

between the male and female mortality ratios from coronary disease is significant in each type of administrative area. The coefficient is largest in the county boroughs, but the difference between this value and those for the urban and rural districts just fails to reach the level of significance.

As might be expected from the lack of correlation between the mortality ratio and the proportion of males in social classes I and II, the grouping of large towns in order of their mortality ratios does not reveal any pattern of industrialization. Seven of the county boroughs may be described as seaside resorts, and four of these had high rates for both social class and mortality ratio, while three had a large proportion of males in social classes I and II but a low mortality ratio. The variations found are illustrated in the data for the towns in which more than one-fifth of the males were in social classes I and II, the three towns with the lowest proportions in social classes I and II, and the three towns with the lowest mortality ratio (Table VII). No

TABLE VII

County Borough	Proportion per 1,000 in Social Classes I and II	Mortality Ratio from Coronary Disease
Southport	306	146
Blackpool	231	120
Southend-on-Sea	274	116
Bournemouth	291	107
Croydon	248	97
Hastings	236	92
Brighton	210	89
Eastbourne	267	84
Bath	230	78
Bootle	78	112
St. Helens	85	108
Warrington	78	107
Dudley	123	63
West Bromwich	106	70
Burton-upon-Trent	125	71

TABLE VIII

Ages:	Death Rates per 10,000 Population during 1950-2			
	25-	45-	65-	75+
Southport	1.7	44.2	137	223
Blackpool	2.0	35.1	124	156
Southend-on-Sea	1.0	30.2	117	193
Bournemouth	2.0	29.8	91	197
Croydon	2.2	22.2	96	171
Hastings	0.5	28.2	87	147
Brighton	1.8	26.9	86	125
Eastbourne	0	21.0	96	128
Bath	0.6	20.2	64	162
Bootle	2.9	29.9	102	141
St. Helens	2.7	34.1	88	139
Warrington	0.8	29.7	85	203
Dudley	1.7	15.7	57	106
West Bromwich	1.4	15.1	83	90
Burton-upon-Trent	0.5	19.4	78	88

specific age group can be incriminated for the variations in the size of the mortality ratio. The death rates at ages for these towns are shown in Table VIII. Southport with the highest mortality ratio and Dudley with the lowest had, respectively, the largest and almost the smallest death rates in the three age groups 45-, 65-, 75+. The ratio of the death rates of these two towns declined with increasing age, the ratios being 2.8, 2.4, and 2.1. With a few minor exceptions the trends of the death rates by age were similar for all the towns.

Summary

At ages of 35 and over a twofold to threefold increase has occurred in England and Wales in the death rates attributed to coronary disease during the past 15 years. The male death rate has increased more rapidly than the female rate at the younger ages, 35-54 years.

The regional distribution of deaths attributed to coronary disease is not very different from that of deaths from all causes, the largest death rates being in

the northern counties. For both sexes mortality is high in the urban areas compared with the rural, but the difference is more distinct for males.

Although the 1951 occupational mortality (1% sample) showed a steep gradient for mortality from coronary diseases with social class, the geographical differences in the mortality ratios in 1950-2 cannot be explained by variations in the social class structure of the populations at risk. The proportion of males in social classes I and II in different areas was not correlated with the level of their mortality ratios, and it seems that some other characteristics must be responsible for the widely varying level of mortality in the different areas.

In each type of area—county borough, urban district, and rural district—there was close correlation between the male and female standardized mortality ratios from coronary disease.

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SOAP AND THE SKIN

WITH AN INVESTIGATION INTO THE PROPERTIES OF A NEUTRAL SOAP

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After the second world war the incidence of dermatitis in housewives greatly increased. Since this was coincident with the introduction into general use of many synthetic detergents, medical men readily assumed that these cleansing agents were the causative factor. As judged by the number of cases referred to hospital, the greatest incidence of such dermatitis occurred in the period 1950-1. The recent fall in the number of hospital cases is probably due to the housewife's greater awareness of the dangers of detergents. The use of protective gloves, tongs, long-handled mops, and washing machines has prevented prolonged contact with the detergent solutions. The family practitioner also, by early diagnosis and prompt advice, usually succeeds in clearing up the dermatitis before irreversible skin changes have occurred. It has also been established that many other substances handled by housewives, such as polishes, insecticides, plants, lacquer hair-sprays, dyes, and rubber, nickel, and plastic objects, may produce dermatitis clinically similar to that caused by detergents.

However, the repeated use of soaps and detergents on the healthy skin may be harmful, especially if the hands are not thoroughly rinsed in running water afterwards. On diseased skin, moreover, even tap-water alone, which is hypotonic and often slightly alkaline, may do damage.

