Marfanil (mesudin, homosulphanilamide, sulphamylon): [*p*-amino-methyl-benzene-sulphonamide].

Introduced by I. G. Farbenindustrie, tested biologically by Domagk, and described by Klarer (1941). It had also been prepared independently by Miller, Sprague, Kissinger, and McBurney (1940). It differs from all the other sulphonamides in that the amino group (H_2N) is separated from the benzene ring by a methyl (—CH_2—) group. Accordingly it is not diazotizable and cannot be estimated by Marshall's method. Also, it is not inhibited by *p*-aminobenzoic acid. Marfanil-fast strains of bacteria are not resistant to sulphathiazole, and conversely (Link, 1943). Apparently the receptor of the organism on which it acts is different from that which is susceptible to the usual sulphonamide action. It is more soluble in water than sulphanilamide (1,970 mg. per 100 c.cm. at 37° C.), and very soluble in dilute acids or alkalis. It is less active than sulphanilamide against streptococci. Domagk (1942) claims that it is much more active against anaerobic infections than this compound; but this claim is not confirmed by Schreus, Brauns, and Schümmer (1941). It seems to be used extensively in the German army for local application to wounds as marfanil-prontosil powder (i.e., 1 part marfanil, 9 parts sulphanilamide), and since it is not inhibited by *p*-aminobenzoic acid it may have real advantages for this purpose. Mitchell, Rees, and Robinson (1944) have recently described a clinical trial for use as a local application to infected wounds; they consider it valuable for this purpose. Their trial was made with German material captured at El Alamein (see also *Lancet*, 1944, **1**, 635)

