Section of Dermatology

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Chemicals in Fabrics as Potential Skin Irritants

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The study of the action of chemicals in fabrics as potential skin irritants is of interest to both the chemist and the dermatologist. It is by their combined efforts in research and practical clinical experience that our knowledge of such reactions will become wider and more accurate. The modus operandi of even a primary irritant is imperfectly understood and when the effects of sensitivity or idiosyncrasy are considered our knowledge is almost nil; facts almost more strange than fiction are duly observed and recorded, but the underlying reactions are unknown. Perhaps this is partly due to the incomplete mental equipment of most of us; so few have the many-sided competence necessary for such study. The chemist is usually without clinical experience and knows little pathology, and the physician or dermatologist generally has but a limited knowledge of chemical industrial materials and processes. So except for those rare individuals who have exceptional qualifications, real understanding must come from co-operative efforts and the free exchange of information. With such thoughts in mind I propose to discuss briefly some of the possible causes of dermatitis mainly arising from fabrics.

It has been well said that the modern miss is the patron saint of chemistry; she is adorned from head to foot by the art of the chemist, and it must be agreed that if she avoids excesses she does look very attractive. I want to present her in another less happy character, that of the experimental animal for which not even a vivisection license is required (but to whom large damages may be payable). The manufacturer aids and abets her in applying to herself all kinds of new compounds the nature and properties of which from our present point of view little or nothing is known. Small wonder that dermatitis cases arise and that their incidence is credibly reported to be increasing. Her hair having been bleached with peroxide and ammonia and shampooed with a soap substitute is dyed with a compound diamine. Her eyelashes may be the product of the grease pencil, her lips and cheeks may derive their beauty not from oxyhaemoglobin but from eosin and ponceau; her teeth—natural or artificial—are brushed with a waterproofed synthetic fibre, her fingers are adorned with nitro-cellulose dissolved in complex solvents and plasticized with still more complex chemicals. Perhaps she has applied chloramine T or an oxyquinoline derivative to her armpits or even used mercapto-glycolic acid as a depilatory. But I want to pass from these personal details to consider more particularly what she is wearing. Perhaps she has a corset made of latex rubber with fillers and antioxidants in it, a bleached woolen vest impregnated with synthetic finishes, other intimate garments made of cotton with synthetic resins as anti-crease, stockings of de-lustred viscose, a flock of rayon containing perhaps regenerated cellulose and cellulose ethers impregnated with...
quaternary ammonium compounds to render them water-resisting; her shoes are of
new plastics resembling snake skin and her fur cape is of leopard skin in which the
familiar spots have been produced by mating a polyphenol with a diamine. Possibly she
has spectacles of synthetic glass with sides of plastic resin, a handbag of suede leather
compounded of cotton and rubber and an orchid made from doped and dyed cellulose
in her button-hole, perfumed with otto of the laboratory, not attar of roses. She is in
fact one grand experiment; small wonder that nature sometimes revolts. A rash appears;
she goes to the doctor. I suppose the principal function of the doctor or the dermatologist
is to effect a cure, but the matter certainly does not end there; he will be concerned to find
out the cause of the outbreak if only to prevent a recurrence, and not infrequently there
may arise questions of liability and of compensation. There is an increasing awareness
of this problem and in truth it is a very difficult one, chiefly because of the variations in
personal idiosyncrasy, sensitivity or allergy. In general there will be little difficulty in
arriving at a shrewd suspicion in cases where the dermatitis is due to clothing and a
patch test may afford strong confirmation or otherwise, but the matter cannot properly
be left there. It is probable that the suspect garment is one of a kind worn by thousands
of people; it may contain a known primary irritant; it may contain some new type of
compound to which many or few people are susceptible; it may contain only substances
believed as result of long experience to be quite innocuous but to which the individual is
idiosyncratic. It is important to ascertain the facts in the interest of all concerned as well
as in the interest of science. Only by accumulating known, well ascertained, facts shall
we be able really to find what substances are harmless or harmful and how they react
with the human subject. In a Report on dermatitis from wearing apparel by Dr. Schwartz
of the U.S. Public Health Service, the Service has devised a questionnaire in which the
importance is stressed of discovering the actual chemical in the fabric which is causing
the irritation and on the methods employed for such determination. In this way certain
potentially dangerous substances introduced in the States have been eliminated from use.