Mechanism of Skin Damage

The reason for skin damage caused by soaps and detergents has been ascribed to a denaturing process, to removal of the protective superficial skin fat, and also to the alkalinity of some cleansers. Most writers agree that the resultant dermatitis is due to a primary irritation rather

than to an acquired sensitivity to the soap or the detergent employed (Brunner, 1954; Schwartz, 1954; Lyon, 1954). Theoretically, however, a true sensitization to one of the many chemical substances added to soap might occur, such as anti-oxidants, "builders," antiseptics, abrasives, and perfumes. Klauder and Gross (1951) found no evidence of sensitization in 75 cases of dermatitis of the hand attributed to the use of soaps and detergents. Jambor (1955) investigated the role of soaps and detergents as primary irritants, and found that the degree of skin damage due to hydration was proportional to the duration of skin alkalinity after immersion. Van Scott and Lyon (1953) tested cleansing products to determine if they damage the keratin molecule in such a way as to expose sulphhydryl groups. Firstly, by the addition of human keratin to aqueous solutions of graded hydrogen-ion concentration, they demonstrated the ability of keratin to act as a buffer and lower the pH to 4-5.5. With some of the detergents tested, where this buffering action was absent, the pH of the detergent solution remained high, and the number of sulphhydryl groups exposed was increased. The authors suggest that this was possibly due to splitting of disulphide linkages at this alkaline pH. Chiego and Silver (1942) had previously demonstrated, on the keratin of hair and nails, that solutions of high pH dissolve keratin by rupturing the disulphide linkages, with the formation of sulphhydryl groups.

The synergistic action of an alkaline detergent (pH 10.3) and "water-glass" (pH 11.2) in the production of dermatitis has been reported by Morris (1953), who failed to reproduce skin reactions, using an acid detergent.

Most ordinary soaps are alkaline, but synthetic detergents can be made of varying pH from 6 to 10. The seven most popular detergents in use in Britain were tested, using a glass electrode and a 1% solution in distilled water (pH 7.4). The pH was found to range from 8.3 to 9.7, with an average of 9.4.

It seems probable, therefore, that the alkalinity of soaps and detergents is an important factor in the production of skin damage, and more especially so in persons with dry skin, where, according to Anderson (1951), the pH is already above normal, with consequently greater impairment to the normal keratin buffering action.

Previous work (Ramsay and Jones, 1955) has implied that when the skin is washed with an alkaline soap a layer of soap is adsorbed on the skin surface. This layer clings tenaciously to the skin and is not normally washed off during the washing process. The adsorbed soap is thought to be hydrolysed to free fatty acids. These fatty acids may be a causative factor in the production of dermatitis after washing with soap.

The alkalinity of normal toilet and washing soaps, as well as the fatty acids formed on the skin from the adsorption layer envisaged, has meant that patients suffering from dermatitis must routinely avoid the use of soap, thus adding to the discomfort of the affliction.

When a soap which, it was claimed, had a pH of 7.5 was recently imported into this country it was considered that an investigation into its actions would be of value.

Laboratory Investigation

The object of the laboratory investigation was to determine if the neutral soap made any alteration in the normal composition of the skin-fat layer, and to compare the action of the soap in this way with other methods of washing.

Method.—The method used to collect fat samples from the skin and for their analysis was described by Ramsay and Jones (1955). The principle is as follows. A sample of skin fat is removed from the skin with ethyl ether. This sample is weighed and then dissolved in petroleum ether. A small aliquot of this solution is then placed on a monomolecular oil film floating on water. The petroleum ether evaporates and the fat spreads on the surface of the water into a colourless monomolecular film. The area of this spread is measured. The ratio of the weight of fatty substance to

the spread is called the skin-fat factor. From this factor the composition of the sample may be estimated. The factor for normal skin fat is approximately 1.2. An increase in the proportion of fatty acids in the skin fat will cause the factor to fall below 1.2.

