HOP DERMATITIS IN HEREFORDSHIRE

BY

J. S. COOKSON, M.D.

County Medical Officer of Herefordshire

AND

ANN LAWTON, M.D.

Dermatologist, Hereford and Shrewsbury Hospitals

The object of this investigation was to try to discover the incidence of hop dermatitis among workers in the hop-yards in Herefordshire and also try to establish the cause and nature of the dermatitis.

The use of hops for flavouring and preserving beer was known long before 1549, when it is thought hops were first cultivated for this purpose on any large scale in England. For a time in the sixteenth century hops were regarded as noxious and their use was forbidden. Hereford City Regulations, 1557 (Morgan, 1945), has the following entry: "And that no bruer shall sett Anye hoppes or asshes in their Ale upon peyne of XXs for evy defalte." Hereford people, however, thought the risk of this "peyne" worth taking, as in 1513 the following culprits were brought before the jury at Views of Frankpledge: "Wyllm Collyer for bere Hoppis in ye ale, Alson Coke for bere hoppis in hyr ale," with a number of other citizens. It can be assumed therefore that Hereford people have been picking hops at least since the early sixteenth century.

In the county "hop rash" is well known by all hop-workers. It is thought to vary in incidence from year to year in relation to the weather and to be fairly common among pickers but rare among other hop-workers. Hop rash is usually assumed by pickers to be caused by the hop-washes.

History of Hop Dermatitis

In 1924 O'Donovan described two cases of acute contact dermatitis on exposed surfaces developing in two girls after visits to the hop-gardens of Kent. He says that, in spite of the annual exodus of Londoners to the hop-gardens, the dermatitis had not been seen previously at the London Hospital, and suggests that this is because the condition is rare, that hop-picking is a holiday, and that people who develop dermatitis do not again go hop-picking. O'Donovan quotes Samuel Dale, who in 1693 wrote on hops: "De Lupulo Salictario—Extrinsicis sedebat dolores," and Badham, who in 1834 described the case of a girl of 14 who developed dermatitis of the hands and face after placing her hands in a bin of hops to warm them.

Lewith (1928) did patch tests with hop-cones on three cases in female hop-pickers, with positive results. His attempt to reactivate the dermatitis by giving lupulin, a hop extract, by mouth failed. He thought there was no doubt that the dermatitis was due to contact with the hop-cones. Smithies (1929) saw 52 cases of hop dermatitis among 1,172 patients attending a clinic for hop-pickers. She quotes the observation of Galbraith (1924) that a number of cases of hop dermatitis appeared in a year when no washes were used, and also points out that the regular garden workers who use the washes most do not suffer from the condition. She suggests that a protein sensitization from inoculation of hop juices or pollen through scratches from the spines on the hop-bines may be the cause. Schwartz *et al.* (1947) state that hop dermatitis is often accompanied by conjunctivitis, but have nothing further to say about the cause of the dermatitis.

Incidence in Herefordshire in 1952

In the previous four years only one case of hop dermatitis had been referred to the dermatological out-patient department in Hereford. The district nurses and medical practitioners working in the hop-picking areas were therefore asked to report cases of hop dermatitis to the dermatologist. As it was thought that this method would miss most of the mild cases, at one hop-yard employing 450 pickers the bushelling clerk, a V.A.D. nurse, who saw all the pickers at work every day, sought out and reported every case.

As dermatitis is almost unknown except at hop-picking time, the investigation started with the picking season on September 4, 1952, and continued until the end of picking on October 7. The first case was reported on September 13, the last on October 4. The estimated number of adults regularly employed in hop-picking in Herefordshire in 1952 was 30,000 (G. P. Chater, 1952, personal communication). This does not include an unknown number of people who visit their friends and relations in the hop-yards for short periods of perhaps half a day. These people make an accurate estimate of the incidence of dermatitis impossible.