Recent legal judgments in this country too have tended to emphasize this aspect. The
Court now requires to know whether the plaintiff's skin was normal or abnormal, or con-
versely—perhaps it amounts to the same thing—was the garment normal or abnormal;
did it contain some trace of substances that ought not to have been there; was it reason-
ably fit to wear by a person not having an idiosyncrasy. So while the dermatologist is
occupied with the patient's skin, the garment comes back to the chemist who must try to
discover any abnormality or imperfection in the material such as would be likely to cause
the troubles experienced. This is often a very difficult problem requiring much knowledge
and skill; let me just indicate the possibilities or probabilities.

FURS*

Furs present what is now perhaps the simplest case. The dyeing of fur by
oxidation of a diamine such as paraphenylenediamine was discovered about fifty years
ago, but only within the past twenty years has fur dermatitis become a recognized
condition and its cause fairly well ascertained. The reason for the method used in dyeing
fur is that while most dyestuffs must be applied by boiling, fur cannot be boiled without
damage (unless it first be chrome tanned). So the colour must be produced by reactions
on the fibres; these reactions are not usually quite complete nor is the pigment completely
absorbed in the fibres, so there is apt to remain on the fibres (1) unoxidized base and
(2) intermediate oxidation products of the base in addition to the real, believed harmless,
pigment formed in the fibres.

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I have described these reactions in detail in another place \cite{1} and it will suffice here
to point out that when a simple diamine such as p-phenylenediamine is oxidized by
peroxide, there is formed first Bandrowski's base and next an insoluble azine in and on the fibres. There is no evidence of the presence of the di-imides which were at one time suspected. The free p-phenylenediamine can be extracted with water, though it is very difficult to remove the last traces on a commercial scale. The Bandrowski's base can be extracted by pyridine and certain other organic solvents, and the evidence seems to be that Bandrowski's base is in fact harmless. So the examination of a suspect with generally resolves itself primarily into a search for traces of unoxidised p-phenylenediamine and allied compounds. Frequently the colour of the dye is modified by a poly-phenol such as resorcinol, pyrogallol or quinol; in such cases an oxazine results instead of a simple azine [2], and again search must be made for phenolic compounds. There are of course other matters to be thought of: there may be an excess of acid or of salt: there may be traces of soluble chromate or chromic acid left from the oxidising agent. Poisonous metals such as lead or antimony may also be present. The chemical aspect may be complicated by the presence of vegetable tannins, by logwood, hustic, gallotannic acid and other such products. If the fur has been chrome tanned different considerations arise: there is unlikely to be free diamine or amino-phenol but there may be soluble chromium compounds and textile dyes and their reduction products, the nature of which must be investigated.

WOOLENS

Wool presents on the whole a more difficult problem than fur usually does: it may be treated in so many ways and with so many substances. It will be within the knowledge of many that both leading judgments ruling dermatitis cases in the Courts arose from woollen garments. In Grant v. the Australian Knitting Mills the plaintiff's skin was normal but the garment contained an excessive proportion of sulphite, whereas in Griffiths v. Peter Conway the plaintiff's skin was abnormal but the garment was normal. White wool, such as a blanket or underwear is quite commonly bleached with sulphite, and garments containing small quantities of sulphite must be worn by millions of people. The sulphite will not be completely removed by even two or three launderings. All such wool—indeed most woollens too—are acid [3]. How much sulphite and what degree of acidity is to be regarded as potentially dangerous? Undyed wool quite commonly shows 2 or even 2-5% of acid reckoned as sulphuric acid. The wool protein is itself acidic and there is evidence [4] that the disulphide (R.CH...S-S.CH...R) linkages in the keratin are continuously oxidized in light with the production of more acid in the form of sulphite and sulphate. In dyed wool some of the acid linkages have combined with the dye and 1% or less acid is found. The amount of sulphite found in normal cases too is somewhat variable; quantities such as 0-2 or 0-3% are common enough in bleached undyed wool. In dyed woolls it is unusual to find any appreciable quantity [5].