Results.—The skin-fat factor obtained after washing the skin with the neutral soap in the normal way is shown in the Table. For comparison the figures obtained in the

Skin-fat Factor Obtained with Different Substances

Group Washed with	Mean Amount of Fat (μ g.)	Skin-fat Factor \pm S.D.
Water	192	1.225 \pm 0.03
Alcohol	157	1.223 \pm 0.05
Toilet soap	162	0.931 \pm 0.03
Neutral ,,	160	1.228 \pm 0.07

previous investigation, using distilled water, alcohol, or common toilet soap for washing, are also given. These results show that washing with the neutral soap does not significantly alter the skin-fat factor from the normal value of 1.2. Washing with ordinary toilet soap—an alkaline super-fatted soap—produces a significant reduction in the factor, indicating an increase in the proportion of free fatty acids in the skin fat. A solution of the neutral soap was extracted with petroleum ether and the resulting extract tested. It was found to have a factor of 1.18. During previous investigations it was found that after washing with common toilet soap the pH of the skin surface was approximately 8, changing over 25 minutes to approximately pH 5. After washing with neutral soap and rinsing in a normal manner, the skin surface was found to be pH 5.8—and did not change over 30 minutes. If the soap was not rinsed off, but the skin just blotted dry, the reaction of the skin surface was pH 6.7 and also remained unchanged for up to 30 minutes. After washing the skin surface with alcohol the pH was 5.8, remaining at this value for up to 30 minutes.

Conclusions.—The fact that after washing the skin with the neutral soap the skin-fat factor was not changed from the normal indicates that the relative composition of the fatty layers on the skin was not changed. An extract of the soap itself was found to have a factor of 1.18, close to that of normal skin fat. The pH of the skin surface after washing with the neutral soap is, however, not different from that after washing with alcohol. These points would indicate that there is no layer of the neutral soap adsorbed on the skin surface, as with the common types of toilet and washing soaps. The additional fact that the skin pH does not alter after washing with neutral soap also indicates that there is no soap layer which can release free fatty acids. The absence of an adsorbed layer of neutral soap may be ascribed to its composition. It is a soap of triethanolamine, a quaternary ammonium compound, and fatty acids, whereas normal types of soap are sodium and potassium salts of fatty acids. With these sodium and potassium soaps the metallic ions still have valency bonds available by which they are "attracted" to the skin surface and so are adsorbed on to the skin surface. The triethanolamine in the neutral soap has no such bonds, being fully conjugated, and therefore is not attracted to the skin surface. This means that the neutral soap is easily and quickly rinsed off after performing its detergent action, leaving the skin clean and with normal pH.

Clinical Investigation

The clinical evaluation was done quite independently of the laboratory work. The samples of soap given to the patients were translucent, amber, and pleasant to use. After washing, the skin felt clean, soft, and pliable, and there was no stinging when the soap was applied to a denuded surface.

At the beginning of the trial the soap was issued to medical colleagues and nurses who had intact skin but in whom excessive scrubbing-up caused the skin to become

dry and rough, with occasional fissuring in cold weather. In all cases it was acclaimed to be less damaging than other toilet soaps, but attention was drawn to the fact that the tablets tended to "sweat" on keeping, owing to the hygroscopic property of this soap. A few fair-skinned patients with mild xeroderma, who claimed that they could not use soap on the face, found that the neutral soap could be used without adverse reaction.

As confidence in its non-irritant quality increased, it was decided to use it in cases of skin disease, where one would normally forbid the use of soap and water and prescribe a liquid paraffin emulsion or a vegetable oil for cleaning. The number of daily washes was at first limited, and the patients were asked to note carefully any deterioration in appearance or irritation of the skin after using the soap.

In the broadest sense these patients suffered from an eczematous reaction of the skin, recognized in the early stage by erythema and vesicle formation and by the appearance of scaling and thickening of the skin in the subacute and chronic stages, with or without lichenification and fissuring.

The cases fall into five main groups, which are considered individually: (1) infantile eczemas (23 cases), (2) eczema of the hands (40), (3) flexural pruriginous eczema (9), (4) ward cases (18), and (5) miscellaneous cases (11).

1. Infantile Eczemas

The difficulty of keeping healthy inquisitive young children clean is well known. When, however, they suffer from eczema and the mothers are forbidden to use soap and water on the skin the problem of cleansing becomes a matter for serious thought. These were therefore the cases of first choice.

There were 23 such cases, with a preponderance of male infants, and the ages ranged from 3 months to 4 years, with an average of 3½ years. The majority were of the atopic type with xeroderma and subacute eczematous areas on the facial prominences, wrists, hands, and folds of the knees. Two were of the seborrhoeic type with exudative crusted areas on scalp and neck spreading down to the chest, and four had become almost generalized with excoriations and secondary infection.

Approximately half these patients had previously attended the clinic and were using cleansing emulsions. Whilst using the soap under trial all cases received appropriate local applications.

