produced at so rapid a rate that the polygonal cells are unable to deal with it *in toto*, the excess is absorbed directly into the blood stream from the Kupffer cells, and forms the immature bilirubin which gives the indirect reaction. An indirect reaction should, then, be obtained in those cases where the pathological factor is increased blood destruction, and it is this variety which occurs in pernicious anaemia and malaria. Such a reaction can be accepted as evidence of intravascular haemolysis.

In haemoglobinuric fever, in the initial stages of the disease, the indirect reaction is strongly positive and the number of units of bilirubin present shows a huge increase on the normal amount of 0.2 to 0.5 unit found in normal controls (unpublished results of one of us, G. R. R.). We have thus indirect evidence that haemoglobinuria in haemoglobinuric fever is accompanied by haemoglobinaemia. There can be no doubt that the haemoglobinaemia must precede the haemoglobinuria. Assuming, then, that haemoglobinaemia exists, it can be postulated that two mechanisms at least come into play in the endeavour to rid the body of the haemoglobin dissolved in the plasma. At first there is an increase in the activity of the reticulo-endothelial system, so that as much as possible of the haemoglobin may be disposed of by the normal methods of converting it into bilirubin. This we know does happen. If, however, the amount of haemoglobin is in excess of the maximum with which the reticulo-endothelial system can deal, then excretion by the kidneys occurs, with consequent haemoglobinuria. We can thus assume that there exists a threshold value for haemoglobin; whether that is constant or whether it varies from individual to individual is not as yet clear. It cannot be assumed at present that the reticulo-endothelial system, on the activity of which the threshold value must in part depend, functions equally in every individual. It is, however, known that if the haemolysis be slow and gradual, as in pernicious anaemia, or even sudden but relatively slight, as in malaria, haemoglobin does not appear in the urine.

Turning now to the question of quinine haemolysis *in vivo*, it is conceivable that if quinine can produce haemolysis sufficient to cause the appearance of haemoglobin in the urine, cases might occur in which the degree of haemolysis is so slight that the free haemoglobin can be disposed of entirely by the reticulo-endothelial system without the appearance of haemoglobinuria. References to this possibility are relatively few. Koch (1898) stated that after the administration of quinine an attack of icterus may occur. Blacklock (1923) believes that haemolysis with slight jaundice can occur without haemoglobinuria and that this condition is frequently due to the same cause as blackwater fever.

The following case is reported as an example of haemolytic jaundice after quinine treatment without the development of haemoglobinuria.

A male European, aged 11, was admitted to Salisbury Hospital under the care of one of us (G. H. P.) as a "pre-blackwater case" on March 4th, 1926. A history was obtained of repeated attacks of malaria throughout the previous six months. The patient was pale, sallow, and thin. He exhibited characteristic malarial cachexia with lemon-yellow conjunctivae. There was, however, no clinical jaundice in the true sense of the term. A blood examination on the day of admission gave the following result: Red blood corpuscles 1,300,000 per c.mm., white blood corpuscles 5,700 per c.mm., haemoglobin 39 per cent. The red cells did not exhibit any abnormality except occasional polychromasia. A differential count showed: Polymorphonuclears 56 per cent., lymphocytes 21 per cent., mononuclears 20 per cent., eosinophils 2 per cent., transitionals 1 per cent. No malarial parasites were seen.

Examination for parasites was also negative on March 6th, 7th, and 9th. The spleen was enlarged to two fingerbreadths below the costal margin. The treatment adopted was on general lines, including the exhibition of liquor arsenicalis and sodium bicarbonate with ample quantities of bland fluids. On March 9th, acting on the assumption that antimalarial treatment was indicated, quinine therapy was instituted, starting with extremely small doses in view of the possible onset of haemoglobinuria.

Thus on March 9th 1/32 grain of quinine bishydrochloride was given; on March 12th the dose was increased to 1/32 grain thrice daily, on March 14th to 1/16 grain thrice daily, on March 15th to 1/8 grain thrice daily, on March 18th to 1/4 grain thrice daily, on March 19th to 1/2 grain thrice daily.

On March 20th the patient complained of severe headache, nausea, and splenic pain. The spleen was now four fingerbreadths below the costal margin. There was slight vomiting, and the temperature, which had been rather febrile for about a week,

rose to 100.2°, and on the two succeeding days reached maxima of 100.8° and 100.6°. On the morning of March 21st the patient was obviously jaundiced, and in the course of a few hours became intensely so. Blood counts done on this day gave the following results: Red blood cells 1,250,000 per c.mm., white blood cells 6,000, haemoglobin 35 per cent. Fouchet's test for bile pigment in the serum was positive. The van den Bergh test gave a positive indirect reaction, and the number of units of bilirubin present, as estimated by the Tannhäuser and Andersen technique, was 2.5. Blood smears were examined on March 21st, 22nd, 23rd, and 24th, but the red cells showed no abnormality and malarial parasites were absent.