REFERENCES

Adair, F. L., Hesseltine, H. C., and Hac, L. R. (1938). *J. Amer. med. Ass.*, **111**, 766.
Alexander, F. (1943). *Quart. J. exp. Physiol.*, **32**, 21.
Ashburn, L. L., Daft, F. S., Endicott, K. M., and Sebrell, W. H. (1942). *Publ. Hlth. Rep. Wash.*, **57**, 1883.
Banks, H. S. (1941). *Lancet*, **1**, 104.
Bellows, J., and Chinn, H. (1939). *J. Amer. med. Ass.*, **112**, 2023.
Black, S., Overman, R. S., Elvehjem, C. A., and Link, K. P. (1942). *J. biol. Chem.*, **145**, 137.
Bogen, E. (1943). *U.S. nav. med. Bull.*, **41**, 1135.
Cantarow, A., Cubberley, C. L., and Rakoff, A. E. (1942). *Arch. intern. Med.*, **69**, 456.
Cutts, F. B., and Bowman, R. O. (1941). *New Engl. J. Med.*, **225**, 448.
Davenport, H. W. (1942). *Yale J. biol. Med.*, **14**, 589.
Davis, B. D. (1942). *Science*, **95**, 78.
—— (1943). *J. clin. Invest.*, **22**, 753.
—— and Wood, W. B. (1942). *Proc. Soc. exp. Biol.*, N.Y., **51**, 283.
Domagk, G. (1942). *Klin. Wschr.*, **21**, 448.
Feldman, W. H., Hinshaw, H. C., and Moses, H. E. (1940). *Proc. Mayo Clin.*, **15**, 695.
Föllmer, W. (1941). *Klin. Wschr.*, **20**, 912.
Frisk, A. R. (1940a). *Nord. Med.*, **7**, 1319.
—— (1940b). Ibid., **7**, 1483.
Harris, J. S., and Klein, J. R. (1938). *Proc. Soc. exp. Biol.*, N.Y., **38**, 78.
Hawking, F. (1937). *Lancet*, **2**, 1019.
—— (1942a). Ibid., **1**, 290.
—— (1942b). Ibid., **1**, 704.
—— (1943). *Practitioner*, **151**, 354.
—— and Hunt, A. H. (1942). *British Medical Journal*, **2**, 604.
Heaf, F. R. G., Hurford, J. V., Eiser, A., and Franklin, L. M. (1943). *Lancet*, **1**, 702.
Heinemann, M. (1943). *J. clin. Invest.*, **22**, 29.
Hepburn, J. S., Paxson, N. F., and Rogers, A. N. (1942). *Arch. Pediat.*, **59**, 413.
Heyl, J. T. (1941). *Proc. roy. Soc. Med.*, **34**, 782.
Hinshaw, H. C., Pfuetze, K., and Feldman, W. H. (1943). *Amer. Rev. Tuberc.*, **47**, 26.
Höber, R. (1942). *Proc. Soc. exp. Biol.*, N.Y., **49**, 87.
Hubbard, R. S., and Anderson, R. K. (1940). *Arch. Pathol.*, **30**, 981.
—— and Butsch, W. L. (1941). *Proc. Soc. exp. Biol.*, N.Y., **46**, 484.
Kinsman, J. M., Moore, J. W., and Harrison, M. M. (1940). *J. Lab. clin. Med.*, **25**, 1235.
Kirchhof, A. C., Racely, C. H., Thompson, A. I., and David, N. A. (1943). *West. J. Surg. Obstet. Gynec.*, **51**, 419.
Klarer, J. (1941). *Klin. Wschr.*, **20**, 1250.
Link, T. (1943). Ibid., **22**, 364.
Long, P. H. (1941). *J. Amer. med. Ass.*, **116**, 2399.
Loomis, T. A., Hubbard, R. S., and Koepf, G. F. (1943). *Amer. J. Physiol.*, **139**, 197.
Macartney, D. W., Smith, G. S., Luxton, R. W., Ramsay, W. A., and Goldman, J. (1942). *Lancet*, **1**, 639.
McChesney, E. W., Sprague, K. D., and Marshall, I. H. (1941). *J. Lab. clin. Med.*, **26**, 1154.
Mackenzie, J. B., Mackenzie, C. G., and McCollum, E. V. (1941). *Science*, **94**, 518.
Mann, T., and Keilin, D. (1940). *Nature*, **146**, 164.
Marquardt, F. (1938). *Klin. Wschr.*, **17**, 1518.
Marshall, E. K., Bratton, A. C., White, H. J., and Litchfield, J. T. (1940). *Johns Hopk. Hosp. Bull.*, **67**, 163.
—— Cutting, W. C., and Emerson, K. (1938). *J. Amer. med. Ass.*, **110**, 252.
—— Emerson, K., and Cutting, W. C. (1937a). *J. Pharmacol.*, **61**, 191.
—— —— —— (1937b). Ibid., **61**, 196.