In 21 cases there was no intolerance. In three of these the mothers claimed that it had actually been of benefit to their children. Of the remaining two cases, one mother did not find it less irritating than a medicated soap she had previously been using, and another claimed that the very apparent deterioration of her child's eczema was due to the soap. The latter was a long-standing case, which had often been observed to flare up from time to time even when on the same previously beneficial local treatment. The exacerbation was not immediate, but occurred after ten days of daily bathing: the mother was not prepared to continue using the soap.

These results indicate that the soap is well tolerated by the vast majority of children with subacute infantile eczema commonly associated with xeroderma. The parents were quite enthusiastic about the soap, and it was noted that most continued to buy it thereafter at their own expense.

2. Eczema of the Hands

The cases selected for trial showed the various stages of eczema in which washing with ordinary soap would be regarded as detrimental. Local therapy was continued during the trial and the number of daily washes gradually increased. There were 40 cases which can be divided into the following three main subgroups.

Contact and Industrial Dermatitis (26).—This group consisted of adults who had plaques of subacute eczema chiefly affecting the fingers, dorsum of the hands, and ulnar aspects of the wrists.

The affected areas were erythematous, were slightly raised, and had superficial scaling. Almost half the cases were industrial, due to contact with mistic and other coolants used in engineering. The others included were caused by detergents, antibiotics, lacquers, flour, nickel, fertilizers, insecticides, and other chemicals.

Acute Cheiropompholyx (5).—In these no culpable exogenous factor was discovered. The patients were mostly of nervous temperament with some hyperidrosis, in whom vesicles developed along the side of the fingers in hot humid weather or under emotional stress. They were allowed to use the soap in the acute vesicular and exudative phase.

Chronic Dermatitis (9).—This group was comprised of mainly elderly female patients who gave a long history of manual eczema. No external cause could be detected, and their general health was good. The skin of the hands was very dry and showed desquamation, with occasional areas of lichenification and usually some fissuring around the finger-joints. These cases probably started as contact dermatitis, but at the time of consultation the condition had been present for many years and no history of present contact could be obtained.

The results were uniformly good in 39 of the 40 cases. No clinical regression was noticed while the neutral soap was being used, and several patients thought it was beneficial and soothing. The one exception was a woman of 36 who suffered from subacute industrial dermatitis of the hands and awaited a compensation claim. She said it caused the hands to smart and become red after use.

3. Flexural Pruriginous Eczema

In this group there were nine cases, mostly females, ranging in age from 7 to 23 years. Some had suffered from infantile eczema and some had allergic manifestations. The typical case presented subacute eczema of the wrists, elbow, and folds of the knees. A few had eczema of the face, upper chest, and hands also, and several showed early lichenification.

Many of these patients could not tolerate the action of ordinary toilet soap as it caused the affected areas to become much more irritant and left the more normal skin dry and tight.

Two of these patients were in hospital with extensive areas of eczema and excoriations. In these severe cases it was possible to compare the action of applicatio detergens *N.F.* and the neutral soap by unilateral control, while both sides received the same treatment. These patients preferred the soap, and its use did not delay the progress of healing.

In none of this group was the soap considered to be harmful to the skin, and most patients continued to buy it in their own interest.

4. Ward Cases

These were in-patients not included in group 3, with fairly generalized dermatoses, showing eczematous skin changes, often with superadded pyococcal infection. There were 18 such cases. Five were elderly men with long-standing dermatitis of the legs, unassociated with varicose veins, and said to have been industrial in origin. Three other cases suffered from generalized seborrhoeic dermatitis with impetigo and folliculitis, and four had nummular eczema chiefly affecting the limbs.

The soap was used mainly in the subacute stages of the various diseases, but the leg cases were washed with it from the early exudative stage, as were the seborrhoeic cases, and no intolerance was observed. Where unilateral control was possible, there was no regression on the side cleansed with the soap. The impression was gained that in the infected seborrhoeic cases progress was more rapid when using the soap than when using cleansing emulsions.

Two patients with generalized exfoliative dermatitis and two with pemphigus, in whom the skin was healed but not yet of normal texture, could indulge in baths, using the soap at an early stage in their convalescence.

A case of Kaposi's varicelliform eruption (infantile eczema with superimposed cowpox virus infection) was treated in the ward with removal of the crusts, using the neutral soap, and application of an antibiotic cream, the result being most gratifying. Another infant, probably

suffering from Brocq's congenital ichthyosiform erythroderma, was washed with the soap, when the collodion-like layer was separating off, without harmful reaction.

5. Miscellaneous Cases

This small group includes three cases of palmar toxic bacteride and two of keratoderma climactericum with deep palmar fissuring. None showed any retrogression which could be attributed to washing with the soap. Two patients with facial pigmentation (melanosis) which was thought to be due to scented cosmetics were much improved when allowed to use this soap, and avoiding the cosmetics. Four cases of genital and anal pruritus associated with inflammation, whilst receiving local therapy, used the neutral soap for cleansing without adverse effect.

