

Raynaud's Disease Treated with Griseofulvin

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Raynaud's disease is uncommon in children. The patient described here developed Raynaud's disease subsequent to rubella when she was 7 years old. Treatment with griseofulvin brought about a rapid disappearance of the symptoms and signs.

Case History

The patient, a 7-year-old girl, with no previous history of circulatory disorder, developed rubella, and a week later a discoloration of her fingers was noted. The index finger of the right hand became purple and cold and then the index finger of her left hand became similarly affected. Other fingers were soon involved (see Fig.) and by the third week some discoloration of the toes was noticed. There was no family history of any similar disorder.

On examination at that time she was a healthy-looking girl of average build. The circulatory changes described above were found, involving mainly the fingers. A trophic lesion was present at the tip of the right index finger. The toes were involved, but to a lesser extent. Arterial pulses in the limbs were normal; blood pressure 90/60 mm. Hg. The skin was mildly ichthyotic.

Investigations. Hb, white blood count, and differential, normal; platelets, 115,000/mm.³ Rubella neutralizing antibody titre, 1/32; antinuclear protein factor, negative. Cold haemagglutinins (taken and separated at 37° C.), negative; cryoglobulins (taken and separated at 37° C.), negative; serum proteins, 7.0%; albumin, 5.0%, globulin, 2.0%. Serum immunoelectrophoresis, IgA, 140 mg./100 ml.; IgG, 1800 mg./100 ml.; IgM, 80 mg./100 ml., all normal for this age. Digital pulp temperatures (Table) implied ischaemia except for the ring finger and thumb of both hands. Plethysmographic measurement of total hand blood flow was 10 ml./100 ml. of hand tissue per min. (adult values at 34° C. are normally 30 ml./100 ml. of hand tissue per minute (Wade, 1965)). There was a good hyperaemic response to local warming of the digits.

After 5 weeks of increasing circulatory disorder, oral treatment was started with fine particle griseofulvin, 125 mg. b.d. A subjective improvement was noticed after 3 days. After 2 weeks of treatment the infection around the finger-nails had disappeared and they were

no longer blue. Digital skin temperatures showed some improvement (see Table).

No abnormality was noticed in the child's fingers by the parents and she had no complaints. The weather was hot during this period and the child swam in an open unheated swimming pool without precipitating any digital circulatory changes.

Because the signs of Raynaud's disease are episodic it was decided to stop treatment at the end of 4 weeks, but within 5 days digital coolness and cyanosis had reappeared in the left hand. Treatment with griseofulvin was restarted and again within 3 days the hands became warm and pink. This treatment was continued into the winter months without any circulatory problems recurring.

Discussion

Ischaemia of the limb extremities causing peripheral gangrene has been reported in children (Lloyd, Kembell, and Fraser, 1967). These cases were thought to result from primary arterial disease, and Lowenthal (1967) states that extensive gangrene suggests arterial thrombosis, embolism, cold haemagglutinins, or the presence of auto-immune disease. The good response of the digits to local heat and the response to the course of treatment in this child's case eliminates such severe obstructive lesions.

Milder ischaemic episodes (Raynaud's phenomenon) can occur in the presence of cold haemag-

TABLE
Effect of Griseofulvin Treatment on Skin Temperatures of Digits of Right Hand

	Temperature (°C.) Before and After Treatment		
	Before	After 2 Weeks	After 4 Months
Thumb	31.5	31.9	34.8
Index	24.6	26.5	30.8
Middle	25.4	26.7	32.8
Ring	30.5	32.8	35.8
Little	26.7	26.8	32.8