Then there are the dyestuffs. It was at one time common to blame the dye in cases of dermatitis from a dyed cloth; often it may have been true, but nowadays most of the known deleterious dyes have gone out of use. Very fast insoluble dyes are now available and standardized tests for fastness and the absence of bleeding have been prescribed by the Society of Dyers and Colorists. Generally speaking it may be taken that the more fast and insoluble a dye the less likely is it to be an irritant [6]. So we must find what kind of dye has been used and whether it is fast to water and to perspiration. The identification of the dyes in a fabric is apt to be very difficult and mixtures are common, so it is not often possible to say exactly what has been used, but it is possible to discover the class of dye present. Here I emphasize that such textile dyes as are usually applied to wool do not contain p-phenylenediamine; this substance is an intermediate and not a dye and is not applied to cloth (though it may have been used in the original manufacture of the dye). The oft-repeated suggestion that a piece of cloth contains p-phenylenediamine or had been dyed with it arises from a misconception of dyeing practice.

Many dyes are fixed to wool with the assistance of a mordant such as chromium salts. Others are after-chromed to improve lustre and fastness. Chromic acid and dichromate are potential irritants, so it is important to ascertain that there is no soluble chrome compound left in the material. Other less common mordants include copper, tin, nickel, zinc, and cobalt.
TEXTILE AUXILIARIES

During recent years great progress has been made in the development of a large range of textile auxiliary agents. In this term are included wetting and levelling agents, dressing and de-lustering compounds, anti-creasing preparations, waterproofing substances, and various other chemical compounds, which improve the texture, feel, appearance, or properties of the fabric. There are reasons for thinking that some of the cases of dermatitis which have been attributed to dyes were in fact due to such a textile agent; as an example may be quoted a recent outbreak in the U.S.A. [7] which was proved to be due to a synthetic resin used as a dressing for textiles.

Most of these compounds depend for the effect upon a property, first discovered by Langmuir, possessed by molecules which consist of a long chain of hydrocarbons attached to a terminal polar group. (A polar group is an ionizable group of which one atom gives up an electron.) The polar group has an affinity for water, whereas the long chain has not, so the molecule when in contact with water stands up on end with the head, or polar group in the water and its tail stretching up. If the proportions are correct a monomolecular layer is so formed. If in such compounds the hydrocarbon group is short (say 12 C. atoms) the result is a wetting agent. In order to dye goods a level shade it is essential that they should be evenly wetted; a small proportion of a sulphonated fatty alcohol, e.g. sulphonated lorol or similar compound, enables the material to be wetted uniformly and quickly and so is a great aid to dyeing. When the carbon chain is somewhat longer, say 16 or 18 C. atoms, a valuable detergent property is developed and a washing compound free from alkali or fat is produced. Such compounds are the basis of soapless shampoos and are much used in the preparation of textile fabrics. The long chain compound may be a sulphonated fatty alcohol (i), or an ester (ii), or may be a quarternary ammonium compound (iii) or pyridinium compound (iv).

The physico-chemical properties of these compounds are truly remarkable and their uses diverse, so it is not altogether surprising that they should have rather marked physiological activities and be capable at times of causing severe skin irritation. I have had occasion to examine some of these substances; two properties stand out, one that they can pass through the skin and the other that they exert a marked hemolytic effect on red blood corpuscles. Such properties may be of significance from the dermatitis point of view. I do not know of evidence which would class them as primary irritants, but there have been sufficient cases of dermatitis following their repeated use to indicate that where susceptibility exists they are capable of being irritants. So it is clear that in our search for the chemical causes of the irritation we must find if any excess of such substances remains in the fabric.

Yet another class of long chain compound with a terminal polar group is used to make the fibres water resistant or water repellent. Such a compound may be a pyridinium compound of the type (iv), which upon being heated in the treatment of the fabric gives rise to a fatty amide and liberates pyridine and acid;
all these substances should be removed. Then there are synthetic resins used to give the fabric anti-creasing properties; they may be condensation products of urea and formaldehyde or of glycerol and phthalic acid. Formaldehyde if not entirely removed may irritate or may combine with ammonia to form hexamethylene-tetramine to which a few people appear to be sensitive [7]. These condensations in general tend to produce insoluble compounds of high molecular weight which are without any marked physiological property. There may, however, be residues of their constituents as impurities, and there is evidence that to some of them some people are susceptible. Cases arising from spectacle frames belong to this category.

