Papers and Originals

Corticosteroids in Heart Disease*

R. I. S. BAYLISS,† M.D., F.R.C.P.

Brit. med. J., 1966, 2, 721-724

Corticosteroids play a limited but nevertheless important part in the treatment of certain cardiac diseases. Before discussing the indications for such therapy it is appropriate, because of its application to the whole subject, to discuss which particular corticosteroid is preferred and why. Cortisone and cortisol (hydrocortisone) are not the steroids of first choice, because both compounds, in addition to their anti-inflammatory and immunosuppressant actions, have mineralocorticoid activity and tend to enhance the renal reabsorption of sodium. Hence except when given over short periods they may in high dosage induce oedema, increase blood-pressure, and precipitate congestive cardiac failure in a patient whose heart is already damaged by some pre-existing condition which it is hoped the corticosteroids will modify.

Prednisone and prednisolone have a less marked influence on sodium retention and are therefore preferred in the treatment of heart disease. The newer analogues, such as triamcinolone, betamethasone, or dexamethasone, have, so far as I can ascertain, no particular advantage (Bayliss, 1959). Nor in this context has corticotrophin any special superiority over prednisone or prednisolone.

Dosage must be flexible, and each individual patient constitutes his own special problem and challenge in experimental therapeutics. There is only one guiding principle, and that is to give an amount of corticosteroid that produces the desired therapeutic response. It is disconcerting to find how in two patients of the same age, sex, and weight the same disease of seemingly equal severity requires for its control dosages of prednisone that may vary by as much as fivefold or tenfold.

Indications

I will not attempt to be comprehensive regarding all the cardiac diseases that may be benefited by corticosteroids. Some are very uncommon or do not normally occur in the British Isles, and I shall limit myself to those conditions of which we have had personal experience in recent months. These comprise (1) certain myocarditides, (2) the post-pericardiotomy syndrome, (3) complete heart-block, and (4) intractable cardiac oedema.

Myocarditis

Corticosteroids do not "cure" myocarditis of any type, but by suppressing the inflammatory reaction in the heart muscle or pericardium they may diminish the ultimate permanent scarring in the cardiac tissue when the primary disease process is spent. Thus corticosteroids are not indicated in the treatment of myocarditis if the cause of the condition is susceptible to some

more specific therapeutic agent. No such specific treatment is yet available for a number of myocarditides, and corticosteroids have proved of value in sensitization and autoimmune reactions involving the heart, such as rheumatic fever, sarcoidosis, disseminated lupus erythematosus, and periarteritis, and also in certain virus infections of the myocardium.

Rheumatic Fever

Opinions regarding the value of corticosteroids in the treatment of acute rheumatic polyarthritis and acute rheumatic pancarditis have largely been governed by the results obtained in the trial conducted jointly by the Medical Research Council and the American Heart Association (1955, 1965). This painstaking multicentre study was designed to answer two main questions. Was cortisone or adrenocorticotrophin (A.C.T.H.) more effective than aspirin in (a) altering the course of the acute disease and (b) preventing the development of permanent rheumatic valvulitis? It was concluded that cortisone caused more prompt relief of certain of the acute manifestations of rheumatic fever, but at the end of one year and of ten years there was no difference in the incidence of chronic rheumatic heart disease. Other workers have also concluded that corticosteroids may shorten the duration of acute rheumatic activity and control the extracardiac manifestations of rheumatic fever without benefiting the ultimate state of the heart or reducing the incidence of chronic heart disease (Houser *et al.*, 1954; Bywaters and Thomas, 1961; Slater, 1961; Thomas, 1961).

There are, however, some criticisms that can be levelled, in the light of modern knowledge, at the design of the Anglo-American trial. Few people seem to appreciate that a fixed dosage of cortisone was used or that the cortisone was given by intramuscular injection rather than orally. The route of administration profoundly influences the plasma level of cortisol, and nowadays the dosage is adjusted in each individual to produce the desired therapeutic response. Thus Wilson (1960) claims better results with larger and individualized corticosteroid dosage, and Illingworth *et al.* (1957) have shown that cortisone plus aspirin not only reduces the duration of the acute arthritis but also prevents, during the course of the disease, the development of such new manifestations as nodules, pericarditis, and heart failure.