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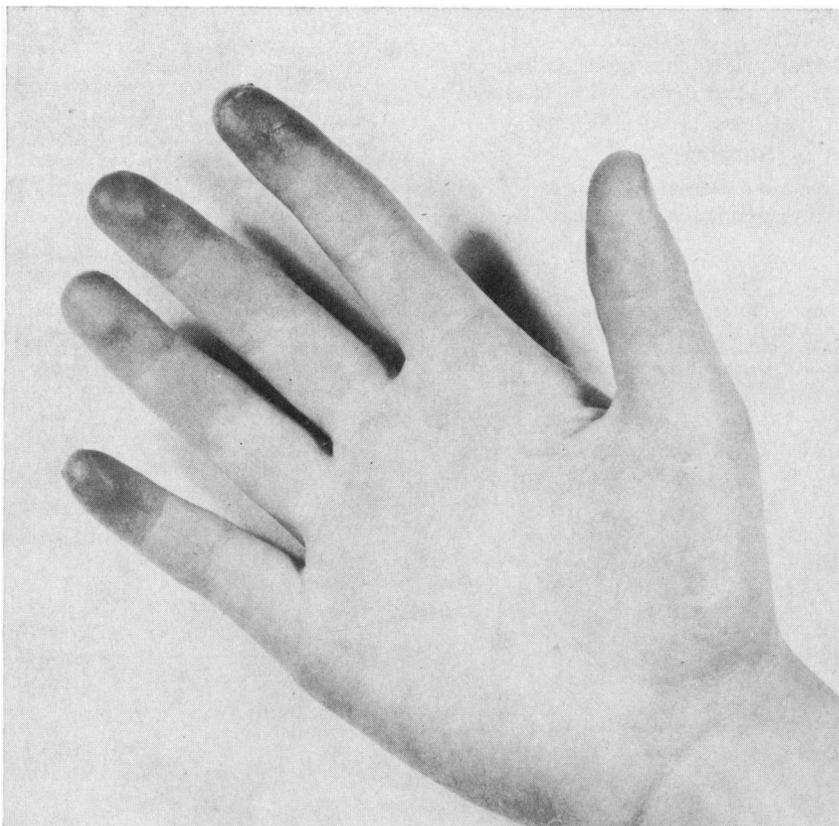


FIG.—*Photograph of right hand before treatment, showing cyanosis of little, middle, and index fingers, with trophic lesions of the index finger.*

glutinins and cryoglobulins, and the term 'Raynaud's phenomenon' should be restricted to these cases.

In this patient the striking symmetry of distribution of the ischaemia (Fig.), the failure to demonstrate a precipitating cause, and the functional nature of the circulatory impairment confirm the diagnosis of Raynaud's disease. The total hand flow found here is also reduced compared with adult values (Wade, 1965), though no strict control flows for children are available. Reduction in hand flow has been demonstrated in adults (Peacock, 1960).

Some authors (Mendlowitz and Naftchi, 1959) still feel that there is sympathetic overactivity in these cases, and it is of interest that the mother volunteered the information that the child had shown increased sweating.

Acquired rubella was possibly incriminated as the cause of the Raynaud's disease in this case. The raised antibody titre supported the clinical diagnosis of a recent infection, and rubella infection

may be associated with increased capillary fragility (Lokietz and Reynolds, 1965). Previously reported cases of rubella have not shown evidence of arterial spasm.

Serre and Simon (1962) thought that griseofulvin exerted its effect through the sympathetic system in cases of shoulder-hand syndrome. Forck and Fegeler (1962) investigated adults with onychomycosis in whom there was associated digital arterial spasm; pulse height tracings showed relief of the spasm after 72 hours of treatment with griseofulvin 750–1500 mg. per day. Rubin (1963) has shown that griseofulvin increases coronary blood flow by a direct effect on vascular smooth muscle. This effect was not altered by blocking of autonomic ganglia (hexamethonium chloride), adrenergic receptors (phentolamine hydrochloride), cholinergic receptors (atropine), and histamine receptors (chlorpheniramine maleate). Sforza and Mossa (1964), following a study of 12 patients with chronic disorders of peripheral arteries, concluded that

griseofulvin was a good vasodilator, probably acting directly on the blood vessels.

Recently Giordano (1967) has reported improvement in a case of scleroderma with Raynaud's disease.

Summary

A case of Raynaud's disease in a 7-year-old girl following rubella responded to oral griseofulvin.

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