and possibly INH. On May 14th, 1956 Dipasic 200 mgm. twice daily was substituted for the previously given anti-tuberculosis drugs. On May 22nd the erythematous, severely pruritic dermatitis recurred and Dipasic was discontinued.

Case 3, No. 1285: C. U., a 48 year old furniture worker, was transferred from the Psychiatric Division on April 6, 1966 with the diagnosis of acute hallucinosis, because of a suspicious-looking x-ray film of the chest. With the history of chronic non-productive cough, 20 pound weight loss, post-tussive rales at the left apex and a chest film showing soft mottling and increased densities throughout both upper lobes, it was felt that there was active pulmonary tuberculosis. Previous examinations by the Board of Health were considered to indicate arrested disease.

On April 12th, he was started on INH and PAS. On May seventh he developed fever, diarrhea and a morbilliform rash over his trunk and extremities. The PAS and INH were discontinued; he received pyribenzamine and by May 14, 1956 his rash and fever had subsided. On this date he was started on Dipasic 200 mgm. twice daily; six hours following his initial dose he experienced nausea, fever, malaise, headache, photophobia, conjunctivitis and had leukocytosis and eosinophilia. The Dipasic was discontinued, he again received pyribenzamine and by May 18, 1956 symptoms had subsided and skin lesions had disappeared.

REFERENCES
3 Publication of Ed. Geistlich Sons Ltd., Wohhusen, Switzerland (097-602-e).