and the prothrombin index of the patient's blood is expressed as a percentage of this normal, as follows:

$$\text{Prothrombin index} = \frac{\text{Normal prothrombin time}}{\text{Patient's prothrombin time}} \times 100$$

With practice a high degree of accuracy can be obtained in assessing the coagulation time. Thus repeated estimations done on the same individual under standard conditions show a deviation of only one or two seconds.

It has been shown by Quick (1938) and by Fullerton (1940) that a marked lengthening of the coagulation time occurs only when the level of the prothrombin in the blood falls to 20% of normal or less. By diluting the blood of both the patient and the control to 20% with normal saline, minor differences in the coagulation time become more apparent. If it is desired to adapt this modification to the present technique, a quantity of normal saline equal to forty divisions of the white-cell pipette are added to the ten divisions of oxalated blood present in the watch-glass. After mixing thoroughly, a quantity of this mixture equal to ten divisions is transferred to a second clean watch-glass, in which the test is completed. It should be noted that the effect of such dilution makes it somewhat more difficult to see the onset of fibrin formation.

Comparison with Kato's Test

Our attention has recently been drawn to a paper by Kato (1940) in which he describes a test for estimating prothrombin using capillary whole blood. He states that many hundreds of such tests have yielded results comparable to those obtained by Quick's method on venous blood. The differences between the method described here and Kato's technique are as follows:

1. The use of a white-blood-cell-counting pipette obviates the need for obtaining the special microhaemopipette designed by Kato (1938).
2. The use of snake venom as a source of thrombokinase as described by Fullerton (1940) eliminates the necessity for preparing a brain extract as used by Kato.
3. The carrying out of the test on a normal control person at the same time and under the same environmental conditions is felt by us to be a fundamental part of the method. In Kato's method no control on normal blood is done, reliance being placed on standardizing the solution of thromboplastin so as to produce a clotting time of approximately twenty seconds. The control eliminates the effect of minor variations in the solutions used and the changes in the clotting time which result from variations in temperature and humidity. In practice we use our own blood as a control, and have found that the clotting time of undiluted normal blood may be as short as twenty to twenty-five seconds in the heated nursery of the maternity pavilion and as long as thirty-five to forty-five seconds in the cooler general hospital wards in winter-time.

One of us (J. I.) was in receipt of the McCosh Bursary and Crichton Scholarship in Medicine during the period of this investigation.

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Dr. Albert B. Sabin and Dr. Joel Warren (*Science*, 1940, 92, 536) point out that the toxicity of most available gold compounds is perhaps the greatest barrier to their more widespread use in the treatment of rheumatoid arthritis. In their search for a compound which does not possess this danger of toxicity they have found in preliminary experiments on mice that calcium aurothiomalate fulfils this desideratum. Whether this compound is equally harmless to human beings has yet to be determined by clinical trials.

MULE-SPINNER'S CANCER

BY

E. M. BROCKBANK, M.D., F.R.C.P.

As a medical referee for industrial diseases I have seen over 150 mule-spinners with epithelioma of the skin in doubtful, early curable, and hopelessly neglected states. Visits to cotton mills, conversations with several hundred men and women spinners over 50 years of age whom I have examined for pensions, and many talks with employers and representatives of the workers' Associations have given me some practical knowledge of cotton-spinning. Frequent visits to the Manchester Cancer Research Laboratories kept me informed on the experimental side of the problem. With such exceptional opportunities for doing so, I have formed certain conclusions on the causes of the disease and on measures which, if

A mule-spinner at work.

systematically adopted by masters and men for its prevention or early recognition and treatment, would greatly diminish its dangers if not avert its onset altogether.

Incidence of the Disease.—Southam and Wilson in 1922 drew attention to the frequent occurrence of the disease, and the numbers of cases notified since then to the Medical Inspector of Factories have been recorded in his Annual Reports from 1923. During the seventeen years ending 1939 its average annual incidence was 64 cases with 21 deaths. In 1939 there were 52 cases with 20 deaths, and as medical referee I saw 16 cases last year. The continuing incidence of a preventable disease is very disappointing.

