BRITISH MEDICAL JOURNAL

LONDON SATURDAY JUNE 4 1960

SOME EFFECTS OF SOAP ON THE SKIN*

BY

F. RAY BETTLEY, T.D., M.D., F.R.C.P.

Physician for Diseases of the Skin, the Middlesex Hospital, London

Views on the action of soap on the skin have changed a good deal in the past; to the Victorians cleanliness came next to godliness, and the consumption of soap in this country increased enormously with advances in chemical techniques of the industrial revolution. Pears soap carried the testimonial of three prominent dermatologists in concert—Erasmus Wilson, James Startin, and John Milton, the founder of St. John's Hospital for Diseases of the Skin. I do not suppose that the nature of soap has changed much since their time, but knowledge of its action on the skin has broadened and the whole position has now altered in that other cleansers are available and the use of soap is not the only alternative to squalor.

The enthusiastic support of soap accorded by the Victorians was followed by a reactionary swing, and some senior dermatologists between the wars considered it almost wholly bad. Henry MacCormac, for example, used to attribute to soap far more harm than good in the cause and prevention of skin diseases. To-day we have perhaps a position somewhere between these two extremes.

Antibacterial Action

Though it is not my purpose to consider at length the cleansing power of soap on the skin, it may be appropriate to mention its effect on the bacterial flora. The antibacterial action of soap was investigated and described by Walker (1924, 1925, 1926). He found that the antiseptic action varied with the soap according to its fatty-acid content and with the bacteria studied. Thus, oleate and linoleate had negligible action in respect of *Salmonella typhi* but were effective against pneumococci; palmitate and stearate soaps were effective against both organisms. The mixed soaps sold commercially contain a variety of fatty acids which should give them good antiseptic action against streptococci, pneumococci, *Corynebacterium diphtheriae*, meningococci, and gonococci. The Gram-negative rods *Escherichia coli, Salm typhi,* and the paratyphoid group are more resistant. In these days it is particularly important to observe that *Staphylococcus aureus* appears to be completely resistant to soap. Colebrook and Maxted (1933) confirmed some of these results and found that in respect of streptococci the antiseptic action of 1 in 400 soap solution was greater than that of 1 in 160 lysol or 1 in 1,000 mercury perchloride.

Perhaps more important than killing micro-organisms is their removal from the skin by washing. Colebrook and Maxted deposited cultures and infected secretions on the skin and under various conditions attempted to recover them later by swabbing. They found that five minutes' ordinary washing was apparently sufficient to remove contamination with streptococci but not with staphylococci—that is to say, they could no longer recover the test organisms after washing. Price (1938) used a standardized technique by which hands and forearms were scrubbed with soap and water for one minute in 14 consecutive bowls. After cultures of the washing water had been examined, the total number of bacteria removed in each washing was calculated, and from this an estimate was made of the total number of micro-organisms which had been present on the skin surface. As might be expected, the number of organisms removed by each successive washing becomes less and less. Price estimated that about half the total flora are removed in the first six minutes and two-thirds in the first ten minutes.

The whole bacterial flora are never removed, and this led to Price's conception of resident and transient flora. The former are fortunately usually not pathogenic, though sometimes a pathogen may become installed as a resident. According to Pohle and Stuart (1940) *Staph. albus* is the most common resident; Pillsbury *et al.* (1942) also identified a coagulase-negative *Staph. aureus. Micrococcus luteus, M. epidermidis,* and others. They found that even after 10 to 12 washings these organisms continued to appear in the washing-water, and all these authors have concluded that it is not possible to remove all the bacteria from the skin surface by washing.

The transient flora are those which are deposited on the skin and which are, apart from washing, at the peril of the self-sterilizing power of the skin. Following the work of Colebrook and Maxted, Price also decided that the transient organisms were easily removed by washing, especially if they were not allowed to remain long on the skin. Their results indicate that, in practice, when the hands are recently contaminated by handling infected material they can be easily cleaned and pathogenic organisms removed by thorough washing with ordinary non-medicated soap.

Property of Cleansing

The property of cleansing or detergency is not altogether straightforward, and in the dermatological literature at least is not well defined. To remove water-soluble dirt a sufficient quantity of water is presumably all that is required. For oily or greasy dirt the usual fat solvents could be used. These are not, however, suitable for repeated application to the skin, and the alternative is to remove fatty material by emulsifying it.