—— and Litchfield, J. T. (1939). Ibid., **67**, 454.
Melton, G. (1941). *Lancet*, **1**, 274.
Miller, E., Sprague, J. M., Kissinger, L. W., and McBurney, L. F. (1940). *J. Amer. chem. Soc.*, **62**, 2099.
Mitchell, G. A. G., Rees, W. S., and Robinson, G. N. (1944). *Lancet*, **1**, 627.
Murphy, F. D., Clark, J. K., and Flippin, H. F. (1943). *Amer. J. med. Sci.*, **205**, 717.
Nicolai, H. (1941). *Münch. med. Wschr.*, **88**, 784.
P'an, S. Y. (1941). *J. Pharmacol.*, **72**, 31.
Peters, B. A., and Easby, M. L. (1943). *British Medical Journal*, **2**, 230.
Peterson, O. L., and Finland, M. (1942). *Amer. J. med. Sci.*, **204**, 581.
—— Goodwin, R. A., and Finland, M. (1943). *J. clin. Invest.*, **22**, 659.
Peterson, O. L., Strauss, E., Taylor, F. H. L., and Finland, M. (1941). *Amer. J. med. Sci.*, **201**, 357.
Philipp, E. (1941). *Dtsch. med. Wschr.*, **67**. 372, 974.
Poth, E. J. (1942). *J. Amer. med. Ass.*, **120**, 265.
—— and Knotts, F. L. (1941). *Proc. Soc. exp. Biol.*, N.Y., **48**, 129.
—— —— (1942). *Arch. Surg.*, Chicago, **44**, 208.
—— and Ross, C. A. (1943). *Texas Rep. Biol. Med.*, **1**, 345.
—— —— (1944). *J. Lab. clin. Med.*, **29**, 785.
Ratish, H. D., Shackman, N. H., and Bullowa, J. G. M. (1942). *New Engl. J. Med.*, **226**, 596.
Reed, H. (1944). *Lancet*, **2**, 535.
Reimers, U. (1939). *Derm. Wschr.*, **108**, 74.
Reinhold, J. G., Flippin, H. F., Schwartz, L., and Domm, A. H. (1941). *Amer. J. med. Sci.*, **201**, 106.
Rieben, G., and Druey, J. (1942). *Schweiz. med. Wschr.*, **23**, 1376.
Roughton, F. J. W., Darling, R. C., Forbes, W. H., Horvath, S. M., Robinson, S., and Talbott, J. H. (1942). *Amer. J. Physiol.*, **137**, 593.
—— Dill, D. B., Darling, R. C., Graybiel, A., Knehr, C. A., and Talbott, J. H. (1941). Ibid., **135**, 77.
Ruegsegger, J. M., Hamburger, M., Turk, A. S., Spies, T. D., and Blankenhorn, M. A. (1941). *Amer. J. med. Sci.*, **202**, 432.
Sadusk, J. F., Blake, F. G., and Seymour, A. (1940). *Yale J. biol. Med.*, **12**, 681.
Schmidt, L. H., and Sesler, C. L. (1943). *J. Pharmacol.*, **77**, 277.
Schönholzer, G. (1940). *Klin. Wschr.*, **19**, 790.
Schreus, H. T., Brauns, A., and Schümmer, H. (1941). Ibid., **20**, 1233.
Siebert, W. J., and Loose, F. (1940). *J. Lab. clin. Med.*, **25**, 1062, and **26**, 371.
Simesen, M. H. (1941a). *Arch. exp. Path. Pharmakol.*, **197**, 12.
—— (1941b). Ibid., **197**, 87, 429.
Speert, H. (1940). *Johns Hopk. Hosp. Bull.*, **66**, 139.
—— (1943). *Amer. J. Obstet. Gynec.*, **45**, 200.
Spink, W. W., Bergh, G. S., and Jermsta, J. (1941). *Surgery*, **9**, 853.
—— and Hansen, A. E. (1940). *J. Amer. med. Ass.*, **115**, 840.
Sprague, J. M., Kissinger, L. W., and Lincoln, R. M. (1941). *J. Amer. chem. Soc.*, **63**, 3028.
Taylor, A., and Agren, G. (1940). *Acta physiol. scand.*, **1**, 79.
Turell, R., Marino, A. W. M., and Nerb, L. (1940). *Ann. Surg.*, **122**, 417.
Turkell, J., and Wilhelm, S. F. (1941). *Proc. Soc. exp. Biol.*, N.Y., **47**, 97.
Vickers, H. E. (1943). *Lancet*, **2**, 760.
Waterhouse, A., and Shannon, J. A. (1942). *Proc. Soc. exp. Biol.*, N.Y., **50**, 189.
White, H. J. (1942). *Johns Hopk. Hosp. Bull.*, **71**, 213.
Wilson, H. E. C. (1943). *British Medical Journal*, **1**, 507.
Wood, E. H. (1941). *Canad. med. Ass. J.*, **44**, 592.