Quinine was immediately stopped and the icterus completely disappeared in the course of two days. The temperature came down to normal, and the pulse, which in the pre-icteric period had varied between 80 and 90, and which during the icterus varied between 120 and 140, returned to its former level. The stools were normally coloured throughout the icterus. An estimation of bilirubin made on March 24th showed 0.75 unit to be present in the serum, which is slightly in excess of normal.

The patient was given injections of sodium methylarsenate and was kept under observation for a period of fourteen days, during which no untoward symptoms developed. The urine was examined daily, in twenty-four hour specimens, for blood pigment, during the icteric period, by the benzidine test and spectroscopically; the results were invariably negative. Urobilin was never present in a greater dilution than 1 in 10 (Marcussen and Hansen technique).

This case, in our opinion, is an example of an intravascular haemolysis, evidenced by jaundice, but with no accompanying haemoglobinuria. There can be no doubt that the jaundice was haemolytic in type. As regards the relationship of quinine to the intravascular haemolysis, it is true that the icterus did not make its appearance clinically until the twelfth day after the institution of quinine treatment, but it must be remembered that the sallowness of the patient and the lemon-yellow conjunctivae, so characteristic of chronic malaria, prevented the appreciation of slight additional degrees of icterus.

Again, the dosage of quinine was exceedingly small; only 1½ grains were being given daily, and only 5½ grains had been administered altogether when the jaundice became clinically apparent.

The disappearance of the icterus on the stoppage of quinine treatment affords additional support to our belief that the quinine acted as a haemolytic agent.

The interest of the case, however, lies mainly in the fact that, while intravascular haemolysis sufficient to produce marked clinical jaundice had taken place, haemoglobinuria did not develop.

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DETOXICATION IN THE TREATMENT OF BURNS.

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DETOXICATION, as part of the treatment of burns and scalds, has not received the attention it deserves, though burns owe most of their deadliness to toxæmia. In the course of prolonged inquiries in many directions I have come across only one man who had used a dressing with detoxicating properties; this was an application of ichthyol and glycerin, covered over with boric fomentations. None of the younger men had heard of such treatment, which is the more remarkable in view of the great advances made in the treatment of infected wounds during the latter part of the war.

In most hospitals burns are treated in the surgical wards, but since there appears to be nothing to do after treating the initial shock and ordering an admittedly unsatisfactory dressing, a "burn" becomes a purely medical case. The patient has a grave systemic disturbance which is not to be benefited by any surgical measures, unless possibly blood transfusion. There is, however, a method of local treatment lying ready to our hands, and only waiting to be applied. It is a great deal easier to prevent poisons from entering the system than it is to get them out before they can do harm, and it is more rational.

Toxaemia, it should be realized, comes on very quickly—long before septic processes have had time to become established. It is caused solely at first by the products of decomposition of the proteins of the tissues which the heat or chemical has killed. According to Dale, in a recently published lecture on the function of the capillaries in the control of the circulation (*University of London Press*, p. 18), "a simple extract, made by boiling the fresh tissue of almost any organ of the body, will be found to contain some substance or substances having this histamine-like action"—histamine being one of the definitely identified and intensely poisonous substances that are formed in protein decomposition. These substances cause relaxation of capillary tonus and general collapse of the patient. Further proof, if it were needed, that local exudations do find their way quickly into the general circulation is afforded by observations on patients who happen to be anaphylactic to such substances. In them the characteristic phenomena will appear within an hour or two, to be relieved again as quickly by applying the treatment to be described.

The first indication, then, is to induce abundant serous exudation, and the second is to get it away from the damaged surface. Wax (containing antiseptics) no doubt forms a valuable first-aid covering, but a patient upon whom I tried a prolonged course of this dressing developed tetanus and died. Such an application is obviously useless as a detoxicating agent. As for oil, how can a dressing impregnated with it, or any greasy ointment, soak up poisonous exudate, even if it be on the surface and awaiting removal? Baths have been advocated, but I have heard of none other than of plain water or normal saline. Picric acid has antiseptic properties, but how can it fulfil the above two indications? It is applied in hypotonic watery solution, or even with the addition of something more hypotonic still—namely, alcohol. Its advocates say: "Keep the skin dry and change the dressings as infrequently as possible." How is that to prevent the absorption of the poisons from the layers that are just too deep to be affected by the drying process? Decomposition progresses there unhindered, and there is nothing to divert the foul products from travelling inwards. Such desiccation can at best be only superficial. Another aqueous dressing that is used is solution of aluminium acetate (1 per cent.), but it is found to be of little value in limiting sepsis, and obviously it will fail in the osmosis test.