Conclusions

From the clinical aspect it can be concluded that this neutral soap is a most useful addition to the armamentarium of dermatological practice. It would seem to prevent excessive denaturing of the normal skin, and can be used with confidence in cases of subacute eczema. Furthermore, in the few cases of acute and secondarily infected eczema it was well tolerated.

It would be imprudent to cite statistical evidence in appraisal of this soap, when the trial consisted of a comparatively small number of selected cases. There are also many psychological factors involved, such as the clinician's enthusiasm, the patients' delight in being allowed to wash normally, and perhaps the novelty of receiving a free sample of an imported soap. Furthermore, apart from ward cases and clinical observation, most of the evidence came from the patients themselves. In some of the new patients the prescribing of topical hydrocortisone for the first time often made the general progress more rapid, and with this the patient's morale improved on the treatment as a whole.

In spite of these and other factors, however, clinical observation confirmed that the soap was well tolerated by patients with eczema and xeroderma. The fact that most patients continued to purchase this not inexpensive soap (whereas cleansing emulsions were supplied free) speaks for the joy afforded them by its use. When unilateral control was possible, it seemed superior to cleansing emulsions. A control using ordinary alkaline soap was not deemed justifiable in the interests of the patients.

Summary

The properties of a neutral soap have been investigated in the laboratory and in hospital.

After the skin had been washed with the soap, the skin-fat factor showed no change from the normal, and the pH of the skin remained unaltered. Thus its use did not involve any denaturing of the skin, and its protective acid mantle remained intact.

Clinically it was found to be innocuous to persons who found the excessive use of ordinary toilet soap to be detrimental to skin health. Furthermore, about 100 patients suffering from subacute eczema, who would normally be forbidden to wash with soap, were able to enjoy using this neutral soap with impunity.

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LIVER FUNCTION IN KWASHIORKOR

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Kwashiorkor is generally accepted as a protein-deficiency syndrome. Since the pioneer work of Trowell (1939) and Cofino and Klee (1942) several workers in Africa have reported on the serum protein spectrum in kwashiorkor (Altmann, 1948, 1953; Janssen and le Roux, 1950; Walt *et al.*, 1950; Gillman and Gillman, 1951; Anderson and Altmann, 1951). Altmann (1953) reported on the thymol turbidity and flocculation tests in 20 cases of kwashiorkor. He could find no prognostic or diagnostic value for the tests in kwashiorkor. The bromsulphthalein test gave positive results in three out of six cases, and Altmann could find no correlation between dye retention and fat content of the liver.

In the West Indies, Waterlow (1948) found normal values for alkaline phosphatase and serum colloidal gold. Serum bilirubin was slightly raised in only very severe cases of the disease. A high degree of correlation was found between bromsulphthalein retention and severity of the disease. Waterlow (1950), using the Cartesian diver technique, also found a significant depression of pseudocholinesterase in liver biopsies from cases of "fatty liver disease." Gómez *et al.* (1952) found that an abnormal thymol test with a normal cholesterol flocculation test is "a phenomenon seen with significant frequency in cases of malnutrition or pellagra in which it is not possible to detect any infection." On the other hand, they suggested that the finding of positive thymol and cephalin tests together was indicative of infection.

At Kampala, Dean and Schwartz (1953) found reduced esterification of cholesterol as well as a reduced pseudocholinesterase value in kwashiorkor. Values for alkaline phosphatase were low for the particular group. The serum protein pattern found by these workers compared well with that of other workers. In Curaçao, Van der Sar (1951) estimated the A:G ratio and the bromsulphthalein retention in 16 cases. Using a dose of 5 mg. per kg. and a 30-minute interval, he found retention of dye in only five cases. His results for 16 total cholesterol and 13 ester estimations were normal. Total lipids in serum were estimated in 16 cases and found to be high. The normal cholesterol esters found by Van der Sar are in striking contrast to the defective esterification found by Dean and Schwartz (1953).

We report the results of liver-function tests carried out on 107 consecutive cases of kwashiorkor treated in the Pretoria Hospital. Bromsulphthalein retention was estimated in 51 cases. There were 19 fatal cases.

Materials and Methods

Blood was withdrawn from the external jugular vein in all cases before treatment was started. The tests were completed within 24 hours of drawing the blood.

Treatment consisted of various high-protein diets with or without added vitamins. The composition of the diets and the clinical data have been published by Brock *et al.*