Whether or not corticosteroids prevent ultimate valvulitis, there is little doubt that in acute rheumatic fever they induce a more rapid symptomatic and clinical improvement than aspirin alone. One is impressed at the striking relief when prednisone is given to a patient with anorexia, continuing pyrexia, acutely painful arthritis, and pericarditis who shows little response to aspirin in doses sufficient to induce salicylism. If it is conceded (Illingworth *et al.*, 1957; Bywaters and Thomas, 1961) that cardiac enlargement, marked rheumatic activity, which increases the risk of cardiac failure, or the actual development of cardiac failure constitutes absolute indications for the use of prednisone,

* Based on lectures given to the Postgraduate Medical School, London, on 5 May and to the Institute of Cardiology on 15 June.

† Physician to Her Majesty's Household, Westminster Hospital, and King Edward VII Hospital for Officers, London.

it seems logical to give corticosteroids in all but the mildest cases of acute rheumatic fever, and certainly such treatment reduces the patients' discomfort and increases their sense of well-being.

Disseminated Lupus Erythematosus and Polyarteritis

In both these conditions cardiac involvement is not uncommon. Indeed, pericarditis may be the presenting symptom of disseminated lupus erythematosus. Less commonly the aortic or mitral valves and the myocardium are involved. Corticosteroids, often in large dosage, are required to control the conditions, but this is the treatment of first choice. The concurrent administration of cytotoxic agents, such as mercaptopurine or azathioprine (Imuran), should be considered if corticosteroids fail to control the symptoms or very large doses are required to do so (Lorenzen and Videbæk, 1965). In some rare instances it may be possible to reduce or discontinue the corticosteroids, maintaining the patient, for a time at least, on azathioprine alone.

Periarteritis is a less well defined entity which runs a variable course and probably has several different causes. Clinical manifestations of cardiac involvement are not common, but E.C.G. evidence of myocarditis occurs in some 40% of patients. Angina pectoris or more prolonged pain due to coronary insufficiency may occur, and we have observed this in a number of women aged 30 to 45 who have had histological proof of periarteritis elsewhere. A diagnosis of periarteritis should at least be considered in any young woman with ischaemic cardiac pain but may be difficult to confirm because a "blind" biopsy of muscle is seldom positive, and histological proof may be obtained only if there is pain or thrombosis in an accessible superficial artery. In these cases the response to corticosteroids may be excellent, and the condition may remain in remission after steroid treatment has been stopped.

Virus Infections

For many years physicians have been reluctant to diagnose myocarditis except in diphtheria or rheumatic fever. It is now clear that involvement of the heart and pericardium may occur in some common virus infections, such as influenza and mumps, and also in such conditions as glandular fever and acute ascending polyneuritis, which are generally conceded to be viral in origin. In most instances the cardiac involvement is unassociated with any clinical symptoms or signs and is detectable only by electrocardiography, which may show abnormalities, for example, in some 5% of adults with mumps (Bengtsson and Örndahl, 1954). When clinical manifestations develop they may take the form of pericarditis, arrhythmias, a syndrome suggestive of acute myocardial infarction, or cardiac failure. The last may be serious, and death has occurred from this in mumps (Roberts and Fox, 1965) and in the Landy-Guillain-Barré syndrome (Haymaker and Kernohan, 1949; Clarke *et al.*, 1954).

The Cocksackie B virus is particularly cardiotropic, and may cause epidemic or sporadic attacks of myocarditis—the former notably in children (Burch and De Pasquale, 1965). As in certain other virus infections, it is often difficult to establish an aetiological diagnosis unless the virus can be cultured from the blood, throat, or faeces (but it may be present in the stools of healthy people) or a rising titre of neutralizing antibodies is found in the patient's serum. Cocksackie B infection is often manifest as a biphasic illness. Initially there is a short period of malaise with symptoms of an upper respiratory infection, to be followed by a more definite illness characterized by pleurisy, Bornholm syndrome, pericarditis, or symptoms and signs suggestive of a myocardial infarction. The pericarditis is manifest by retrosternal pain, often aggravated by deep breathing, movement, or lying flat. There is usually an irritating un-

productive short cough, and the patient is more comfortable sitting upright or leaning forward. The T waves are flattened or inverted and the ST segments may be raised, but Q waves seldom develop, and the levels of serum glutamic oxaloacetic transaminase and lactate dehydrogenase are not elevated. There may be an accompanying pleural effusion. No doubt some cases of so-called benign acute pericarditis or acute non-specific pericarditis are caused by this virus.

