patient lies in defining as specifically as possible the particular subcategory of disease most applicable to him.

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To the Editor:

I appreciate Dr. MacAlpin's comments about our recent paper, "Further Variant Patterns within Prinzmetal Angina Pectoris" (Chest 66:622-627, 1974). Since Dr. MacAlpin is an important contributor to the literature of this syndrome, his comments are of special interest.

It would seem that our differences rest essentially on the definition of the disorder; Dr. MacAlpin's definition serves to restrict and exclude the preinfarction and immediately postinfarction patients. We feel that the phenomenon described by Dr. Prinzmetal has a much broader clinical significance; in essence, recurrent ischemic episodes with reversible ST segment elevations may, in fact, reflect the participation of coronary spasm in a number of different coronary syndromes. The definition which will ultimately emerge to be generally accepted by the profession as a whole seems as yet uncertain.

More important, we do not find a clean distinction between the various categories Dr. MacAlpin lists; rather we find considerable overlap in the anatomy, electrocardiographic findings, and the clinical course in the disorder labeled Prinzmetal's angina. In addition, we do not find intermittent ST segment elevation after acute myocardial infarction to be at all common; rather it seems to us to definitely reflect a special group of patients who fall within a broader definition of the disorder.

Again, I appreciate Dr. MacAlpin's comments.

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Aerosolized Isoproterenol and Myocardial Infarction Analog

To the Editor:

I would like to comment on the article by Aelony et al entitled "An Electrocardiographic Pattern of Acute Myocardial Infarction Associated with Excessive Use of Aerosolized Isoproterenol" (Chest 68: 107-110, 1975).

While I would agree with the importance of the authors' emphasizing the potential for cellular toxicity with overuse of almost any pharmacologic agent, the reader should be cautioned against assuming that the patient described in the report of Aelony et al experienced an ischemic necrotic analog to classic myocardial infarction. Indeed, there is serious doubt as to the kinship of catecholamine-induced myocardial necrosis and myocardial infarction resulting from the atherosclerotic process and blood flow deprivation.

In any event, I would make a plea for this sort of report stimulating a search for mechanism rather than suggesting (as I am sure was not the authors' intent) a simplistic and probably erroneous lumping of pathogeneses.

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BIBLIOGRAPHY


Acute Abdomen

An Unusual Reaction to Isoniazid

To the Editor:

An increasing awareness of the possible untoward reactions to isoniazid has led many physicians to modify their approach to the chemoprophylaxis of tuberculosis.1-3 A comprehensive review by Goldman and Braman4 has categorized the three major types of adverse reactions to isoniazid as (1) side effects, (2) idiosyncrasy, and (3) toxicity. We report here a new type of idiosyncratic response to isoniazid, manifest as a reproducible acute abdomen or peritonitis and rapidly reversed by withholding the drug.

CASE REPORT

In 1951, sarcoidosis was diagnosed by scalene node biopsy in a 43-year-old woman after the typical histologic picture was identified. Her tuberculin skin test in 1951 produced a 5-mm induration. She was well without specific treatment until 1967 to 1970 when recurrent episodes of pneumonitis failed to adequately respond to antibiotic therapy. The results of sputum examination were repeatedly negative for acid-fast bacilli, and the results of tuberculin skin tests were unchanged.

In June 1971 a skin test with purified protein derivative of
tuberculin produced a 13 × 15-mm induration; chemophylactic therapy with isoniazid was prescribed. Within four days the patient developed rapid onset of abdominal pain, vomiting, and fever to 40°C (104°F). On examination she appeared acutely ill and flushed. The abdomen was rigid with marked tenderness, guarding and rebound, particularly in the left lower quadrant. Bowel sounds were diminished with occasional high-pitched tinkles. The results of the pelvic examination were normal. The hemogram showed a leukocyte count of 5,800/cu mm with a left shift.

The patient was treated with fluids and antibiotic therapy; isoniazid was withheld. All cultures were negative. There was gradual but complete resolution of the symptoms and signs over the next three days. Isoniazid (300 mg) was given again on the fourth day, and within two hours an identical picture of peritonitis and fever was noted, with marked improvement by the following morning. The same spiking fever and signs of peritonitis were observed on two further days about two hours after isoniazid administration, with improvement by the next morning. Isoniazid was no longer given; complete and permanent remission ensued.

The following month, a papular skin rash developed; a biopsy showed granulomatous changes consistent with sarcoidosis. However, the special stains revealed acid-fast bacilli; cultures of the skin biopsy for acid-fast bacilli were negative. The patient was treated uneventfully for two years with ethambutol and rifampicin.

**RESULTS AND DISCUSSION**

Antinuclear antibodies were absent, and lupus erythematosus preparations were negative four years prior to the development of the acute abdomen, when the initial episodes of fleeting pulmonary infiltrates failed to respond to antibiotic therapy. A collagen disease was suspected. However, after repeated episodes of peritonitis following isoniazid administration, the antinuclear antibody tests became positive; lupus erythematosus preparations remained negative. Eosinophilia of 4 to 8 percent was noted during the acute illness. Results of liver function tests were all normal, except for a transient rise of the alkaline phosphatase level to 8.4 Bodansky units/100 ml (normal, 1.0 to 4.5 units/100 ml). The results of urine tests for porphyrins and porphobilinogens were negative.

A lymphocyte transformation test to isoniazid was performed utilizing the patient’s serum. Tritiated thymidine studies, using the patient’s lymphocytes, revealed that she did react to minute quantities of isoniazid. The observed ratio of four to five times the radioactive counts to isoniazid over control counts is significant; drug sensitivity to isoniazid was verified by this test.

The sudden occurrence of peritonitis as a manifestation of drug sensitivity is distinctly unusual. Erythromycin estolate can rarely cause cholestatic jaundice with a clinical picture of severe abdominal distress, eosinophilia, and an elevated level of alkaline phosphatase.5 The time sequence of symptoms occurring after a few days of drug ingestion and the prompt recurrence on subsequent administration suggest a sensitization phenomenon and parallel the pattern seen in our patient. Occasionally the picture seen in erythromycin estolate sensitivity can lead to a mistaken diagnosis of an acute surgical abdomen, as was nearly the case in our patient.

The frequent development of antinuclear antibodies in patients taking isoniazid is well known. A genetic predisposition has been postulated as the cause of the overt lupus-like syndrome which develops rapidly in individuals receiving isoniazid. To date, over 20 cases of isoniazid-induced lupus have been reported. In the first reported case of lupus dramatic fever induced by isoniazid (INH) therapy, bilateral pleural effusions and pericarditis occurred after two months of isoniazid administration. Greenberg and Lutcher noted a man who developed life-threatening pericardial tamponade due to isoniazid sensitivity. We believe that our patient’s illness demonstrates that the peritoneum is another of the serous surfaces which can act as a “shock organ” in drug-induced lupus syndromes. To our knowledge, this manifestation of isoniazid idiosyncrasy has not been reported.

**ACKNOWLEDGMENT**

We are indebted to Dr. Quinton Callies, Allergy Division, Henry Ford Hospital, for performing the lymphocyte transformation tests.

**REFERENCES**

4 Goldman AL, Braman SS: Isoniazid: A review with emphasis on adverse effects. Chest 62:71-77, 1972