*The Watson Smith Lecture delivered at the Royal College of Physicians of London on January 12, 1960.

Skin cleansers are therefore surface-active substances, emulsifiers which lower surface tension at the oil-water interface and bring grease away from the skin in an emulsified form. The removal of insoluble dirt particles, including bacteria, is sometimes said to result from merely floating them off the skin, as the skin and the foreign bodies are more readily wetted by a low-surface-tension aqueous solution. This explanation is not enough.

McBain (1920) stressed the importance of the colloidal nature of soap solution and attributed the removal of solid dirt particles to the formation of sorption compounds with soap molecules. He quotes Shorter as mentioning that, in the presence of alkali, dirt particles and the surface to be cleansed both carry a negative charge. Lane and Blank (Fishbein, 1945) quote evidence that at a *p*H above its isoelectric point keratin carries an increasingly negative charge. Most solid dirt particles and bacteria are also negatively charged, so that they are actively repelled from the keratin surface in the presence of an alkali, but are attracted and held to the skin at an acid *p*H, when the skin surface is positively charged. Blank and Coolidge (1950) confirmed these findings in respect of human keratin.

The active part of the soap molecule, the fatty-acid anion, also bears a negative charge ; hence it is repelled by the skin surface and remains free in the solute. In the case of cationic detergents, such as the quaternary ammonium compounds, the surface-active cation is attracted to the keratin and adsorbed on to the skin surface, with consequent loss of detergent power. It appears from this that the most efficient cleanser for the skin should be an anionic detergent and should be alkaline. Ordinary soap, of course, fulfils this requirement ; and the alkalinity of soap, which is so often regarded as a disadvantage, in fact makes a valuable contribution to its cleansing power on the skin. The keratin, surface-active anion, and the solid dirt or bacteria will then all bear negative charges and will repel each other.

As Blank and Coolidge point out, this has an important bearing on investigations into the degerming (killing and removal of bacteria) of the skin. Many of these investigations have assumed that the number of organisms which can be removed from the skin surface is a direct indication of the number present. When it is now appreciated that the ease of removal is greatly influenced by *p*H and by the nature of the cleanser, this assumption seems to be unjustified and some of this work therefore may need to be reassessed.

One may also observe that the efficiency of a cleanser will depend upon the nature of the surface to be cleansed. Keratin, a protein with an isoelectric point of 3.5 to 5.5, is clearly very different from cotton, nylon, and crockery. This point is of importance not only to achieve efficiency and economy in cleansing, but, by choosing cleansers where possible which have little effect on the skin, to minimize the risk of irritant effects.

Self-sterilizing Power of the Skin

We must also consider the possible effect of washing on the self-sterilizing power of the skin. It has for many years been held that organisms deposited on the living skin are likely to die more quickly than if they are placed under comparable conditions on an inanimate surface. Even the skin of a cadaver loses its sterilizing power as soon as 15 minutes after death (Arnold *et al.*, 1930). They concluded that the acid *p*H of the normal skin was important for this function. However, Cornbleet (1933) found that staphylococci survived indefinitely in thermal sweat at *p*H down to 3, but that a skin surface at *p*H 7 inactivated those organisms. Burtenshaw (1948) found that fat-soluble extracts of skin were strongly bactericidal, especially the fatty acid and soap fractions. The bactericidal action of these substances may depend, as Walker suggested, not upon *p*H but upon the lowering of interface tension on the surface of the bacterium.

Washing with soap removes these substances from the skin and raises the *p*H but tends to leave behind a deposit of the soap (Ramsay and Jones, 1955) which may in some degree make up for the loss. Rebell *et al.* (1950) found that the self-sterilizing power of the skin was greatly decreased if the surface lipoids were removed with ether, but I am unable to find any report of investigations into the self-sterilizing power of the skin after it has been washed with soap. The results would be interesting and possibly important, for these various effects of washing with soap are antagonistic. One may observe in passing that furunculosis commonly affects chiefly the areas of skin which are washed most frequently and that the avoidance of shaving-soap is often sufficient to cure folliculitis of the beard region ; similar considerations apply to chronic paronychia, in so many cases of which exposure to soap and water seems to play a major part.