Twenty-two cases were reported to the dermatologist and were classified as follows:

Severe: forced to give up picking	11
Moderate: carried on picking, rash persisted but cleared when picking stopped	5
Mild: carried on, rash cleared before the end of picking	6

Apart from the difficulty of casual pickers, this total does not give a true picture of the real incidence of hop dermatitis for the following reasons: (1) Hop-picking is a pleasant and lucrative occupation; pickers will not give up before the end of the short season unless forced to do so by the severity of their dermatitis. (2) Many cases are mild and even transitory, the cause is known, and recovery is certain when picking stops, therefore pickers do not seek medical help even in 1952. However, the 11 severe cases may be a fairly accurate figure for the incidence of this type of case among the 30,000 (plus) pickers in 1952, as such cases would have been forced to seek medical help. The most that can be said, therefore, is that in Herefordshire in 1952 severe dermatitis was uncommon, about one case in 3,000 pickers.

Some idea of the incidence of all types of hop dermatitis can be obtained from the figures supplied by the V.A.D. nurse working in a hop-yard employing 450 pickers. She reported 12 cases: six were of a mild transient type and were not seen by the dermatologist; six were seen—one severe, two moderate, and three mild. From this report, so far as it goes, it seems possible that a mild dermatitis was fairly common in Herefordshire in 1952, about one picker in 30 being affected.

Clinical Findings

Unlike most cases of contact dermatitis seen in out-patients, the history in these cases could be obtained fairly accurately, and the dermatitis appeared in healthy cheerful people bent on a lucrative holiday and not bedevilled by thought of compensation. The dermatitis was therefore seen in an unusually clear field.

Of the 22 cases reported, 17 were seen personally—of whom 12 were given patch tests—three were seen by other doctors, and two were not seen. The patients came from 11 hop-fields situated in all the different hop-growing areas in Herefordshire. There were five men and 17 women. This is of no significance, since there are many more female than male pickers. At one farm, for example, there were 410 women and only 40 men. The ages range from 15 to 71. This agrees with the usual finding that contact dermatitis is rare among children. Apart from two cases in sisters, no family history of hop dermatitis was dis-

covered. Two patients gave a history of contact dermatitis to other irritants. There was no obvious evidence of psychological stress and strain, patients compared favourably with the average run of dermatological patients in this regard. No one wanted to give up picking, in fact the patients were upset if they were forced to do so, and the cry of compensation was not heard once.

Socially patients varied from the poorest caravan dwellers to undergraduates. Secondary infection of the dermatitis was seen in only two cases. The dermatitis was papular and oedematous rather than weeping, and this would help to prevent secondary infection.

The following case histories illustrate typical hop dermatitis.

Severe Dermatitis.—A healthy housewife aged 29 had no previous history of skin trouble other than dermatitis due to hops. She was born in Herefordshire, but lived away and was visiting the county for the hop-picking. Her mother had picked hops during many seasons without trouble. The patient had often been in hopyards for odd days as a child, but had had no sign of dermatitis until the age of 21, when after picking hops for one afternoon she developed a rash on her face, arms, and legs which lasted for three days. She had not visited a hop-yard again until 1952. She started picking on September 10, and by the evening felt a rash under the skin of her face. She picked again on the following afternoon, but the rash became worse and she did not pick again. When seen on September 13 she had gross oedema of eyelids, nose, and lips, with erythema, and an itchy papular eruption on the face, between the fingers, and on the dorsum of the hands, extending up the flexor surface of the forearms to the elbows. Antihistamines by mouth and sedative applications were prescribed. By September 15 the condition was beginning to settle down, and by the 22nd the oedema had subsided completely, the skin was peeling, and there was a slight vesicular eruption on the fingers which disappeared during the next seven days. Patch tests to hop-cone on September 22 and October 25 were strongly positive.

Moderate Dermatitis.—A healthy male undergraduate with no previous history of skin trouble was working as a busheller. He plunged his right arm with the bushel measure into the picker's crib of hops and helped the hops into the measure with his left hand. He started work on September 4, having never previously seen a hop. After eight full days of bushelling he developed an irritable papular eruption on the back of his hands and the flexor surface of his forearms, corresponding fairly accurately to the site of staining from the hop juices. He carried on with his work and the dermatitis was little different when he was seen 10 days later. He then had a slight erythema round his eyes and at the side of his nose. A patch test to hop-cone on his back was strongly positive. He was treated similarly to the previous case and went on with his work until October 3 without much discomfort. On October 6 his skin was almost clear.

