

MEDICAL GRAND ROUNDS  
PARKLAND MEMORIAL HOSPITAL

APRIL 7, 1960

STEROIDS IN INFECTION

Bibliography

Review articles

1. Thomas, L. The effects of cortisone and adrenocorticotrophic hormone on infection. *Ann. Rev. Med.* 3, 1, 1952.
2. Kass, E.H. and Finland, M. Adrenocortical hormones in infection and immunity. *Ann. Rev. Microbiol.* 7:361, 1953.
3. Spink, W.W. Adrenocorticotrophic hormone and adrenal steroids in management of infectious diseases. *Ann. Int. Med.* 43:685, 1955.
4. Kass, E.H. and Finland, M. Adrenocortical hormones and the management of infections. *Ann. Rev. Med.* 8, 1, 1957.
5. Kass, E.H. and Finland, M. Corticosteroids and infections. *Adv. Int. Med.* 9:45, 1958.

These articles list the wide variety of infections in which steroids have been used. In most infections in which measurement is readily accomplished, i. e. mostly bacterial infections, sufficiently prolonged steroid administration must be said to depress host resistance. Symptomatic improvement, defervescence and reduction of "toxicity" occur uniformly without regard to the nature of the infecting microorganism.

Effects in viral infections

6. Nelson, R.S. Present indications for cortisone therapy in acute viral hepatitis. *Ann. Int. Med.* 46:685, 1957.  
The immediate apparently beneficial effects of steroids in hepatitis are followed by an unexpectedly high incidence of relapse.
7. Mandel, W., Marilley, R.J., Jr. and Gaines, M.C., Jr. Corticotropin in severe angiose infectious mononucleosis. *JAMA*, 158:1021, 1955.
8. Bernard, J., Mathe, G. and Segal, S. Treatment with cortisone of 22 cases of infectious mononucleosis with positive Paul-Bunnell reactions. *Sang*, 27:245, 1956.
9. Frenkel, E.P., Shiver, C.B., Jr., Berg, P. and Coris, T.N. Meningo-encephalitis in infectious mononucleosis. *JAMA*, 162:885, 1956.
10. Solem, J.H. The effect of corticotropin in the orchitis of mumps. *Acta. Med. Scand.* 149:341, 1954.
11. Petersdorf, R.G., and Bennett, I.L., Jr. Treatment of mumps orchitis with adrenal hormones: Report of 23 cases with note on hepatic involvement in mumps. *Arch. Int. Med.*, 99:222, 1957.
12. Klemola, E. and Somer, P. Corticotropin och cortison vid parotitorchit. *Nord. Med.*, 56:1128, 1956.

Relapse has not been a problem in other viral infections. e.g. infectious mononucleosis and mumps orchitis.

Reference 12 is of special interest because in a well-controlled study of mumps orchitis these investigators found that a placebo gave as prompt symptomatic response as did steroids.

Effects on some infections described as no apparent harmful effects.

13. Coreill, T.L., Siegel, A.C., Cook, C.D., Murphy, L. and Stokes, L., Jr. Use of pituitary adrenocorticotrophic hormone in poliomyelitis. JAMA. 142:1279, 1950.
14. Helm, E.O., Houser, H.B., Rammelkamp, C.H., Jr., Denny, F.W. and Wannamaker, L.W. Effect of cortisone on acute streptococcal infections and post-streptococcal complications. J. Clin. Invest. 30:274, 1951.

Effects on reticuloendothelial system.

15. Bennacerraf, B., Halpern, B.N., Biozzi, G. and Benos, S.A. Quantitative study of the granulopoietic activity of the reticuloendothelial system; effect of cortisone and nitrogen mustard on the regenerative capacity of the R.E.S. after saturation with carbon. Brit. J. Exper. Path. 35:97, 1954.

Effects on Antibody production.

16. Berglund, K. Studies on factors which condition the effect of cortisone on antibody production. 1. The effect of time of hormone administration in primary hemolysin response. Acta Path. et Microbiol. Scand. 38:311, 1956.
17. Berglund, K. Studies on factors which condition the effect of cortisone on antibody production. 2. The significance of the dose of antigen in primary hemolysin response. Acta Path. et Microbiol. Scand. 38:329, 1956.

Steroids may activate latent infections, and may permit infections by microorganisms which under ordinary circumstances would be saprophytic.

See references 2 and 4.

18. Le Maistre, C., and Tompsett, R. The emergence of pseudotuberculosis in rats given cortisone. J. Exper. Med., 95:393, 1952.
19. Haggerty, J. and Eley, R.C. Varicella and cortisone. Pediatrics, 18:160, 1956. (Details the gravity of varicella in children receiving steroids.)
20. Denny, F.W., Jr., and Thomas, L. Persistence of Group A streptococci in tissues of rabbits after infection. Proc. Soc. Exper. Biol. & Med. 88:260, 1955
21. Batten, J.C., and McCune, R.M. The influence of corticotropin and certain corticosteroids on populations of mycobacterium tuberculosis in tissues of mice. Brit. J. Exper. Path. 38:413, 1957.

Effects on hypersensitivity in infections.

22. Fitz, R.H. and Meikeljohn, G. Varicella pneumonia in adults. Am. J. Med. Sci., 232:489, 1956.
23. Thompson, C.A. and Cantrell, F.P. Chickenpox pneumonia treated with prednisilone: A case report. Ann. Int. Med. 49:1239, 1958.  
Describe apparently favorable effects of steroids in varicella pneumonia, an infection which has been considered by some to have a major element of bronchospasm.