When the pericarditis is associated with a myocarditis the condition may be confused with a myocardial infarct, or, if there are additional pulmonary symptoms, with a bronchial carcinoma with pleural and pericardial metastases. A proportion of patients have recurrent attacks of pericarditis over a number of months or years (Swan, 1960).

One hesitates to use corticosteroids to suppress virus-induced inflammation, and the natural course of the disease makes it difficult to assess the value of any treatment. Most patients need no specific therapy, but administration of prednisone should be considered in viral myocarditis when there is heart block or cardiac failure; in some instances steroids have seemingly saved life (Clarke *et al.*, 1954). Such treatment is also indicated in patients who are having recurring attacks of pericarditis.

Recently, for example, we looked after a 56-year-old man who had had four episodes, each lasting six to seven days at intervals of six weeks, characterized by fever, retrosternal pain, a pericardial rub, and mild heart failure. A diagnosis of repeated myocardial infarction had been made, although the serum transaminases were never raised and the E.C.G. changes were atypical. In his fifth attack, the first which we were able to observe, a pleural effusion developed, and the sixth attack was cut short by giving prednisone. A striking rise in the antibody titre to Cocksackie B virus was found in his blood, and no recurrences have occurred since treatment with prednisone.

Post-pericardiectomy Syndrome

It is difficult to find an appropriate name for this syndrome, which most commonly occurs after cardiac surgery but may also develop without cardiectomy after myocardial infarction, traumatic pericarditis (presumably with associated damage to the myocardium), and even after pericardiectomy without incision of the heart muscle (van der Geld, 1964). There is usually a latent period of a week or so after the primary illness before the syndrome develops, with malaise, fever, a raised sedimentation rate, precordial pain, and pericarditis with or without pleurisy and pericardial or pleural effusions. There is experimental evidence, derived from studies with a haemagglutination reaction with the use of tanned red cells sensitized with a crude saline extract of heart muscle, that this syndrome is an expression of autoimmunity to heart tissue (Ehrenfeld *et al.*, 1961; Robinson and Brigden, 1963). This hypothesis finds indirect support in that the clinical and laboratory manifestations of the condition can be suppressed and the natural course of the syndrome curtailed by corticosteroids. The oral dosage of prednisone is determined by the patient's clinical response; treatment should not be discontinued too soon, and should be withdrawn gradually for fear of a relapse.

Complete Heart-block

Acute complete atrioventricular block may occur in association with a recent myocardial infarction. The main dangers in this situation are a further reduction in cardiac output, with diminished perfusion of the coronary vascular tree, and the occurrence of transient ventricular asystole (Stokes-Adams attacks) or more permanent ventricular asystole or fibrillation. The complete heart-block is often transitory with spontaneous

resumption of normal rhythm, which makes it difficult to assess the value of any therapeutic measure used. However, an increasing number of reports seem to indicate that corticosteroids, by reducing ischaemic inflammation in the conducting tissues, help to restore sinus rhythm (Prinzmetal and Kenamer, 1954; Phelps and Lindsay, 1957; Aber and Wyn Jones, 1960, 1965; Caramelli and Tellini, 1960; Dall and Buchanan, 1962; Dall, 1964). Such treatment may be rapidly effective and obviate the need to consider artificial pacing. Corticotrophin gel (40 units b.d.), hydrocortisone hemisuccinate (200–400 mg. intravenously), or prednisolone-21-phosphate (50–100 mg. intravenously) has been used in the acute stage, followed by prednisone, 5 mg. q.d.s. orally, for some days.

Chronic heart-block, persisting for longer than a month, was formerly attributed to ischaemic heart disease, but there is now good evidence that other causes are more common. Zoob and Shirley Smith (1963) drew attention to the frequency of scattered foci of myocardial fibrosis in such cases, and in a careful post-mortem study Davies (1966) found coronary artery disease in only 3 out of 22 cases of chronic heart-block, 10 of which had a cardiomyopathy and three a myocarditis. Corticosteroids may restore sinus rhythm or abolish or reduce the frequency of Stokes-Adams attacks (Friedberg *et al.*, 1960; Verel *et al.*, 1963). The success rate of this treatment is, however, very variable, ranging from complete failure in 10 patients (Caramelli and Tellini, 1960), failure in 12 out of 14 patients (Dall, 1964), success in 5 out of 6 patients (Pay and Waverley, 1961), and success in 17 out of 26 (60%) patients (Aber and Wyn Jones, 1965). In such patients the dosage of prednisone should be high initially (60 mg. daily) and continued for two weeks unless sinus rhythm is restored earlier. If normal rhythm occurs maintenance therapy is continued for three months in a dose of 15–20 mg. of prednisone daily. In some patients atrio-ventricular block may return when corticosteroid treatment is withdrawn (Friedberg *et al.*, 1960; Pay and Waverley, 1961; Verel *et al.*, 1963), and it is wise to prescribe in addition a long-acting isoprenaline preparation such as Saventrine to accelerate the heart rate.

