

MEDICAL GRAND ROUNDS  
Parkland Memorial Hospital  
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SALICYLATES

CASE #1: [REDACTED] ( [REDACTED] ) is an 18-year-old [REDACTED] female who was admitted on [REDACTED]/63 with a two day history of migratory joint pain starting in her left shoulder, then involving both knees and the right wrist. Because of dysuria, frequency, and a finding of bacilluria she was given antibiotics without any effect on her temperature which ranged between 100° and 103°. A history of a sore throat 3 weeks was also obtained. After therapy with penicillin, streptomycin and chloromycetin failed to affect her signs and symptoms, ASA 0/3 gm. every 4 hours was started. Her temperature dropped to 97.5° and her joint symptoms disappeared by the following morning. She had no further symptoms.

CASE #2: [REDACTED] ( [REDACTED] ) is a 41-year-old [REDACTED] female who was admitted on [REDACTED] 4/63 complaining of a generalized symmetrical poly-arthritis for one day prior to admission. She also complained of headache and a feverish feeling. Subcutaneous nodules were noted in both elbows. Physical examination showed temperature 100.8°, tenderness at the shoulders, elbows, wrists, MCP's, PIP's, knees and ankles. The wrists, knees and ankles were swollen and warm with fluid in the latter.

The patient was given ASA 0/6 gm. every 4 hours on the second hospital day. ESR = 50 mm/hr., ASO = 50, Slide Latex = 4+, SSCA = 1/112.

There was a dramatic response after one day of therapy with most of the joints resolving. She became afebrile. There was some residual effusion and swelling in a few joints. Biopsy of a subcutaneous nodule showed it to be typical of a rheumatoid arthritis.

The patient subsequently had a relapse after stopping ASA and was subsequently poorly controlled on larger doses (4.5 gm/day). She is now resolving again on gold therapy.

CASE #3: [REDACTED] [REDACTED] is a 16-year-old [REDACTED] male with juvenile rheumatoid arthritis since age 4. Since that time he has had continuous low-grade activity in his joints along with fever appearing daily to biweekly with spikes to 105°. He has been on steroids ever since. When placed on Aspirin his mother states that severe nose bleeds occurred. When the aspirin was stopped the bleeding stopped to recur whenever salicylate was restarted.

ASA was restarted [REDACTED]/60 with no ill effects until [REDACTED]/61 when melena developed and the ASA was stopped. The ASA was restarted [REDACTED]/61 with another episode of melena 4 weeks later. ASA was continued at 1.2 gm/day with intermittent episodes of melena. On [REDACTED]/61 he was changed to enteric-coated ASA. He was subsequently placed on liquid aspirin and has had no bleeding since.

Prothrombin times during periods of melena varied from 64 to 72% with the platelet count 600,000. The hemoglobin from 1960 to the present has ranged between 8 and 12 grams.



## SALICYLATES

### I Metabolic effects of salicylates

- 1) Uncoupling of oxidative phosphorylation ref. 19
- 2) Inhibition of transaminoses ref. 23
  - a) glutamic-pyruvic
  - b) glutamic-oxaloacetic
  - c) inhibition of transaminase ref. 26  
(Fructose-6-P  $\rightarrow$  Glucosamine-6-P)
- 3) Inhibition of malic and isocitric dehydrogenases ref. 29
- 4) Inhibition of xanthine oxidase ref. 30
- 5) Depression of thyroid activity ref. 42

### II Circulatory effects leading to congestive heart failure ref. 46, 47

- 1) Increased sodium intake (if sodium salicylate used) ref. 48
- 2) Increased plasma volume ref. 49
- 3) Sodium retention ref. 50
- 4) Potassium loss  $\rightarrow$  hypokalemia ref. 51
- 5) Increase in free circulating thyroxine ref. 44
- 6) Increased cardiac output ref. 47

### III Anti-inflammatory effects ref. 62

- 1) Anti-bradykinin ref. 55
- 2) Anti-erythema ref. 57, ref. 1 p. 127 f.
- 3) Anti-SRS-A ref. 58
- 4) Decrease of vascular permeability ref. 1 p. 141 f.
- 5) Inhibition of phagocytic activity of PMN leukocytes ref. 60
- 6) Anti-hyaluronidase ref. 61

### IV Blocking of immunologic phenomena and wound healing

- 1) Anti-anaphylactic (rabbit) ref. 65
- 2) Suppression of Schwartzman phenomenon ref. 66
- 3) Inhibition of immune hemolysis ref. 67
- 4) Inhibition of antigen-induced histamine release ref. 68
- 5) Depression of antibody response ref. 69
- 6) Partial dissociation of preformed antigen-antibody precipitates r. 70



## V Side effects in man

- 1) Thrombocytopenic purpura ref. 73
- 2) Hypoprothrombinaemia ref. 74
- 3) Asthma ref. 75, 76
- 4) Celluria ref. 77
- 5) Gastric erosions ref. 78, 80, 81, 83

## VI Changes in serum components with salicylate therapy

- 1) Increased transaminase activity ref. 25
- 2) Changed uric acid levels (depending on serum salicylate level) ref. 27
- 3) Decreased blood sugar (in diabetes) ref. 35
- 4) Increased serum lactate (in diabetes) ref. 34
- 5) Increased serum pyruvate (in diabetes) ref. 32
- 6) Decreased ketones (in mild diabetic ketonuria) ref. 33
- 7) Increased  $T_3$  (RBC) ref. 36
- 8) Decreased PBI ref. 42
- 9) Decreased cholesterol (in hypercholesterolemia) ref. 45
- 10) Decreased phospholipids ref. 30
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