INVESTIGATION AND RESULTS OF TREATMENT OF 1,000 CASES OF VAGINAL DISCHARGE

BY

OSWALD LLOYD, M.D., F.R.C.S., M.R.C.O.G.

Assistant Gynaecological Surgeon, Addenbrooke's Hospital, Cambridge; Late Gynaecological Registrar, Middlesex Hospital

The following account embodies the results of the investigation and treatment of 1,000 women complaining primarily of vaginal discharge. Each was carefully interrogated and all necessary bacteriological and serological investigations were made. Details of clinical examination and findings are purposely omitted, as the routine is now well established. The cases were all directly under my care for a period of at least six months. The services of a trained nurse were at all times available, and this has contributed greatly to the excellence of the end-results. The case incidence of the various types will be found in the Table, and each group will be briefly discussed and conclusions drawn from the results.

Case Incidence

(*a*) Trichomonas vaginitis	447
(*b*) Gonococcal infection	178
(*c*) Combined trichomonas vaginitis and gonococcal infection	32
(*d*) Residual and non-specific erosions	193
(*e*) Monilia vaginitis	57
(*f*) Vulvovaginitis of infancy	14
(*g*) Senile vaginitis	41
(*h*) Non-inflammatory leucorrhoea	27
(*i*) Polypi, neoplasms, and foreign bodies	11
Total	1,000

(a) Trichomonas Vaginitis

The literature dealing with this condition is considerable. At first there seemed to be some doubt as to the pathogenicity of the organism, but now it is widely accepted as capable of producing a vaginitis—acute, subacute, and chronic. The primary source of the infection is still debated: the rectum is a potential origin, but is by no means definitely incriminated. Almost all cases occur during the reproductive period, but this series includes one pre-pubertal and four post-menopausal. It affects undoubted virgins and has a predilection for the vagina in pregnancy. The association of gonorrhoea and trichomonas vaginitis in 32 cases draws attention to the need for careful exclusion of Neisserian infection even if *Trichomonas vaginalis* has been demonstrated. The following method of treatment has yielded the best results, both immediate and remote.

As soon as diagnosis is established, one stovarsol vaginal compound tablet is inserted daily for at least eight weeks, including during the menstrual period. Once a week the vagina is thoroughly irrigated with sodium bicarbonate solution, one drachm to the pint, then dried, and finally swabbed out with half-strength Bonney blue solution. This must be done at least once during two consecutive menstrual periods. At the conclusion of the eight weeks the patient is given enough tablets to insert one daily during the next three menstrual periods. The vaginal painting can with advantage be done once a week. Certain modifications have to be made in individual cases; for example, when the hymen is intact the Bonney blue solution is run in through a small rubber catheter. During pregnancy an arbitrary time period of eight weeks has been adopted.

One case of trichomonas vaginitis deserves special mention, because it was among the first few in the series, and it remains after five years the only one that has resisted all efforts to dislodge the causative organism.

The patient, then aged 30, had had an irritating discharge for several months. The only positive laboratory finding was *Trichomonas vaginalis*. She was treated with 5% negatol vaginal packs—a method then being used by me, and reported in the *Lancet* in 1939. This failed, and in company with many others she was insufflated with silver picrate. Moderate success attended this treatment; a number were cured, but recurrences were not infrequent, and this patient was among them. She was then given a full routine treatment as outlined above, and obtained several weeks' freedom from discharge; but once more it recurred. In addition she complained that her periods were profuse and irregular. Little improvement was obtained by medicinal measures, and curettage on two occasions brought only temporary relief. Accordingly, subtotal hysterectomy was carried out. The *Trichomonas* infection continued to thrive after discharge from hospital, and the patient was readmitted. The cervical canal was cauterized and the vagina lightly packed with gauze soaked in half-strength Bonney blue solution; this was removed after 12 hours, and douches of flavine 1 in 1,000 were given three times a day. In addition stovarsol vaginal compound was inserted daily into the rectum, and the urethra was swabbed with 10% protargol. After six weeks' treatment the patient was sent home, only to return in three weeks with a typical acute *Trichomonas* infection.

She was advised to douche three times a day and to "grin and bear it." This she did for several months; then she once more appealed for help. She was readmitted to hospital and given a full course of 40 g. of prontosil album, without benefit. This was followed by a course of stilboestrol up to 5 mg. a day for six weeks, without tangible improvement. The vagina was packed with gauze soaked in 5% N.A.B. paint for three weeks; after this improvement occurred and hopes ran high. She left the hospital with the vagina looking normal for the first time in three years. Recurrence was noted in less than a month, and a repetition of the N.A.B. led to local soreness and had to be abandoned. She was once more admitted; the vagina was irrigated with a solution of quinosan and she was given a course of quinosan by mouth. Relief was only temporary, and she remained infected in spite of all the above treatments.

(b) Gonorrhoea

This review serves to illustrate that gonorrhoea is far from being the commonest cause of discharge in women. The diagnosis in earlier cases was made by smears only, but, on the recommendation of the American Neisserian Society, cultures of the cervical pus were made. This is said to lead to more positive diagnosis, but in the present series positive cultures were obtained only if positive smears had been reported.