Mild Dermatitis.—A healthy female publican aged 45, with no previous history of skin trouble, had been in the hop-yards every year since the age of 1. Her mother had also picked hops for many seasons without trouble. She started picking on September 4, and 11 picking days later developed an oval erythematous area with itchy papules on the dorsum of her right forearm and erythema and slight swelling round the eyes. This persisted for five days and disappeared, in spite of continued picking, without treatment. The site of the eruption on the forearm was the same as a painful area due to tenosynovitis or hop gout. No embrocation had been used, but she had rubbed the area with hop-stained fingers. A patch test to hop-cone was negative on a day when the rash had recovered.

The degree of severity and the number of days picking before the development of dermatitis in 18 cases classified according to their previous history of hop dermatitis or of contact with hops is summarized in Table I. From these results it seems that hop dermatitis is a true sensitization

dermatitis, in that the skin has to be previously exposed to the sensitizing agent and the dermatitis recovers when this is removed (Hellier, 1950).

Cases with a previous history of dermatitis all developed an attack within 48 hours of exposure in the hop-yard. In new cases length of exposure varied widely and did not seem to depend on the type of the subsequent attack. As is usual in contact dermatitis, there seemed to be no reason why these particular individuals should be sensitive to hops.

Prognosis could also be assessed and was in accordance with the view of Hellier (1950) that hardening in contact

TABLE I

Case No.	Previous History of		No Contact Except "Stripping"	Type of Dermatitis
	Dermatitis	Picking		
1	½ day			Severe
2	1 "			"
3	2 days			Moderate
4	1 day			Severe
5	1 "			Moderate
6	Not known			Severe
7	" "			Moderate
8		1 day		Mild
9		2 days		"
10		4 "		Severe
11		14 "		Mild
12		9 "		"
13		13 "		"
14		11 "		"
15			8 days	Moderate
16			10 "	Severe
17			17 "	"
18			10 "	"

dermatitis, as described by Schwartz *et al.* (1947), occurs only in mild cases, while the more severe ones become progressively worse with each exposure.

Apart from the mild cases which recovered during this season, a case of hardening was found in the sister of one of the cases. This woman had picked for three seasons without trouble, but developed moderate dermatitis during her fourth season, mild dermatitis during her fifth season, and this season had picked free of trouble again. One case of moderate severity seen two months after the end of the season still had a chronic eczema of the hands at the site of previous dermatitis. This result may be an alternative to hardening in some patients.

Daily weather reports were obtained from the county observatory to try to correlate the development of new cases with periods of sunshine. This was not possible, but it is probable that the weather over the whole picking season may affect the incidence of dermatitis. September, 1952, was the coldest in Herefordshire for 80 years, the mean daily maximum temperature of 59° F. (15° C.) being without precedent (F. G. Parsons, 1952, personal communication). This may account for the low incidence of severe dermatitis this year. It is hoped to study weather influence in subsequent years.

Possible Causative Factors

To discover the cause of hop dermatitis a search was made for a sensitizing agent. Three possibilities were explored.

(1) **Insecticides and Other Washes.**—The evidence against these is as follows. First, hop dermatitis was described by Badham in 1834. Sulphur was first used as an insecticide for hops in about 1850 (Parker, 1934). All other insecticides were introduced later. Secondly, hop dermatitis is almost unknown among cultivators. One case which was thought to be due to hop pollen was reported by Dr. J. C. Taylor, of Goudhurst. The number at risk must here be taken into account. For example, on a first-class Herefordshire hop-farm employing more than 450 pickers, only 23 people are employed regularly in cultivation, with an additional 15 at hop-tying. Hop-pickers would come into contact with sprays if these were present on hop-cones. The fate of the following sprays was therefore investigated:

(1) Nicotine : this evaporates (A. H. Burgess, 1952, personal communication). (2) Sulphur : this may remain on hops until they are dried in kilns, when it is usually driven off (Burgess, 1952). (3) Bordeaux mixture : correctly applied the hops should be free of copper at picking (Lloyd Hind, 1948). (4) Pestox : contamination with organo-phosphorus compounds may be fatal in a few days (Barnes and Davies, 1951)—these are applied according to regulation to prevent contamination. Sulphur, therefore, is the only one of these insecticides which need be considered.