Though Burtenshaw laid emphasis on fatty acids in skin self-sterilization, he nevertheless stated that the *p*H of the normal skin would alone be enough to kill many organisms. Eggerth (1926) found that the antibacterial action of soap was enhanced by an acid *p*H. The *p*H of the skin surface has been measured with indicators, by direct application of the electrodes of a *p*H meter, and by determining the *p*H of distilled water which has been left in contact with the skin. Though the results obtained by individual workers vary, there is complete agreement that the normal skin surface has an acid reaction—usually found to be between *p*H 5 and 6—and that certain regions are less acid, notably the flexural surfaces of the axillae and groins. This acid reaction may derive partly from sweat, since the *p*H of exocrine sweat is about 5.5 to 6 (Talbert, 1922). Furthermore, exocrine sweat may become more acid as it evaporates (Levin and Silvers, 1932), a change attributed by Bergeim and Cornbleet (1943) to increased concentration of lactic acid as the water disappears. These authors also found that if sweat is incubated without being allowed to evaporate its *p*H rises to 7 or more owing to the production of ammonia by bacteria. This may account for the relative alkalinity of the flexures, though, in addition, Marchionini (1929) found apocrine sweat to be nearer neutral or even slightly alkaline. Szakall (1955) decided, however, that the *p*H of the skin surface is due not to sweat but to amino-acids which are released or discarded in the formation of keratin, and the work of Dowling and Naylor (1960) points in the same direction.

There is no doubt that the use of soap on the skin leads to loss of its normal acidity. Bernstein and Herrmann (1942) found that the ordinary process of washing with toilet soap raises the *p*H of the skin surface by 1 to 1.5 units and that it takes about three and a half hours for the normal reaction to be restored. Martin-Scott and Ramsay (1956) found a greater rise in alkalinity after washing—up to *p*H 8—but a more rapid restoration to *p*H 5 in only 25 minutes. Evidently much will depend upon the thoroughness and the duration of

washing, the amount of soap used, and whether small amounts of soap remain on the skin from inadequate rinsing.

Effect of Prolonged Exposure

Klauder and Gross (1951) made particularly valuable observations on the effects of more prolonged exposure. They found that after ordinary washing the *p*H was restored to normal in three-quarters to two and a half hours. Longer periods of exposure while washing dishes raised the *p*H of the skin for four and a half hours; in canteen workers exposed several times during the day the recovery period was prolonged to 19 hours, so that in these subjects the hands were seldom at their normal *p*H. Each period of exposure to soap at *p*H 9.2 led to an increase of alkalinity of the skin from which recovery was so delayed that it was only on days off that the *p*H of the skin returned to normal.

The consequences of this are difficult to assess. The effect on the self-sterilizing power of the skin is doubtful. The *p*H of the skin is raised in eczema and in seborrhoeic dermatitis (Levin and Silvers, 1932), and Bernstein and Herrmann (1942) found that in eczematous patients the restoration of the *p*H to its former level after washing with soap takes longer than normal. This agrees with the findings of Burckhardt (1935) that the alkali-neutralizing time is longer than normal in eczematous subjects. The work of Anderson (1951) and of Beare *et al.* (1958) shows that this high *p*H is not restricted to the affected areas and that it persists after the eruption has cleared up. It is still not possible to say, however, whether the higher *p*H predisposes to eczematous eruptions, or to seborrhoeic dermatitis as Anderson suggested, or whether it is a consequence of these disorders. Many dermatologists believe that exposure to soap predisposes to dermatitis of the hands, but if this is so then several additional factors may be involved other than the mild elevation of *p*H which occurs with ordinary use of soap. There seems to be no clear evidence that maintaining the skin surface at a *p*H around neutral is in itself in any way harmful.

Soap and Skin Diseases

As to how often soap causes dermatitis there is great divergence of opinion. It is easy to believe that excessive use of soap may lead to degreasing of the corneous layer, to cracking, and hence to some degree of soreness—changes resembling chapping. Much greater difficulty arises in respect of frankly eczematous lesions with vesiculation or weeping. Klauder and Gross (1951) stated that 13% of their cases of industrial dermatitis were due to soap and water or to similar cleansers. Downing (1939) blamed soap and water as a contributing factor in nearly a quarter of his cases, and mentioned soap as the primary hazard in hotel and restaurant workers. Jordon *et al.* (1940) described a series of 239 cases of soap dermatitis in housewives, many of these taking the form of patchy vesicular eczemas involving the backs of the hands and one or several fingers. In the discussion which followed, their diagnosis was not questioned, and there appears to have been general agreement on the harmful properties of soap. But Gross (1941) regarded the cases of Jordon *et al.* as nummular eczema—which may indeed be expected to improve with rest and avoidance of soap, but the primary cause of which remains obscure.