Treatment in the first year was by the routine administration of 40 g. of prontosil album by mouth, daily douches, high vaginal packs of gauze soaked in glycerin, and urethral swabbing with 10% protargol. The prontosil album was replaced by sulphapyridine, and this eventually by sulphathiazole. Local treatment was discontinued, but 5 g. of prontosil album powder was insufflated into the vagina twice within the first week. In 203 cases the gonococcus could not be demonstrated after the conclusion of the treatment, but 7 were still positive, and recourse was had to local treatment as previously described. This was continued until two post-menstrual smears were negative following the use of a provocative vaccine.

Groups c and d

Combined gonococcal and Trichomonas infections were treated with sulphonamides by mouth, and locally by means of stovarsol and Bonney blue. The results were satisfactory in all cases.

Treatment of *residual and non-specific erosions* was by application of pure negatol to the eroded area twice weekly. The results were satisfactory for small erosions, but larger erosions required electric cauterization.

(e) Monilia Vaginitis

This group deserves wider recognition, and will be discovered more often if search is made. In a typical case the vaginal mucosa is covered with the white patches characteristic of *Oidium albicans*. The predominant symptom is a white musty-smelling discharge causing much irritation. The first treatment adopted was douching, followed by painting of the vaginal walls with 2% gentian violet at intervals of a few days. This yielded fair results, but was varied in an attempt to find a completely satisfactory method. Monsol (1/200) douches were equally satisfactory, but the best treatment, and the one used solely during the past year, was the local application of mersogel fungicidal jelly (Glaxo). The patient attended the clinic for treatment, to ensure that the fungicide reached the upper vagina. The results were very satisfactory; the average duration of treatment was three weeks. The infection is apparently more common during pregnancy.

(f) Vulvovaginitis of Infancy

The number of cases of this disease is small, but the results were excellent. Each patient was admitted to hospital and examined under anaesthesia. Material was obtained for smears and culture, after which the vagina was irrigated with a bland lotion; finally a few c.cm. of 10% argyrol were instilled into the vagina, and the child kept recumbent, with the foot of the bed on blocks. Sulphonamides were given to all these patients in doses proportionate to their age, and stilboestrol, 1 mg. t.d.s., was administered for 21 days. The argyrol instillation was repeated after a week. All cases were free from any evidence of infection six weeks from the start of treatment.

Groups g, h, and i

Most cases of *senile vaginitis* presented in a typical fashion—thin purulent discharge causing irritation of the vulva, with punctate haemorrhages appearing on the vaginal walls. Treatment was by lactic acid douches and the administration of stilboestrol by mouth in doses averaging 3 mg. a day. The results were eminently satisfactory in all cases, resolution occurring within two months of the beginning of treatment.

Non-inflammatory leucorrhoea is diagnosed by examination of a high vaginal swab, the findings being epithelial cells and Döderlein's bacillus with no pus cells. Such cases are often made worse by ill-advised douching with various antiseptics. Relief was obtained by the use of sodium bicarbonate solution, but the very nature of the complaint precludes complete cure.

Group i requires no discussion. Treatment was by the usual methods.

Conclusion

This account is incomplete in that no attempt has been made to give detailed figures of each subsection of each group; but such details would produce a maze of figures that would only bore and confuse. The object has been to give as briefly as possible my own methods and conclusions, in the hope that they will help others engaged in dealing with similar problems.

I wish to acknowledge with gratitude the help given by the Bland-Sutton Institute of Pathology and the Pathological Department of Addenbrooke's Hospital, and, in particular, that given by the nurses who carried out the treatment in the clinic.

A Polish Military Hospital in the Middle East is now equipped with a laboratory for making penicillin, and is the only military place in the Middle East for making this drug. Prof. Odrzywolski is in charge of the manufacture. The first two phials of mould were sent to the Polish Hospital by Sir Howard Florey in May, 1944. The Poles have carried out their own experiments, and Prof. Odrzywolski came to England recently to visit one of our chief penicillin research centres, in order to exchange scientific information and learn improved methods. The Polish Hospital in the Middle East supplies not only other Polish hospitals but other Allied military medical institutions in the Middle East.