(2) *Insects on Hops*.—At least 11 caterpillars are found on hops (Theobald, 1925). Of these the caterpillars of the pale tussock-moth, or hop-dog, the vapourer moth, and the dock-moth are hairy and in the caterpillar stage in September. Hop dermatitis often starts on the face, but never round the neck, which is the usual site for caterpillar dermatitis. "Hop-fleas" are present and bite the legs of pickers. The spots caused by these are distinguished easily from dermatitis by the pickers.

(3) *Hop-cones*.—These are the female inflorescence of the dioecious hop-plant and ripen in early September, when they are aromatic and sticky with resin. The aroma is due to hop-oil and the pickers are in contact with this in the atmosphere and also have it on their hands mixed with hop-resin. In view of the importance of hops in the brewing industry, much work has been done on hop-oil and hop-resin, so that in addition to patch tests with hops it was possible to use the different hop products as well. The content of these oils and resins is at a maximum when the cones are ripe in September. The bines are pulled down from the wires and the cones picked off one by one. A good picker can pick up to 20 bushels in a day, and picks for about 30 days each season, from 7 a.m. to 4 p.m. The contact with the hops is therefore a concentrated one.

Results of Patch Tests

Hop-cone.—The cone was bisected and the cut surface applied to the skin away from the site of dermatitis under lint, jaconet, and strapping for 48 hours. A control test, omitting the cone, was used. Severe cases were not tested until the dermatitis had subsided. The results (see Table II) were :

Cultivated hops possibly contaminated with sulphur: eight tested—six positive, one doubtful, one negative.

Escape hops from bine on telegraph pole, no possibility of contamination with sulphur: five tested, all positive.

Controls: 12 used, all negative.

The doubtful and negative tests occurred in patients whose dermatitis had recovered, although picking continued, before the test was read. Oedema was severe around the erythematous positive patch test. From this it seems highly likely that the hop-cone itself is the cause of the dermatitis. In order to exclude contamination with caterpillar hairs and to try to pin down the sensitizing agent, further patch tests were done using hop-oils and hop-resins. The oil would be present on the face and hands; the resin would be on the hands and brought to the face by the fingers.

Soft Resin, Total Resin, Humulone, Lupulone.—These were prepared by Messrs. Bencard. Appropriate control tests were made from material supplied by the Brewery Research Association. Nine patients were tested, all of whom had previously given positive results to hop-cone. Two were positive to all four tests; one was positive to soft resin and total resin; and six patients negative to all four tests.

Hop-Oil.—This was obtained from three sources. *Oil A* (from Messrs. Bencard) on prepared patch tests. This oil was known to be one year old. The nine patients tested were all positive to hop-cone; eight were negative and one was positive to hop-oil. *Oil B* (from Cheltenham Brewery). This also was an old oil. It was applied on lint under jaconet and strapping. Two patients were tested, one was positive and one was negative. The positive patient was one of those who gave positive results with the four resin patch tests. *Oil C* (from Messrs. White, Tomkins, and

Courage) was freshly distilled oil from fresh green hops and was applied on lint as above. Seven patients were tested, six were positive and one was doubtful, possibly due to evaporation of oil before test could be used. Two of these positive patients gave positive results with some or all of the resin patch tests.

TABLE II.—Results of Patch Tests

Case No.	Hop-cone		Resins				Hop Oils		
	Culti-vated	Escape	Soft Resin	Total Resin	Humu-lone	Lupu-lone	Old		Fresh
							A	B	C
1		+	+	+	+	+	+	+	
2		+	+	+	+	+	+	+	+
17	+		+	+	—	—	—	—	+
3	+		—	—	—	—	—	—	+
4	+		—	—	—	—	—	—	+
16	+		—	—	—	—	—	—	+
18		+	—	—	—	—	—	—	+
15	+	+	—	—	—	—	—	—	?
8	?	+	—	—	—	—	—	—	
9	+								
10		+							
14	—								

Discussion of Results of Patch Tests

Where accurate histories could be obtained it was found that dermatitis started on the face in seven patients, and in three of these the hands were not affected. In three patients the dermatitis started on the hands and spread to the face. In view of this, and the probable variation in incidence with the weather, a volatile agent seemed likely. Hop-oil is such an agent, as it consists of a mixture of essential oils. Fresh hop-oil is known to differ from old oil in that it contains 40% myrcene which is oxidized and disappears in old oil (Lloyd Hind, 1948). From the patch tests it seems possible that myrcene might be one of the sensitizing agents responsible for hop dermatitis. If the sensitizing agent is in fresh hop-oil, it seems surprising that kiln workers do not commonly develop dermatitis. Again the number at risk has to be considered—10 kiln workers in proportion to 450 pickers. In the kilns, also, the fresh hops are not handled by the workers but spread with flat shovels. The hops awaiting drying are kept in sacks and on the drying racks; some of the oil myrcene is lost in the air current used in drying (A. H. Burgess, 1952, personal communication).