Seat of Election of Scrotal Cancer

Mule-spinners work in bare feet on a wooden floor saturated with oil. They are constantly walking to and fro along the front of the machine, leaning well over but not actually against its front bar, whilst the carriage is moving outwards towards them, in order to join up very rapidly, or piece, broken ends of the yarn. This is almost invariably done with the thumb and finger of the left hand. In most men the bar is on a level with the pubis and groins, and above the scrotum. In the hot room the spinners, in vest

and overalls only, perspire freely, and this must tend to wash off the natural grease of the skin and allow the oil to get on it.

Over 80% of cases occur on the left side. This may be due to one or more of the following causes:

1. The left side hangs anatomically lower than the right. This will be more pronounced when the spinner, in bending forward to piece with his left hand, stands on the left leg, sometimes on his toes, and balances with the right shoulder well above the left. The pelvis is correspondingly tilted.

2. Perspiration from the lower part of the abdomen may therefore tend to run down the left side of the scrotum more than the right.

3. The left side and, less often, the middle of the scrotum will come in contact with the left thigh and the oily trousers some hundreds of times a day.

Piecing with the right hand may, in the same way, be the cause of the trouble on the right side.

Mineral Oil as a Cause of Skin Cancer

Mineral oil was known in the middle of the last century to be a cause of epithelioma of the skin in the paraffin and shale-oil industry. The first case in a mule-spinner was found in the Manchester Hospital records in 1887, thirty-five years after the introduction of shale oil for lubrication of cotton machinery (Henry, 1926). It was proved in 1922 to cause the disease when painted on the skin of mice (Leitch, 1922), and many observations since then have shown that oils from certain fields of origin are more carcinogenic than those from other sources.

Oil on the Clothes.—The spinner oils the spindles twice a day, and these, revolving many thousands of times a minute, throw off some oil on to the clothes in the earlier moments after starting. A little will get on the hands when the oil-can is used and refilled twice a day, and will probably be wiped off on the clothes about the hips to clean the fingers for piecing. In some mills a special attachment to the machine reduces the need for oiling the spindles to once a week. A heavier oil is used twice daily on the carriage and wheels of the mule, and there is a general weekly overhaul and cleaning. More oil will then get on the hands, arms, and clothes, and the face is quite likely to have a little smeared on it unintentionally during all this work. Dermatitis of the face produced by dust or liquids not uncommonly arises in this way.

Oil in the Atmosphere.—Dr. E. L. Middleton (1926) found a definite amount of oil in a fine state of division in the atmosphere of the mule-room, and the hotter the room and the nearer to the machine the more there is. Some of this oil will get on the face and bare arms of the mule-spinners. There was less oil in the rooms where the earlier processes for mule-spinning are carried out, and very little or none in the air of the rooms of a ring-spinning mill. The preliminary processes of all spinning are carried out in hot rooms; but the men wear more clothes about the groins and are not in such constant movement about their work, with tilting of the body and pull on the trousers, as mule-spinners are. They come into daily contact with mineral oils, but do not often suffer from epithelioma of the skin generally or of the scrotum in particular.

Heat and Perspiration.—These alone will not cause the disease. Coal-miners are remarkably free from it, and yet in some hot pits they work in shorts and clogs and perspire freely. Coal dust, unlike its combustion-product soot, does not contain tar, and is not itself a cancer-producing irritant to the skin. In the shale oil and paraffin industry work is carried out in the open—in some processes in very cold temperatures, even as low as zero—and perspiration is not excessive. Both these substances, however, are much more carcinogenic than the mineral oils

now in use in the cotton trade, and probably need no contributory cause in producing the disease.