Another synthetic resin used on textiles is ester gum, which is reported by L. Schwartz and others [8] to have caused quite a number of cases of dermatitis last year in the U.S.A. Ester gum is formed by heating glycerol with colophony resin, the principal constituent of which is abietic acid. Colophony is known to cause irritation in various other industries; it contains abietic acid and unsaturated acid anhydrides related to the terpenes, pinene and retene, which are possible causes of its irritant effects.

So an examination of woollens and other fabrics must include consideration of and tests for all these diverse and rather difficult compounds which may be implicated in any particular case, and it may be necessary to conduct patch tests on the separated suspect substance if complete proof is to be obtained.

COTTON AND SILK.

These fabrics are unlikely to contain acid or bleach, but they may be weighted with a variety of inorganic compounds such as tin salts or titanium oxide, not that these substances are harmful; and it will be necessary to consider the dyes which have been used and any traces of impurities arising therefrom, also to find out if any active chemical auxiliaries are present in an uncombined state. Anti-crease compounds such as urea-formaldehyde polymers and the glyptals are possibilities and water-resistant substances of the amido-pyridinium class may have been used; if so there should be no free acid or free pyridine or formalin. In the practical examination of these materials it is desirable to differentiate clearly the different kinds of fibres and so far as the dyes are concerned to examine different colours separately. The reason for this is of course that different classes of dye will be used for vegetable fibres and animal fibres. The use of suitable quaternary ammonium compounds greatly increases the fastness of the direct cotton dyes.

RAYON.

In my experience various kinds of rayon are suspected in more cases of dermatitis than the natural animal or vegetable fibres. Union fabrics are more likely to be concerned than single component fabrics and black is more likely than most of the colours. There are, however, considerations which modify the force of such general observations; for example, rayon is immensely popular, union fabrics are more difficult to dye uniformly than others and black is by far the most used colour. It is also the colour which requires a maximum quantity of dye and the one most frequently applied in re-dyeing an already other coloured garment. In examining a rayon garment it is particularly needful to consider what the fibres are made of. The type of dye applicable to acetate-silk may be quite different from that used, say, on viscose. Cellulose acetate was for some years difficult to dye, and new types of colour have been evolved since 1920 to meet the difficulty. Notable among these are the ionamines (1922) and insoluble azoic colours prepared by coupling aminoazo compounds with \( \beta \)-hydroxynaphthoic acid or one of its arylamides.

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\text{COOH}
\end{align*}
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Traces of this \( \beta \)-hydroxynaphthoic acid are difficult to remove completely, particularly in the case of union fabrics, and in my experience a few cases of dermatitis have been traceable to such cause. In testing one has to avoid producing it by hydrolysis during
the extraction and when it is found consideration must be given to the quantity. A few parts per million seem to be inevitable, but larger quantities may be found which are irritant to susceptible individuals. It is not a primary irritant, but one to which some people are sensitive.

Like cotton and silk, rayon is very frequently treated with a filler or some textile auxiliary compound. The material and its manufactures are so versatile that quite aesthetically beautiful new fabrics are constantly being produced, new colours, new textures, new properties giving nothing but delight to the vast majority of purchasers but unfortunately producing irritations in a few idiosyncratic individuals.

**RUBBER GARMENTS.**

In my experience quite a number of cases of irritation have arisen from the wearing of latex rubber often in immediate contact with the skin. Most people can do this with impunity and the garments last for quite a reasonable time. Breakdown ultimately occurs, the rubber loses its elasticity and becomes sticky. The curious feature is that this change is much accelerated by sweat and the sweat of some people is much more potent than that of others. Chemically the breakdown is really a polymerization of isoprene

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\text{CH}_2 = \text{CH}_2
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resulting in the formation of a resin [9]. In terms of analysis this is marked by a sharp rise in the solubility in acetone. In a degraded rubber it may reach 20 or 25% instead of some 3 or 4%. The active agent in the degradation is an oxidase present in the sweat of some people, and it is on this account that artificial sweat mixtures are not entirely comparable with the natural product. To counteract this natural tendency to oxidation many substances known as antioxidants are or may be added. Usually these are complex hydroxylated phenols, amines or sometimes quinones. What are their physiological properties? Little is known, though in the case of quinone there is some evidence that it is harmless when fed to rats for several generations. Another aspect is that these oxidases and antioxidants are very potent substances; they are active when present in quite minute percentages and exert a most marked effect. Oxidation and reduction in the tissues is a fundamental biological activity and my suggestion is that any substance which inhibits it is *prima facie* suspect. As an example may be cited the familiar p-phenylenediamine, which has been shown by Keilin and others [10, 11] to exert a considerable influence on tissue respiration; if this is so it is not probable that di-β-naphthyl-p-phenylenediamine will be similarly active.