If dry hops contain little myrcene they may be less likely to cause dermatitis, as seems to be the case both in breweries (R. Webb, 1952, personal communication) and in the hop-markets. The commercial manager at the Hop Marketing Board (Mr. F. H. Job) gave the following interesting information. Among about 250 people employed he has heard of only one case. These people are constantly taking samples from the pockets of dry hops and testing them by rubbing between the palms, which are then put up to the nose to obtain the full aroma. It seems highly likely, therefore, that the sensitizing agent has been removed in the drying, otherwise cases of dermatitis might be expected frequently among the samplers.

Unfortunately this explanation does not cover the patients who gave positive patch tests to resins. The fact that they were positive to all four tests in two cases might be explained if the substances provided for the tests were not absolutely pure. There is probably no chemical relationship between the constituents of the oil and those of the resins (A. P. Tatchell, 1952, personal communication). The two patients who gave positive patch tests to both fresh hop-oil and resins had severe dermatitis, two of them with rapid development of acute oedema and erythema after a short contact. The patch tests were not part of a general sensitivity, however, as the controls were negative and the tests did not reactivate the dermatitis which had subsided.

It is possible that two sensitizing agents are involved, with fresh hop-oil as the more usual one. On the other hand, the explanation may lie in further elucidation of the chemistry of the hop-cone.

Summary

Hop dermatitis in Herefordshire was studied during the 1952 picking season, which was regarded as a light season for dermatitis.

Accurate estimation of the incidence of dermatitis was impossible, but it was thought that most of the severe cases were seen. The incidence of this type of case in Herefordshire in 1952 was found to be about 1 case in 3,000 pickers.

Daily observations of 450 pickers showed a much higher incidence of mild dermatitis: approximately 1 in 30 of these pickers developed some type of dermatitis.

It therefore seems probable that, while severe cases are rare, mild cases may be fairly common.

Hop dermatitis in some cases tested seemed to be due to a sensitivity to fresh hop-oil, of which myrcene may be the active ingredient. In three cases sensitivity to hop resins was also present. No satisfactory explanation of this is forthcoming at present.

It is suggested that the rarity of hop dermatitis among workers in dried hops is due to the fact that the sensitizing agent is driven off in the drying process. It is concluded that this is just as well, in order that the use of hops may continue. Harrison's words in his *Description of England* in 1577 are still true in 1952: "For if your Ale may endure a fortnight your Beere through the benefice of the hop shall continue a month, and what grace it yieldeth to the taste all men may judge that have sense in them."

We thank the medical practitioners and district nurses of Herefordshire who sent us the patients, and particularly the patients themselves, who were most helpful about patch testing. We also thank Dr. A. H. Burgess, head of hop research, Wye College; Mr. R. Webb, of Cheltenham and Hereford Brewery; Mr. Milner, of Messrs. Bencard; Dr. Bernard Tate; and the Davies family, of Claston, Herefordshire, for much help.

REFERENCES

- Barnes, J. M., and Davies, D. R. (1951). *British Medical Journal*, 2, 816.
 Galbraith, S. N. (1924). *Lancet*, 2, 885.
 Harrison, William (1577). *Description of England*. Quoted by Parker (1934).
 Hellier, F. F. (1950). In *Modern Practice in Dermatology*, edited by G. B. Mitchell Hegg, p. 123. London.
 Lewith, R. (1928). *Arch. Derm. Syph., Berl.*, 154, 345.
 Lloyd Hind, H. (1948). *Brewing Science and Practice*, 1, 335.
 Morgan, F. C. (1945). Transcriptions of the Regulations of the City of Hereford.
 O'Donovan, W. J. (1924). *Lancet*, 2, 597.
 Parker, H. H. (1934). *The Hop Industry*.
 Schwartz, L., Tulipan, L., and Peck, S. M. (1947). *Occupational Diseases of the Skin*, p. 589. Philadelphia.
 Smithies, B. M. (1929). *Lancet*, 2, 494.
 Theobald, F. V. (1925). *Cultivation, Diseases, and Insect Pests of the Hop Crop*. Ministry of Agriculture Miscellaneous Publications No. 42.