Intractable Oedema

With the advent of increasingly potent diuretics, intractable oedema is becoming less intractable, and there are few patients, except those in terminal cardiac failure, whose oedema cannot be eliminated by a combination of diuretic agents such as ethacrynic acid or frusemide, which impede sodium reabsorption in the proximal tubule and the loop of Henle, and spironolactone or triamterene, which block sodium reabsorption in the distal renal tubule (Ledingham and Bayliss, 1965b). Such intensive treatment requires constant vigilance and supplements of potassium chloride to prevent the development of hypokalaemia, hypochlorhaemic alkalosis, or azotaemia (Ledingham and Bayliss, 1965a; Sherlock *et al.*, 1966). Everything possible must be done to improve cardiac output and renal blood-flow, a reduction in which is the primary cause of the sodium retention. Sometimes this means repairing a damaged valve under most unfavourable circumstances, as, for example, in a patient who was still oedematous after two months' intensive treatment but had a massive diuresis in the operating theatre immediately after aortic valvotomy.

The use of corticosteroids in the treatment of cardiac oedema is largely empirical and stems from their use in nephrotic and cirrhotic oedema, where a good response is more common than in cardiac patients, probably because of the anti-inflammatory effect of the steroid on the glomerular lesions in nephrosis and on the hepato-cellular damage in cirrhosis.

The rationale for the use of prednisone in the treatment of cardiac oedema has been based on a number of premises which are probably false. Because the serum sodium concentration is often low in intractable cardiac oedema it has been suggested

that there is adrenal or pituitary failure and that the hyponatraemia is analogous to that found in severe cases of Addison's disease (Mickerson and Swale, 1959). This supposes that the total body sodium is reduced, which is not the case in patients with cardiac oedema, nor is the plasma level of cortisol low, being normal or even raised. In these patients no reliance can be placed on the urinary excretion of corticosteroids and their metabolites as an index of adrenal function, because steroid excretion falls when urine volume is reduced (Hatfield and Shuster, 1959). Nor does corticosteroid restore the ability to eliminate promptly a water load in cardiac failure as it does in patients with adrenal insufficiency (Lasché and Durant, 1957). It seems more probable that the hyponatraemia is mainly due to the intracellular migration of sodium from the extracellular fluid, a condition which is often of evil omen and has been termed "the sick-cell syndrome." Any diuretic action of prednisone cannot be attributed to suppression of aldosterone secretion, which is not controlled to a significant degree by the pituitary secretion of A.C.T.H., nor to competition between prednisone and aldosterone in the distal renal tubules.

Although a number of investigators have reported a diuretic response to corticosteroids or A.C.T.H. in cardiac failure (Cámara and Schemm, 1955; Heidorn and Schemm, 1955; Riemer, 1956; Cattan and Vesin, 1956; Gutner *et al.*, 1957; Dresdale *et al.*, 1958), this has not been our experience. On the other hand, like others, we have found that prednisone may potentiate the response to conventional diuretics. The Chart shows in a group of cardiac patients on a constant sodium

Urinary sodium excretion per 24 hours after 2 ml. of mersalyl given intramuscularly to seven patients with intractable cardiac oedema before and during administration of prednisone 5 mg. q.d.s. The patients were on a constant low sodium intake (22 mEq/day). Note the increased natriuresis during prednisone treatment.

diet the 24-hour urinary sodium excretion after single doses of 2 ml. of mersalyl intramuscularly given before and during administration of prednisone. There is no doubt that prednisone enhanced sodium excretion, and in some of the patients who had hyponatraemia the serum sodium level returned to normal. Similarly we have found that prednisone may potentiate the action of mersalyl and spironolactone or other diuretics. This effect of prednisone is of more physiological interest than therapeutic benefit in intractable oedema, and is probably related to an action on the cell membranes of renal and extrarenal tissues influencing the fluxes of sodium, potassium, and water (Dingman *et al.*, 1958) and increasing glomerular filtration and renal plasma flow (Raisz *et al.*, 1957; Pechet *et al.*, 1959).