In a general discussion on eczema of the hand Sulzberger and Baer (1948) consider primary irritants to be major influences, especially as predisposing or perpetuating factors, and they name soap as an outstanding cause. The part played by soap in individual cases is, however, extremely difficult to assess. Specific allergic sensitivity to soap is very uncommon, so that patch tests are of no value whatsoever in any given case. The behaviour of the eruption in relation to exposure to soap is seldom clear-cut, and patients' own statements upon which we may have chiefly to rely are often coloured by preconceived notions and by the opinions of their friends. To distinguish between a primary cause and an aggravating or perpetuating factor is usually impossible.

Jambor and Suskind (1955) carefully investigated 57 patients, of whom 35 were housewives, all having hand eczema attributed by the patients to the use of soap. On further investigation 30% of these cases were proved to be caused by other specific sensitivities.

The diagnosis of soap dermatitis often can be no more than surmise; eczemas of the hand have a high incidence in women in the fourth decade, and most women of that age are housewives, but we cannot necessarily assume that these two facts are causally related. The hands are a common site for eczema even in the absence of any identifiable external factor.

The experiments of Jambor (1955) and of Suskind (1957) are of particular interest. Jambor studied the effect of two kinds of soap, a neutral non-soap detergent, and an alkaline non-soap detergent, on 22 patients with hand eruptions which had been attributed to soap. One hand was immersed in 0.5% soap or detergent solution for half an hour daily and compared with the other, which was immersed in plain water. No difference between the hands or aggravation was seen in any case. As Jambor remarks, this may be because the solutions were not strong enough or because the exposure was not long enough or not frequent enough. Nevertheless, this strength of soap is that given by Fishbein (1945) for dish-washing (0.3 to 1%), and half an hour's immersion daily is indeed a considerable exposure. Suskind obtained the same entirely negative results in 45 subjects when the exposure was increased to half an hour twice daily.

One may recall that Brain (1956) has found that moderate use of soap does no harm to infants with eczema, for which, of course, it is the customary practice to forbid the use of soap. In my own wards I have used 5% toilet soap and 5% pure potassium palmitate as a cleanser in the treatment of eczema, seborrhoeic dermatitis, and psoriasis. The solution was rubbed on to the affected skin twice daily in order to remove applications such as Lassar's paste and zinc cream. The effect of these soap solutions was compared with that of applic. deterg. *N.F.* 1957 and liquid paraffin. Over a trial period of one month neither patients nor nurses nor doctors observed any irritant property in the soap solutions, except in contact with ulcerated surfaces. Their use was not continued because the other cleansers mentioned were found to be more efficient.

I do not wish to imply that soap plays no part in hand eczemas; but the observations I have just mentioned indicate a need for caution in arriving at general conclusions. The test of usage—the chief evidence upon which we can rely—is not easily arranged under properly controlled conditions. It is nowadays unusual to find a married woman who can completely avoid using soap, and the effect of rubber gloves is often, I think, clearly more harmful still. The occasional cases where hand eczemas have been ascribed to soap in paid employment,

where a change of occupation enables soap to be avoided, have not in my experience been at all impressive. Most of these eczemas have continued indefinitely and have thus given rise to the grave suspicion that the diagnosis of industrial (soap) dermatitis was wrong in the first place.

In the cases of Jordon *et al.*, mentioned above, the eruption was described as patchy, and I find it difficult to understand how total immersion of the hands in a liquid can produce well-outlined patches resembling nummular eczema with the adjacent skin completely normal. My own clinical observations lead me to believe that a truly eczematous soap dermatitis—that is, anything beyond the stage of fissuring and chapping—is uncommon and rarely severe. When it does occur the eczematous eruption, though perhaps patchy in degree, appears on a hand the whole skin of which shows some redness and chapping, a picture quite different from that of nummular eczema, which occurs in sharply outlined patches with completely normal skin between. Aggravation of eczema by soap is probably more common, though easily overrated; some burning and itching at the time of exposure followed by a degree of soreness is probably much more likely than any objective worsening directly caused by soap. In clinical practice we should be aware of the possibility of soap-aggravation, but the invariable and total prohibition of soap in eczema patients is often unjustified and inflicts an unnecessary hardship on the patient. These remarks are not intended to apply to ichthyotic subjects or to those middle-aged and elderly men in whom a dry eczematous eruption on the legs seems to be mainly due to washing.