The joint committee set up in 1946 by the National Institute for the Blind and the London County Council to advise on the use of optical aids for the partially sighted has now published its report (*N.I.B. Bulletin No. 19*). The search for a good magnifying lens capable of covering an entire printed page has resulted in the production of special binoculars which fit over the nose. Various types of desk lenses are also described and illustrated. Another method advocated is the projection on to a screen of micro-filmed books, newspapers, etc.; the advantage of books on micro-film over other aids is that greater magnification can be obtained without loss of contrast and with no distortion. Suitable projectors cost about £20. Tests on partially sighted children show that in some cases the use of contrasting colours, such as blue chalk on yellow board, improved the visual impact of reading and writing. At one school a preference for black crayon on white paper was expressed. The report may be obtained from the National Institute for the Blind, 224, Great Portland Street, London, W.1.

RAPID METHOD FOR DETECTION OF BARBITURATES IN URINE AND STOMACH CONTENTS

BY

R. MARSHALL, M.B., M.R.C.P.

Registrar, Medical Professorial Unit, St. Bartholomew's Hospital

Treatment of barbiturate poisoning by analeptics is not without danger, and a rapid method for the detection of barbiturates in urine and stomach contents is of value in doubtful cases. Several "rapid" methods (Griffon and Le Breton, 1938; Denis and Lambrechts, 1940; Merley, 1948; Goldbach and Opfer-Schaum, 1949; Selwyn and Dark, 1950) have been described for detecting barbiturates in urine, but the procedures take from one to three hours.

A micromethod for the detection of barbiturates in urine, cerebrospinal fluid, and blood has been described by Kresbach and Gomahr (1951), and a modification of this method, making it less sensitive but more rapid, has been used for the detection of barbiturates in urine and stomach contents.

Principle of the Method

The acidified urine or stomach washings are extracted with chloroform. This is carried out in one stage, and the volume of chloroform is kept small so that the time required for evaporation is not excessive. Chloroform is used in preference to ether because of the inflammatory nature of the latter. The chloroform extract is dried and decolorized. Activated charcoal is used for decolorization because, although it absorbs some of the barbiturate, it is more effective than any other agent and the loss of some of the barbiturates is not serious. The chloroform extract is evaporated to dryness and the presence of barbiturate in the residue is tested for by its reaction with cobalt nitrate and ammonia vapour.

Reagents Required.—Chloroform; dilute sulphuric acid (approximately 10% w/w); sodium sulphate (anhydrous); a mixture of activated charcoal 3 parts and magnesium oxide 1 part; cobalt nitrate 1% w/v in absolute methyl alcohol; and ammonia solution (S.G. 880).

Procedure

About 50 ml. of urine or stomach contents are acidified with 4 ml. of dilute sulphuric acid and shaken with 20 ml. of chloroform in a separating funnel for one minute. Stomach contents should be strained to remove solid material, although any portions of tablets or capsules which are present should be included in the sample.

After allowing the chloroform emulsion to settle out, the chloroform layer is run off into a 250-ml. conical flask. Enough anhydrous sodium sulphate (5–10 g.) is added to dry the chloroform emulsion, so that, after shaking, the sodium sulphate separates out from the clear or slightly opalescent chloroform. About 0.5 g. of the activated charcoal mixture is added, the resultant mixture being shaken and filtered through a No. 43 Whatman paper into a 100-ml. beaker. The filtrate should be crystal clear. The filtrate is then evaporated to dryness on a boiling water-bath. Towards the end of the process the beaker is tilted so that the final residue is confined to a small area of the beaker.

The residue is rubbed off the bottom of the beaker, using a small piece of filter paper fastened over the rounded end of a glass rod so that most of the residue, which is of a pale yellow colour, is concentrated on an area about 2 mm. in diameter in the centre of the paper. The paper is then removed from the glass rod, flattened out, and a drop of