



FIG. 1. Isolated spiral strips of pulmonary artery (upper tracing) and pulmonary vein (lower tracing) taken from a 6 week old Friesian calf sensitized with hen egg albumin (15 mg/kg intravenously). Tissues are contracting to 5-hydroxytryptamine (5-HT), histamine (H) and hen egg albumin (OA). Doses in ng/ml. The marker shows injection time and 30 s.

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#### Effects of azathioprine and phenylbutazone in rat adjuvant arthritis

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A single intraplantar injection of heat-killed tubercle bacilli in liquid paraffin (Freund's adjuvant) causes local and migratory peri-arthritis and other connective tissue lesions in rats (Pearson, 1956). This experimental arthritis can be suppressed to different degrees by various anti-inflammatory and immunosuppressive agents (Newbould, 1963; Ward, Cloud, Krawitt & Jones, 1964; Graeme, Fabry & Sigg, 1966). Piliero & Colombo (1967) showed that serum from rats treated with certain

anti-inflammatory drugs and also from rats with adjuvant arthritis showed reduced turbidity on heating. The present studies define the stages in the development of the arthritis when the immunosuppressant azathioprine is effective in suppressing symptoms and explore the relationship between the appearance of swelling and of serum changes in arthritic controls and in similar rats also given either azathioprine or phenylbutazone.

Arthritis was induced in male Wistar rats by injection of 0.1 ml Freund's adjuvant into one hind-foot pad. A primary swelling in the injected foot was seen within about 24 h while secondary, arthritis-like lesions appeared in the other feet about 14 days later.

Azathioprine completely prevented secondary swelling but had no effect on primary lesions when oral doses of 25 mg/kg were given daily from the day of adjuvant injection (day 0) until day 10. There was marked reduction in secondary swelling when the drug was given only on days 0-4, 2-6 or 4-8 and slight reduction with treatment on days 8-12. Dosing after day 12 was ineffective.

To examine the serum changes blood was drawn from the tail on alternate days after adjuvant injection; 0.1 ml of serum from each rat was diluted with 2.9 ml M/15 phosphate buffer and heated at 69° C for 30 min. The resulting turbidity was measured on a spectrophotometer. In arthritic controls there was an approximately 50% decrease in the turbidity measurement by day 2. The value remained low during the course of the arthritis and often dropped further around day 14. The drop was related to the severity of the ensuing arthritic lesions and rats which did not develop arthritis showed normal serum turbidity. Adjuvant-injected rats given azathioprine (25 mg/kg) daily from days 0-10, although protected against arthritis, also showed lowered turbidity measurements, but at 21 days the drop was less than in arthritic controls ( $0.01 < P < 0.05$ ). When phenylbutazone (100 mg/kg) was similarly administered the appearance of secondary arthritic swelling was largely prevented while primary swelling was reduced. Turbidity changes resembled those in arthritic controls on days 2 and 4, but were significantly less than in arthritic controls from day 7 onwards ( $P < 0.1$ ) and from day 11 the values were not significantly different from those in untreated controls.

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#### Some effects of *Escherichia coli* enterotoxin on fluid and electrolyte transfer in calf small intestine

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Certain enteropathogenic strains of *Escherichia coli* produce an enterotoxin which causes dilatation of ligated loops of intestine (Smith & Halls, 1967).