Tests for Irritancy

It is well known that patch tests with soap solutions in normal people commonly give rise to positive results. It is probably equally well accepted that these are non-allergic primary irritant reactions. Lyon (1954) drew attention to the variability and uncertainty of these reactions, and this is discernible in comparisons of the various published series. Most of these reactions are mild, varying from a faint erythema to a slight degree of oedema and papulation. Nevertheless, even the mildest erythema from a soap patch test must surely indicate an irritant property, and it may be that the irritant property thus revealed is related to the irritancy of soap in ordinary use. Indeed, Kooyman and Snyder (1942) assessed the irritancy of soap by patch-testing and by user tests, and the results of the two methods were in close agreement. It seems likely, therefore, that the more convenient method of patch-testing probably gives a fair indication of the irritancy of a soap in actual use.

The irritancy of soap has been variously ascribed to alkalinity, to degreasing, to the essential irritancy of fatty acids, or to a combination of these factors. It has also been suggested that soap itself is not an irritant, or but rarely so, and that the irritancy usually observed results from the presence of free alkali, alkaline builders, resins, or other added substances.

Dr. Donoghue and I have carried out a series of experiments which were intended to throw some light on this problem (Bettley and Donoghue, 1960a). The effect of alkali alone in the *p*H range of soap solutions is negligible. My own experiments of patch tests with carbonate-bicarbonate buffer at *p*H 10 showed no primary irritancy. Other workers, such as Pillsbury and Shaffer (1939), have found the same, and patch tests with various soaps show no correlation between irritancy and alkalinity. The experiments of Blank (1939) indicate that the fatty acids of lower molecular weight, especially caprylic and capric, are primary irritants. In order to isolate the effect of these fatty acids of low molecular weight we compared the irritancy of potassium palmitate and verified Blank's view that the latter is much less irritant than an ordinary commercial soap. We found also that a soapless detergent, "teepol," is less irritant than soaps but becomes somewhat more irritant if its *p*H is brought up to 10. We suggest from these experiments that, though soap owes some of its irritancy to its fatty-acid content, and perhaps also to its degreasing effect on the skin, a further factor is present. We suggest that this factor is an increase in skin permeability which allows alkali and perhaps other irritants to reach the malpighian cells.

The living cells of the epidermis are normally protected from the outside by a barrier zone which is nearly waterproof and which resists penetration except by fat-soluble substances. Dr. Donoghue and I believe we have shown (Bettley and Donoghue, 1960b) that this barrier layer is attacked by soap in a way that makes it far more permeable to water and perhaps, therefore, to water-soluble irritants as well. We similarly examined a few other substances which may act as detergents or emulsifiers, and have gained the impression that their influence on the barrier zone is less or negligible.

These experiments seem to support the view that the irritancy of soap depends partly on its power of penetrating the epidermal barrier and reaching the cells of the malpighian layer, where fatty acids and probably alkali may exert their irritant properties. The irritant effect of free alkali, builders, resins, antiseptics, and other additives will presumably be much enhanced by, or even mainly dependent upon, the destruction of the epidermal barrier; thus the presence of soap may be a more important factor in producing irritation than these various additives which are often blamed.

Soap in Barrier Creams

Finally, I should mention briefly the use of soap in barrier creams. Soap is a common constituent of oil-resistant creams, being insoluble in most oils, and it is claimed to have a further advantage in helping to cleanse the skin at the end of work. In 1954 the Barrier Substances Subcommittee of the B.P.C. Revision Committee recommended certain type formulae. The composition of an oil-resistant barrier cream included 12% soap, and I think this is of doubtful wisdom. The Ministry of Labour (1946) pamphlet had already implied that a barrier cream should have a *p*H between 5.6 and 6.5. Yet the oil-resistant cream mentioned above gave a *p*H of 9.2 in 25% solution, and gave 25 positive reactions in 29 subjects patch-tested by Donoghue and me. Kooyman and Snyder (1942), as I have already mentioned, showed that the irritancy of patch tests goes hand in hand with the irritancy of soaps in a user test, so that we need not be too hesitant in drawing conclusions from patch tests. If, therefore, this barrier cream is applied often, and if it remains on the skin—as it is supposed to do—for several hours, then it is almost certain to be an irritant. The effect of soap in increasing the permeability of the epidermis, thus potentiating the effect of other irritants and sensitizers encountered during work, adds another grave disadvantage. Goldsmith and Hellier (1954) quote Tzank

et al. as believing that barrier creams may facilitate penetration of the skin by noxious substances.