Summary

The value of the anti-inflammatory and immunosuppressant actions of corticosteroids in the treatment of certain cardiac diseases is discussed. Rheumatic pancarditis, virus pericarditis and myocarditis, and the post-pericardiotomy syndrome may respond favourably, and the treatment may sometimes obviate the need for artificial pacing in complete heart-block. The use of corticosteroids in intractable cardiac oedema is also discussed.

REFERENCES

- Aber, C. P., and Wyn Jones, E. (1960). *Brit. Heart J.*, **22**, 723.
 — (1965). *Ibid.*, **27**, 916.
 Bayliss, R. I. S. (1959). *Proc. roy. Soc. Med.*, **52**, 929.
 Bengtsson, E., and Orndahl, G. (1954). *Acta med. scand.*, **149**, 381.
 Burch, G. E., and De Pasquale, N. P. (1965). *Viral Myocarditis in Cardiomyopathies*, edited by G. E. W. Wolstenholme and M. O'Connor, p. 376. Churchill, London.
 Bywaters, E. G. L., and Thomas, G. T. (1961). *Brit. med. J.*, **1**, 1628.
 Cámara, A. A., and Schemm, F. R. (1955). *Circulation*, **11**, 702.
 Caramelli, Z., and Tellini, R. R. (1960). *Amer. J. Cardiol.*, **5**, 263.
 Cattani, R., and Vesin, P. (1956). *Sem. Hôp. Paris*, **32**, 712.
 Clarke, E., Bayliss, R. I. S., and Cooper, R. (1954). *Brit. med. J.*, **2**, 1504.
 Dall, J. L. C. (1964). *Brit. Heart J.*, **26**, 537.
 — and Buchanan, J. (1962). *Lancet*, **2**, 8.
 Davies, M. J. (1966). Communication to the Association of Physicians.
 Dingman, J. F., Finkenstaedt, J. T., Laidlaw, J. C., Renold, A. E., Jenkins, D., Merrill, J. P., and Thorn, G. W. (1958). *Metabolism*, **7**, 608.
 Dresdale, D. T., Greene, M. A., and Guzman, S. V. (1958). *Amer. Heart J.*, **55**, 851.
 Ehrenfeld, E. N., Gery, I., and Davies, A. M. (1961). *Lancet*, **1**, 1138.
 Friedberg, C. K., Kahn, M., Scheuer, J., Bleifer, S., and Dack, S. (1960). *J. Amer. med. Ass.*, **172**, 1146.
 Gutner, L. B., Moses, J. B., Dann, S., and Kupperman, H. S. (1957). *Amer. J. med. Sci.*, **234**, 281.
 Hatfield, C. B., and Shuster, S. (1959). *J. Endocr.*, **18**, 262.
 Haymaker, W., and Kernohan, J. W. (1949). *Medicine (Baltimore)*, **28**, 59.
 Heidorn, G. H., and Schemm, F. R. (1955). *Amer. J. med. Sci.*, **229**, 621.
 Houser, H. B., Clark, E. J., and Stolzer, B. L. (1954). *Amer. J. Med.*, **16**, 168.
 Illingworth, R. S., Lorber, J., Holt, K. S., and Rendle-Short, J. (1957). *Lancet*, **2**, 653.
 Lasché, E. M., and Durant, T. M. (1957). *Amer. J. med. Sci.*, **233**, 80.
 Ledingham, J. G. G., and Bayliss, R. I. S. (1965a). *Clin. Pharmacol. Ther.*, **6**, 474.
 — (1965b). *Brit. med. J.*, **2**, 732.
 Lorenzen, I., and Videbæk, A. (1965). *Lancet*, **2**, 558.
 Medical Research Council and American Heart Association (1955). *Brit. med. J.*, **1**, 555.
 — (1965). *Ibid.*, **2**, 607.
 Mickerson, J. N., and Swale, J. (1959). *Brit. med. J.*, **1**, 876.
 Pay, B. W., and Waverley, A. (1961). *Ibid.*, **2**, 139.
 Pechet, M. M., Bowers, B., and Barter, F. C. (1959). *J. clin. Invest.*, **38**, 681, 691.
 Phelps, M. D., and Lindsay, J. D. (1957). *New Engl. J. Med.*, **256**, 204.
 Prinzmetal, M., and Kennamer, J. W. (1954). *J. Amer. med. Ass.*, **154**, 1049.
 Raisz, L. G., McNeely, W. F., Saxon, L., and Rosenbaum, J. D. (1957). *J. clin. Invest.*, **36**, 767.
 Riemer, A. D. (1956). *Bull. Johns Hopk. Hosp.*, **98**, 445.
 Roberts, W. C., and Fox, S. M. (1965). *Circulation*, **32**, 342.
 Robinson, J., and Brigden, W. (1963). *Brit. med. J.*, **2**, 706.
 Sherlock, S., Senewiratne, B., Scott, A., and Walker, J. G. (1966). *Lancet*, **1**, 1049.
 Slater, J. D. H. (1961). *Ann. rheum. Dis.*, **20**, 173.
 Swan, W. G. A. (1960). *Brit. Heart J.*, **22**, 651.
 Thomas, G. T. (1961). *Brit. med. J.*, **1**, 1635.
 van der Geld, H. (1964). *Lancet*, **2**, 617.
 Verel, D., Mazurkic, S. J., and Rahman, F. (1963). *Brit. Heart J.*, **25**, 709.
 Wilson, M. G. (1960). *Advanc. Pediat.*, **11**, 243.
 Zoob, M., and Smith, K. S. (1963). *Brit. med. J.*, **2**, 1149.