So one might continue reviewing the different garments—hats, shoes, brassieres, corsets, &c.—our modern miss may wear. In the manufacture of all of them potent chemicals have been used, and traces may remain which may be themselves irritant or to which our daimel may be supersensitive. But the point I really want to make is the need for more careful co-operative study between the dermatologist and the chemist, of the substances used on garments or otherwise in contact with the skin. One property these substances have in common, be they auxiliaries, dyes, antioxidants or what, is that their value depends upon special reactivity. They are substances of which a fractional percentage exerts a great effect; they can wholly alter the physical properties of the fibres or the penetrating effect of dyes. It has been shown that some of them are intensely active when in contact with blood or serum, so it is not surprising that sometimes unwanted effects develop on the human subject. Unwittingly Miss Blank may thus become our experimental animal. This ought not to be; the physiological properties of substances applied to our outsides as well as to our insides ought to be very carefully explored and in general the results if favourable should be made known to all concerned; if unfavourable then, of course, the substance is unfit for use. The great difficulty is arranging for a sufficient number of experiments to complete the necessary research; it is not difficult to discover the properties and reactions of a new product, nor is it difficult to detect and eliminate the primary irritants, but it is very difficult to foresee and provide against the
supersensitive and idiosyncratic individual. The law has recently been distinctly more helpful to industry in this direction, and that I think makes it still more desirable that we should together explore more thoroughly the relationship between chemical constitution and irritant propensities, together with the cognate subject of induced sensitization.

REFERENCES

2. Id. (1940), ibid., 65, 303.
5. Cox, H. E. (1939), Analyst, 64, 570.

President—H. C. Semon, M.D.

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DISCUSSION ON A SELECTION OF THERAPEUTIC PROBLEMS

ACRODERMATITIS (DORE)

Dr. S. E. Dore, who was asked by the President to speak on a condition to which his name was appended, said: I have never made any special claim to this condition. Some years ago at a meeting of the British Association of Dermatology and Syphilis1 I described a short series of cases characterized by vesicular and pustular lesions on the thenar and hypothenar eminences of the hands and on the soles of the feet, the eruption being very chronic, relapsing, refractory to treatment, and sterile on culture. At the same time Dr. Barber wrote a much more comprehensive paper describing the histology of the disease which he subsequently included in his group of "pustular psoriasis" and showed cases in which the two conditions occurred together, a combination which I had never seen in my own cases.

Dr. Goldsmith typified the condition I had described as an eczema of the pompholyx type entirely different from psoriasis and coupled my name with it. Naturally I was somewhat surprised and gratified when Dr. Goldsmith called it by my name, but I am quite willing to abide by Dr. Barber's verdict regarding the nature and classification of the disease. It is a characteristic eruption in view of the peculiar "lacunar" pustules in the epidermis accompanied by eczematization, the special localization, the chronic history, refractoriness to treatment, and tendency to relapse. Dr. Barber pointed out that in some cases focal sepsis was an important factor in its causation, but in my cases I have not found this to be a prominent feature of the disease.

Dr. Prosser Thomas: So far as treatment goes, ordinary measures clear up the attacks temporarily. Crude coal tar in Lassar's paste is probably the most useful local application. Some of the dyes, such as gentian violet, are helpful, also silver nitrate, and I think Castellan's carbolfuchsin paint has been advocated. Whether or not the condition is related to pustular bacteride, it is important to find a focus of infection. It might be allowable to use one of the sulphonamide group of drugs in this condition as it may be directly or indirectly of microbial origin. I have not had an opportunity of doing so. I should suggest sulphathiazole. I have had at least temporary success with thorium X. The eruption is supposed to be resistant to X-rays and they have been known to make it

1 Brit. J. Dermat. & Syph., 1928, 40, 12.