Friction of Clothes.—Dr. Robertson (1927), medical officer of health for Darwen, in 1926 endeavoured by very careful practical investigation to prove that scrotal cancer was caused by friction on the scrotum by the upward pull of the overalls or braces during the piecing movements of the body. The disease is unknown in the woollen industry, in which spinners piece with both hands at once without any tilt of the body. His observations were also directed to prove that very little, if any, oil was thrown from the rotating spindles, but he agreed that some got on the clothes during the general oiling of the machines. Dyes or stiffening materials that may be in overalls are in his opinion a source of irritation, but these will be removed in their early washings.

Ichthyosis.—After an examination of 400 spinners, L. Savatard formed the opinion that ichthyosis is an important aetiological factor in the causation of mule-spinner's cancer.

Want of Bodily Cleanliness.—Some managers of mills who have given close attention to the subject are of the opinion that neglect of soap-and-water cleanliness is a definite factor in causation.

Skin Protectives.—The sebaceous-gland secretion is protective against the action of a mineral oil, and, in control mice, if washed off with soap and water before painting with oil epithelioma will develop more readily than in the unwashed skin. A mixture of lanolin and olive oil applied to the unwashed skin before the application of mineral oil prevents the development of dermatitis and epithelioma. This observation led Dr. Alexander Scott in 1930 to try such an ointment to protect the shale and paraffin workers in Scotland from dermatitis and epithelioma of the skin, to which they are very liable. He informs me that the protection it afforded has proved so satisfactory that a proprietary preparation for the same object is still regularly used by the men. A similar preparation is applied daily in other industries as a preventive of dermatitis due to dust or liquids. These proprietary substances are preferred because they are easier to wash off than a grease like lanolin. Protective application for the thousands of spinners in cotton mills is not practicable, but it could be adopted by those over 50 years of age or those with specially dry skins, of whom there are comparatively few at work.

Conclusions as to Causation

1. The primary cause of epithelioma of the skin in mule-spinners is undoubtedly mineral oil.
2. A predisposing cause is probably an abnormally dry skin, especially in older men.
3. Excessive perspiration, by washing off the natural protective grease, allows oil close access to the skin. This is especially likely to happen on the scrotum.
4. Irritation may arise from friction of trousers or overalls on the scrotum during the movements of the body for piecing broken ends some thousand times a day.
5. Want of reasonable use of soap and water may be an occasional cause.

Protective Measures

Regular periodical examination of spinners should be carried out by a medical man for the earliest appearance of an epithelioma, which may be merely a local ichthyotic thickening of the skin or like a simple papilloma or wart. A microscopical examination is often necessary to settle its exact nature. Any one of these early changes can be excised or be treated with radium or x rays with such

slight bodily disturbance that there is a good prospect of ability to resume work in ten to fourteen days and of freedom from any recurrence. Immediate removal from the scrotum is especially advisable to prevent hopeless extension to the groins, which may take place very rapidly by the lymphatics (Morley, 1911).

The value of such regular examination every six months for ten years has been established by Dr. Grey at a group of Lancashire mills. He found several suspicious changes which proved to be early stages of epithelioma. Dr. Scott also carries out a similar examination in the shale-oil industry.

Selection of Oils.—The regular use of only the safer oils or blends recommended by the Manchester Committee's scientific staff is advisable; but even if this be done it will be some years before all danger from the disease ceases in spinners who have worked with carcinogenic oils.

Protection of Skin.—The wearing of an additional trouser garment, such as shorts, diminishes contact with oil on the overalls and lessens friction; reasonable attention should also be paid to washing, especially in the scrotal region.

A protective ointment should be used by men over 50 and by those who have an unusually dry skin.

An advisory handbill on epithelioma, with illustrations of its appearance when in a stage suitable for early removal, on lines similar to the one prepared by the Home Office on anthrax (1930, Form 1893), would be helpful.

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THE DERRIS ROOT TREATMENT OF SCABIES

BY

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The varied factors responsible for the prevalence and transmission of scabies are to a large extent unavoidable, but the question of its prevention and control must be faced in the light of present-day circumstances as one of the most difficult public health problems. New factors have arisen which probably account for the increase in the incidence of scabies seen in civilian practice. For example, many citizens are now huddled together throughout the night in over-populated shelters where sanitary arrangements are inadequate, and some have been unable to remove their clothes for several weeks. Facilities for bathing have in addition become difficult. It is obvious that with the increasing strain thrown on the medical profession to-day scabies assumes an unpleasant but realistic problem, and one which is becoming unduly prevalent in the Army.