From these considerations it follows that the use of soap-based barrier creams, so far from preventing industrial dermatitis, may substantially increase the risk. The substitution of ethanolamine soaps may reduce alkalinity, but their effect in potentiating other industrial irritants remains problematical. Until more evidence is available it would certainly seem best to avoid any type of soap in a barrier cream.

Summary

Though soap has a considerable antiseptic activity, its action in washing bacteria off the skin surface is probably more important, particularly as regards recent contamination.

The power of the skin surface to sterilize itself may be impaired by washing with soap.

The normal acidity of the skin surface is changed towards alkaline by exposure to soap; the consequences of this are difficult to assess.

The irritant effect of soap on the skin tends to be overestimated. Such as it is, it depends upon primary irritancy of fatty acids and also upon the power which soap has to penetrate into the skin.

The inclusion of any soap in barrier creams is inadvisable.

REFERENCES

Anderson, D. S. (1951). *Brit. J. Derm.*, **63**, 283.
Arnold, L., Gustafson, C. J., Hull, T. G., Montgomery, B. E., and Singer, C. (1930). *Amer. J. Hyg.*, **11**, 345.
Beare, J. M., Cheeseman, E. A., Gailey, A. A. H., Neill, D. W., and Merrett, J. D. (1959). *Brit. J. Derm.*, **71**, 165.
Bergeim, O., and Cornbleet, T. (1943). *Amer. J. med. Sci.*, **205**, 785.
Bernstein, E. T., and Herrmann, F. (1942). *N.Y. St. J. Med.*, **42**, 436.
Bettley, F. R., and Donoghue, E. (1960a). *Brit. J. Derm.*, **72**, 67.
—— —— (1960b). *Nature (Lond.)*, **185**, 17.
Blank, I. H. (1939). *Arch. Derm. Syph. (Chicago)*, **39**, 811.
—— and Coolidge, M. H. (1950). *J. invest. Derm.*, **15**, 249.
Brain, R. T. (1956). *Brit. med. J.*, **2**, 299.
Burckhardt, W. (1935). *Arch. Derm. Syph. (Berl.)*, **173**, 262.
Burtenshaw, J. M. L. (1948). In *Modern Trends in Dermatology*, edited by R. M. B. MacKenna, p. 158. Butterworth, London.
Colebrook, L., and Maxted, W. R. (1933). *J. Obstet. Gynaec. Brit. Emp.*, **40**, 966.
Cornbleet, T. (1933). *Arch. Derm. Syph. (Chicago)*, **28**, 526.
Dowling, G. B., and Naylor, P. F. D. (1960). *Brit. J. Derm.*, **72**, 57.
Downing, J. G. (1939). *Arch. Derm. Syph. (Chicago)*, **39**, 12.
Eggerth, A. H. (1926). *J. gen. Physiol.*, **10**, 147.
Fishbein, M. (1945). *Medical Uses of Soap*. Lippincott, Philadelphia.
Goldsmith, W. N., and Hellier, F. F. (1954). *Recent Advances in Dermatology*, 2nd ed. Churchill, London.
Gross, P. (1941). *Arch. Derm. Syph. (Chicago)*, **44**, 1060.
Jambor, J. J. (1955). *J. invest. Derm.*, **24**, 387.
—— and Suskind, R. R. (1955). Ibid., **24**, 379.
Jordon, J. W., Dolce, F. A., and Osborne, E. D. (1940). *J. Amer. med. Ass.*, **115**, 1001.
Klauder, J. V., and Gross, B. A. L. (1951). *A.M.A. Arch. Derm. Syph.*, **63**, 1.
Kooyman, D. J., and Snyder, F. H. (1942). *Arch. Derm. Syph. (Chicago)*, **46**, 846.
Levin, O. L., and Silvers, S. H. (1932). Ibid., **25**, 825.
Lyon, J. B. (1954). *Brit. J. Derm.*, **66**, 308.
McBain, J. W. (1920). *3rd Report on Colloid Chemistry*, p. 2. D.S.I.R. and Brit. Ass. Adv. Sci. H.M.S.O., London.
Marchionini, A. (1929). *Klin. Wschr.*, **8**, 924.
Martin-Scott, I., and Ramsay, A. G. (1956). *Brit. med. J.*, **1**, 1525.
Ministry of Labour (Factories Dept.) (1946). Form 330.
Pillsbury, D. M., Livingood, C. S., and Nichols, A. C. (1942). *Arch. Derm. Syph. (Chicago)*, **45**, 61.
—— and Shaffer, B. (1939). Ibid., **39**, 253.
Pohle, W. D., and Stuart, L. S. (1940). *J. infect. Dis.*, **67**, 275.
Price, P. B. (1938). Ibid., **63**, 301.
Ramsay, A. G., and Jones, K. K. (1955). *Brit. J. Derm.*, **67**, 1.
Rebell, G., Pillsbury, D. M., de Saint Phalle, M., and Ginsburg, D. (1950). *J. invest. Derm.*, **14**, 247.
Sulzberger, M. B., and Baer, R. L. (1948). *The Year Book of Dermatology and Syphilology*. Chicago.
Suskind, R. R. (1957). *J. Amer. med. Ass.*, **163**, 943.
Szakall, A. (1955). *Arch. klin. exp. Derm.*, **201**, 331.
Talbert, G. A. (1922). *Amer. J. Physiol.*, **61**, 493.
Walker, J. E. (1924). *J. infect. Dis.*, **35**, 557.
—— (1925). Ibid., **37**, 18.
—— (1926). Ibid., **38**, 127.