Concentration of Chloramphenicol in the Urine and Blood in Relation to Renal Function

A. A. LINDBERG,* M.D.; L.H.:son NILSSON,† M.D.; H. BUCHT,†, M.D.; L. O. KALLINGS,* M.D.

Brit. med. J., 1966, **2**, 724–728

Because of the occurrence of multiresistant bacterial strains in chronic infections of the urinary tract the physician is often faced with the necessity of choosing a therapeutic agent differing from those normally resorted to in the first instance. According to *in vitro* determinations, these multiresistant strains are often relatively sensitive to chloramphenicol. Treatment is often complicated by the occurrence of anatomical changes in the kidneys and the urinary tract, and by impairment of the renal function.

Most antibiotics are eliminated from the body by the kidneys, and so the concentration of such substances in the blood and urine is dependent on the renal function. If this function is impaired an antibiotic and its metabolites may be retained in the blood in concentrations which may have toxic effects (Erlanson and Lundgren, 1964). When giving antibiotic therapy, therefore, the renal function should be taken into consideration, with regard to the risk of overdose as well as the difficulty of attaining a sufficient concentration in the urine. Kunin and Finland (1959) discussed the connexion between renal function and the excretion of various antibiotics. Principally, they found that if the concentration of the substance in the blood and the volume of urine are constant, then the concentration of the substance in the urine is directly

proportional to the clearance of the substance and to the renal function. In treatment of the urinary tract, therefore, relatively high concentrations in the urine are attained if the substance is excreted rapidly, even if the renal function of the patient is much impaired. On the other hand, antibiotics with low clearance values do not give effective urinary concentrations even in patients with good renal function, provided the serum concentrations of the substances are not raised very much. When estimating the renal function, determination of non-protein-nitrogen and serum creatinine is often insufficient; considerable variation in the glomerular filtration may be found when these values are normal.

At the Renal Clinic of St. Eriks Sjukhus, Stockholm, we believe we have found an unsatisfactory correlation between the determination of the sensitivity of the bacterial strains *in vitro* and the results of chloramphenicol therapy. On reading the published reports of treatment with chloramphenicol in infections of the urinary tract we found varying results. Not unexpectedly, these were better when treating acute infections of the urinary tract than in the treatment of chronic cases (Chittenden *et al.*, 1949; Hewitt and Williams, 1950; Turck *et al.*, 1962).

Högman and Tillegård (1954) studied the parallelism between bacterial sensitivity *in vitro* and the clinical therapeutic results obtained with various antibiotics in the treatment of infections of the urinary tract. The parallelism for sulphanilamide,

* From the National Bacteriological Laboratory, Stockholm.

† From the Renal Clinic, St. Eriks Hospital, Stockholm.