The generally accepted method of treatment in civilian practice is the three-day use of sulphur ointment. Other specific drugs which have been used to destroy the parasite are balsam of Peru, beta-naphthol, and benzyl benzoate. Storax ointment, pernil, kathiolan, mitigal, and the sodium-thiosulphate-hydrochloric-acid method all have their advocates. It is often left to the patient to arrange the disinfection of his bedding and clothing: little wonder is it, then, that recurrences are so frequent. The disadvantages of sulphur ointment are: (1) its greasy

and messy qualities, whereby pyjamas become quickly dirty and uncomfortable to wear; (2) the disagreeable odour of the ointment; (3) the confinement of patients to their own rooms during the course of treatment; (4) the likelihood of sulphur dermatitis arising from prolonged application, and therefore its danger in inexperienced hands.

All the mentioned methods of treatment essentially require baths and disinfection of bedding and clothing. The treatment detailed below will show that neither bathing nor disinfection of clothing is necessary for obtaining a cure.

Thomas and Miller (1940) stated that rotenone in a 1 or 2% lotion produced prompt cure in twenty-four unselected cases. I had been in medical charge of a main dressing station where many cases of scabies were seen, and their results induced me to try the treatment. However, instead of using the rotenone solution, which was relatively expensive and difficult to procure, I made a solution of derris root powder, from which rotenone is extracted. The powder was of tested strength and was guaranteed to comply with the requirements of the Ministry of Agriculture as a dressing against the warble-fly.

Derris or tuba root consists of the dried rhizome and roots of the *Derris elliptica* Benth and *Derris malaccensis* Prain, climbing plants that are cultivated in the Federated Malay States, Sarawak, Singapore, Sumatra, and Johore. The powder has a slight odour and a bitter taste, and on inhalation produces a feeling of numbness in the tongue and throat. The root contains up to 10% of the crystalline substance rotenone ($C_{23}H_{22}O_6$), which is known as tuba toxin. Three other crystalline substances—deguelin, tephrosin, and toxicarol—have been isolated. The active constituents are soluble in acetone, benzene, chloroform, ether, and carbon tetrachloride. They are insoluble in water, weak acids, and alkalis. Derris is used extensively in horticulture and agriculture as an insecticide, especially against the warble-fly.

The results of the investigations with derris root may be grouped into three classes.

(A) Experimental Investigation

Solution Used.—A warm solution of 1 gallon of water and 1 oz. of soft soap was prepared, and to this was added 4 oz. of the derris root powder. The mixture was stirred thoroughly, and with the resulting lotion treatment was instituted on 21 unselected cases of scabies. The diagnosis was made in the majority of cases by the combined features of the itch and burrows. In addition these cases had been previously diagnosed as scabies by one or two other medical officers. In view of this and of my own diagnosis based on clinical grounds the spotting of the parasite in every case was considered unnecessary. The parasite cannot always be seen owing to the existing pyoderma; and, again, particularly in patients of cleanly habits, no burrows are in evidence and the search for the parasite proves fruitless. The diagnosis in these cases has to be made by the history of itching at night and the signs of scratching in the areas of characteristic distribution.

Method of Application.—Each patient was given a preliminary bath. He was then instructed to rub the lotion with cotton-wool all over the body from the neck down to the toes, paying particular attention to the spots on the hands, wrists, armpits, and groins. A nursing orderly was detailed to assist in the application on the back and buttocks. The lotion was allowed to dry on the body, and the patient, wearing only pyjamas, was then isolated in a ward. His clothing and bedding were disinfected. One application was given during the morning and one at night, and this procedure was continued until all irritation had ceased. On an average ten applications were found to be sufficient (Table I).