### Adrenal insufficiency in infections.

See reference 5. This describes effects of cortisone on pneumococcal infection in adrenalectomized mice. An optimal dosage restores the animals to a susceptibility comparable to that of intact mice. Larger or smaller doses increase susceptibility to infection.

24. Browne, J.S.L., Aronovitch, M., Beck, J.C., Leith, W. and Meakins, J.F. The treatment of coexisting Addison's disease and active pulmonary tuberculosis. *Am. J. Med. Sci.* 228:491, 1954.

25. Crispell, K.R., Parson, W., Hamlin, J., and Hollifield, G. Addison's disease associated with histoplasmosis. *Am. J. Med.* 20:23, 1956.

26. Ingle, D.J. The functional interrelationship of the anterior pituitary and the adrenal cortex. *Ann. Int. Med.* 35:652, 1951.

Points out that anatomic changes in adrenal seen in acute infections can be reproduced by stimulation with corticotropin.

27. Melby, J.C. and Spink, W.W. Comparative studies on adrenal function and cortisol metabolism in healthy adults and in patients with shock due to infection. *J. Clin. Invest.* 37:1791, 1958.

See also reference 5.

28. Tobin, J.L. Complications of meningococcus infection in a series of sixty-three sporadic cases. *Am. J. Med. Sci.* 231:241, 1956.

Largest series of patients with Waterhouse-Frideriksen syndrome treated with steroids. Author doubts if they contributed significantly to favorable outcome (5 of 9 patients survived).

29. Robinson, H.J. Adrenal cortical hormones and infection. *Pediatrics*, 17:770, 1956.

Suggests that small doses of steroid may be significantly better than usual doses used.

### Potentiation of pressor responses by steroids.

30. Kurland, G.S. and Freedberg, A.S. The potentiating effect of ACTH and of cortisone on pressor response to intravenous infusion of L-nor-epinephrine. *Proc. Soc. Exper. Biol. and Med.* 78:28, 1951.

### Effects on fever.

31. Kass, E.H. and Finland, M. Effect of ACTH on induced fever. *New Engl. J. of Med.* 243:693, 1950.

32. Recant, L., Ott, W.H. and Fischel, E.E. The antipyretic effect of cortisone. *Proc. Soc. Exper. Biol. & Med.* 75:264, 1950.

33. Douglas, W.W. and Paton, W.D.M. The hypothermic and antipyretic effect of preparations of ACTH. *Lancet*, 1:342, 1952.

34. Kass, G.H. Hypothermia following cortisone administration. *Am. J. Med.*, 18:146, 1955.

Describes profound hypothermia following cortisone therapy in a febrile patient.

In infections which are predominantly intracellular under ordinary circumstances, the administration of steroids apparently results in diminished phagocytosis. Although this might enhance the action of antimicrobial drugs, any such theoretical advantage could well be offset by increased density of the bacterial population.

35. Lurie, M.B. Constitutional factors in resistance to infection. N.Y. Acad. Med. Section on Microbiology. The effect of ACTH and cortisone upon infection and resistance. (N.Y. Columbia University Press, 1953) page 84. See also reference 21.

36. Bacos, J.M. and Smith, D.T. The effect of corticotropin, dihydro-streptomycin and corticotropin/dihydrostreptomycin on experimental bovine tuberculosis in the rabbit. Am. Rev. Tuberc. 67:201, 1953.

This article and reference 21 describe course of experimental tuberculosis in animals given steroids and antituberculous drugs. Steroid treatment was not harmful under these circumstances.

Additional references on clinical use of steroids in infections.

See ref. 27. Use of Steroids in bacteremic shock.

37. Smadel, J.E., Ley, N.L., and Diercks, F.H. Treatment of typhoid fever. I. Combined therapy with cortisone and chloramphenicol. Ann. Int. Med. 34:1, 1951.

38. Woodward, T. E., Hall, H.E., Dias-Rivera, R., Hightower, J.A., Martinez, E. and Parker, R.T. Treatment of typhoid fever. II. Control of clinical manifestations with cortisone. Ann. Int. Med. 34:10, 1951.

39. Spink, W.W. and Hall, W.H. The influence of cortisone and adreno-corticotropic hormone on brucellosis. II. Adrenocorticotrophic hormone in acute and chronic human brucellosis. J. Clin. Invest. 31:958, 1952.

40. Johnson, J.R. and Davey, W.N. Cortisone, corticotropin and anti-microbial therapy in tuberculosis in animals and man. Am. Rev. Tuberc. 70:623, 1954.

41. Lewis, R.A., Dane, B.T., Joag, G.G. and Patel, J.C. Hydrocortisone in severe tetanus. Lancet. 508, 1956.

42. Appelbaum, E. and Abler, C. Treatment of measles encephalitis with corticotropin. Am. J. Dis. Child. 92:147, 1956.

43. Lepper, M.H. and Spies, H.W. A clinical study of the use of cortisone, hydrocortisone and corticotropin in the treatment of seriously ill patients with infections. Antibiotics Annual. Medical Encyclopaedia, 1956-1957, p.447.

44. Schmidt, L.H. and Squires, W.L. The influence of cortisone on primate malaria. J. Exper. Med. 94:501, 1951.

45. Trowell, H.C. and Vaizey, J.M. Treatment of blackwater fever with prednisone. Lancet, 2:128, 1956.

#### Hospital Course

<u>Date</u>	<u>Diet</u>	<u>Reducing Substance in Urine</u>
2/15	Milk	2%
2/17	Nutramigen	0
(2/21)	Restart Milk)	
2/22-3/1	Milk	2%
(3/1)	Restart Nutramigen)	
3/2-3/3	Nutramigen	0