The only substances I have used to provoke osmosis towards the surface are sodium chloride and glycerin. Professor McLeod of Leeds has tested them for me in various concentrations against fresh red cells. He found that with sodium chloride it was possible to go up to 4 or 5 per cent. without readily haemolysing, but he found glycerin haemolytic in all strengths from 2 per cent. upwards. Nevertheless, the presence of sodium chloride of 3 to 5 per cent. along with it afforded appreciable protection to the cells. Other substances more suitable may be found, but there is no gainsaying the physical effectiveness of the two mentioned. Professor McLeod tried magnesium sulphate and sodium sulphate also, but found the results variable, owing to difference in composition. Both salts are capable of holding two different quantities of water of crystallization.

I have used this method in four or five bad cases.

CASE I.

A girl, aged 18, received burns over about two-thirds of the surface of both legs and thighs and her buttocks. Within a few hours she began to vomit—the next grave symptom after the initial shock. The special dressing was applied and the vomiting ceased within three or four hours, and she was able to take

plenty of food. She improved steadily week by week till some six or eight weeks later, when I consented to a less troublesome form of dressing being tried—namely, boric fomentations. Care was to be taken to keep them hypertonic, by adding no more water to the lint than was needed to wet it. (A semi-saturated solution of boric acid is, I believe, isotonic.) The result was tragic. Vomiting began again within a few hours, and the patient died the next day.

CASE II.

This patient was a child, who was burnt about the chest, shoulders, and neck. He was in hospital three months or more, and several times the lines originally laid down for treatment were departed from. Ointment, though less painful in use, was always accompanied by a change for the worse in the general condition, and much the same happened with boric fomentations.

CASE III.

This patient was a healthy young farmer who weighed 19 st. His injuries were caused by the accidental ignition of petrol, and, as in the first case, they affected chiefly the backs of his legs, thighs, and buttocks, though his face and hands were touched also. I saw him about an hour and a half after the accident. There was then little evidence of shock, though he was in a good deal of pain. I gave him 1/4 grain of morphine hypodermically and wrapped him up in blankets over what clothes he still had on—his legs were burnt quite bare—and sent him to a nursing home. The remaining portions of his clothing were removed without an anaesthetic, and the special dressings applied to all burnt parts. He vomited four times during the first night, and twice more in the next twenty-four hours, and that was all. The skin sloughed over larger areas for its whole thickness, and behind the knees and on the left calf the burns were deeper still, one tendon being exposed. Although his evening temperature was about 100° F. for the first fortnight or so, his appetite was good throughout. He ate well of fish and such-like light diet, and drank large quantities, for he was often genuinely thirsty. Towards the end of his seventeen weeks in the home he was touched up in a few places with blue-stone and had a few applications of direct sunlight. Apart from these he had no treatment other than hypertonic saline containing also eusol and glycerin. He made a perfect recovery, without undue scarring.

CASE IV.

A child, aged about 12, was scalded over the lower abdomen and thighs through the tearing of a rubber hot-water bottle. She did not do well, dying at the end of three weeks with bronchopneumonia and a scarlatiniform rash. The solution used for the dressings was eusol of one-quarter of standard strength, containing also glycerin to the amount of 11 per cent. by volume and sodium chloride 2½ per cent. The burnt surfaces never looked healthy. I think now that she had a great deal too much glycerin and too little sodium chloride.

CASE V.

The only other case extensive enough to record was that of a girl, aged 22, who spilt boiling water down the side of her leg. I could not observe her progress closely, but she had neither glycerin nor eusol, but boric lint moistened with salt solution of about 4 per cent. She made good and rapid progress all the time.

I prefer eusol as a germicide for two reasons. The first is the obvious one that it really is germicidal, provided only that it is not destroyed by overheating—even by pouring hot water into it. The second is that any harmful effect it has on the tissues is only intermittent in character, owing to its instability. Its characteristic odour is gone in two hours or less in spite of a covering of jaconet, after which the dressing remains as an aseptic one only. I think it ought to be used for the first few days in every case, though the experience of my last case seems to suggest that an antiseptic stronger than boric acid is possibly not needed at all with this method.

Hypertonic dressings need to be changed frequently, for in remaining they rapidly lose this special property, besides endangering the cleanness of the bed. A macintosh is essential. The dressings should be thoroughly wet when applied, and may be expected to be absolutely dripping when taken off, besides leaving pools on the macintosh sheet. My third patient used to complain pretty regularly of increasing discomfort whenever a dressing had remained on three hours. He would ask to be re-dressed, in spite of the pain attached to the process.

Convenient solutions can be prepared thus:

I.			
Standard eusol solution	...	...	1 part (20%)
10 per cent. saline solution	...	...	2 parts (NaCl 4%)
Water	...	...	2 parts
II.			
Standard eusol solution	...	...	1 part (25%)
10 per cent. saline solution	...	...	1½ parts (NaCl 3.75%)
Water	...	...	to 4 parts