NEW STICK TEST FOR P.A.S. IN URINE

REPORT ON USE OF "PHENISTIX" AND PROBLEMS OF LONG-TERM CHEMOTHERAPY FOR TUBERCULOSIS

BY

GEORGE R. W. N. LUNTZ, M.R.C.P.

Consultant Chest Physician, Birmingham Chest Clinic, Yardley Green and Romsley Hill Hospitals, Birmingham Consultant Physician in Charge of Tuberculous Diabetic Service, Birmingham Regional Hospital Board

AND

RAYMOND AUSTIN, M.B., B.Ch., B.A.O.

Assistant Chest Physician, Birmingham Chest Service

Since para-aminosalicylic acid (P.A.S.) became generally available in the British Isles in the spring of 1948, streptomycin a year later, and the introduction of isoniazid in the treatment of tuberculosis in 1952, there has been an increasing weight of evidence of the value of effective long-term chemotherapy in the management of pulmonary tuberculosis.

The low toxicity in therapeutic dosage, ease and convenience of administration, together with potency, make P.A.S. and isoniazid the most satisfactory chemotherapeutic combination for tuberculous patients who have completed their hospital treatment and continue to have antibacterial drugs whilst living at home and working. Many such patients continue their ambulant combined therapy for two to three years.

Several methods have been described for determining the presence of P.A.S. in urine, depending on the colour produced with Ehrlich's reagent (Venkataraman *et al.*, 1948; Herold, 1951; Penman and Wraith, 1956; Ruiz, 1957), hypochlorite (Simpson, 1956), or ferric chloride (Simpson, 1956; Penman and Wraith, 1956; Dixon *et al.*, 1957). Though existing tests are reliable and sensitive when carefully applied in the laboratory or out-patient department, none have the simplicity of "clinistix" for glucose (Luntz, 1957) or "albustix" for proteinuria (Macgregor, 1958; Baron and Newman, 1958; Frazer, 1958).

In view of the comparable simplicity of "phenistix" reagent strips (primarily designed for the detection of phenylketonuria), and because it is based on the same principle as the ferric-chloride test, it was decided to examine in detail the suitability of this new test for the detection of P.A.S. in urine. With phenylpyruvic acid the reagent strip changes to a green colour (Rupe and Free, 1958; Baird, 1958; Nellhaus, 1959; Gibbs and Woolf, 1959), whereas with P.A.S. it turns a pink or purple, according to the amount present.

Material and Methods

Phenistix Test

This new test for P.A.S. in the urine employs impregnated paper sticks (phenistix reagent strips), which remain yellow when dipped in normal urine but become purple if the urine contains P.A.S. The test is based on the colour reaction which occurs with ferric ions and phenylpyruvic acid. Phenistix is impregnated with a mixture containing ferric and magnesium salts plus cyclohexyl sulphaminic acid.

Before embarking on clinical trials of phenistix in hospital wards, on chest clinic out-patients, and by patients themselves it was necessary to examine the sensitivity and specificity of phenistix in some detail.