

Original Articles.

THE USE OF IZAL IN THE TREATMENT OF TROPICAL DYSENTERY.

BY J. C. S. VAUGHAN, M.B., C.M. (EDIN.),

MAJOR, I.M.S.

THE remarkable properties possessed by izal by virtue of which we have in this substance a low toxic value combined with marked germicidal powers, and the results of recent research with regard to its pharmacology and its value as an antiseptic *in vivo* when administered by mouth have induced me to make a trial of this substance in the treatment of tropical dysentery. I am aware that it has been already used in the treatment of this disease, but I do not know of any published results of its use in India in this connection. Before introducing my subject proper, I would venture shortly to sum up what we know of izal itself. Izal oil is a proprietary article discovered by Mr. J. H. Worrall among the by-products occurring during the conversion of coal into coke. Chemically it consists of hydrocarbons oxidized, and having a higher proportion of hydrogen to carbon than the phenol (C₆H₆O) group and a lower proportion than the methyl alcohol (CH₄O) group. It has a high boiling point and is insoluble in water. Three preparations are met with in Europe: (1) the pure (?) izal oil; (2) "medical izal," which is an emulsion containing 40% of izal oil, and (3) disinfectant izal which, like the medical izal, is an emulsion containing 40% of izal oil, but the latter is not specially refined as it is for the preparation of the "medical izal." Nevertheless this want of refining does not make the disinfectant emulsion unfit for medicinal uses as the sequel will shew.

The germicidal properties of izal were worked out by Dr. Klein in his "Report on the Disinfecting properties of Izal", and a solution of 1 in 200 is quite strong enough for the most antiseptic purposes, while a strength of 1 in 500 has been found by Major F. J. Drury, I.M.S., to be enough to destroy the plague bacillus. As compared with carbolic acid, its germicidal power is much higher, being four times as great while its toxicity is about $\frac{1}{2}$ or less of that of carbolic acid.

Its effects on the living organism have been worked out by Tuncliffe. To sum up his results—(1) To invertebrates izal is rapidly fatal in very great dilution [1cc. of 1% solution to 100 cc. of tap water]; (2) On the frog's heart or on muscle-nerve preparations from the same animal it has a marked action and when given in relatively large doses it destroys the functions of the medulla and spinal cord; (3) On mammals its action was tested in guinea-pigs,

rabbits, cats and dogs. Rabbits were found least, and cats most susceptible to its action. Doses of from 0.2c.c. to 0.8c.c. per kilo of body weight produced absolutely no symptoms, and it can be injected under the skin in doses of 0.1c.c. and into the blood in doses of 0.02 cc. in the form of a $\frac{1}{2}$ per cent. or 1 per cent. solution without producing any toxic effects. Large doses taken into the stomach pass down the alimentary tract, and evidence of the presence of the drug practically as izal unchanged can be found in the fæces, while at the same time appetite is unaffected, and there is no evidence of any irritant effect on the alimentary tract. This substance further appears to be by the respiratory organs, for the breath smells excreted of it, while on *post-mortem* examination the lungs smell of it, but not the kidneys or liver or other vascular organs. Hence izal appears to be excreted as izal unchanged by the respiratory organs. On the circulatory system it appears to have no action beyond inducing, when given in large doses, a slight temporary fall in blood pressure. If the dosage be increased beyond 0.25 c.c. per kilo of body weight and administered without break for several days, a definite train of symptoms occurs, *viz.*, restlessness soon followed by inco-ordination of movement. Next by twitching of the limbs especially in any attempt to perform a co-ordinated act. Next follows a spastic gait. If no larger dose be given, these symptoms pass off. If, however, the dosage be increased to 0.5 or 1.0cc. per kilo of body weight, a stage of paralysis supervenes, varying in degree with the dosage adopted. The sensory part of the reflex are remaining practically unaffected, the temperature falls and death occurs from paralysis of the respiration, the heart continuing to beat for some considerable time; after the respiratory movements have ceased the paralytic stage is sometimes absent, and animals can recover even after the paralytic stage has supervened. The action of the drug is somewhat cumulative. Dr. Tuncliffe goes on to say, that judging from the above, it is obvious that the doses required to produce toxic symptoms are much larger than and far in excess of those required to produce the ordinary therapeutic effects of izal, and that when administered to man izal may be given "in doses of from m.xv to ʒi or more of the emulsion, made into an ordinary ounce or half ounce mixture or diluted with milk or water, three or four times a day. If prolonged treatment is desired as for instance in cases of obstinate fœtid diarrhœa or auto-intoxication, a day's pause should be allowed at first after from ʒiv to ʒvi have been administered, to avoid the possible accumulation of izal in the system."

So much then for the general action of izal on the organism. Next I would invite attention to its antiseptic properties as they are exerted *in vivo* when administered by the mouth,

and more especially on the contents of the alimentary tract.

In this connection among the most recently published work are the experiments of Dr. M. H. Gordon [*Lancet*, March 8th, 1902]. To quote his own words Dr. Gordon proceeded to enquire whether "the number of micro-organisms in the fæces is diminished when izal is taken by the mouth and, if so, to what extent," and this enquiry was undertaken in connection with a comparative investigation into the relative merits of various antiseptics when administered *in vitro*. In his experiments the pure izal oil was administered in capsules, each containing m. 2 of the oil. These were given with food, "one capsule before and one or two after the meal according to its size" and the largest amount given in 24 hours, was m. 24 of the oil, no unpleasant symptoms resulting. In the details of these experiments I must refer the reader to the paper already quoted; for my own purposes I shall summarize Dr. Gordon's results as follows:—

izal oil in six days, which means a daily average dosage of m. 13 per diem of pure oil or say an equivalent of 33·5, or say 34 minims of either form of izal emulsion per diem, or, roughly speaking, doses of some 17 m. of izal emulsion given twice, or say 11 or 12 minims three times a day, which is just about the minimum dosage noted by Tuncliffe as based in his research already quoted.

Thus far I have been directing attention to the properties and qualities of izal, and I must apologize for the amount of detail given, but I wish to emphasize certain points, *viz.* (1) the extremely large dosage required to produce any physiological effects; (2) the remarkable demonstration of germicidal power when given *in vivo*.

Next as to dysentery. Broadly speaking and for practical purposes, we may regard it as a specific inflammation of the gut, always associated with the presence of a specific responsible virus which is a micro-organism and, added this, we have the circumstance that the

Summary of Gordon's experiment.

NO. OF EXPERIMENT.	EXPERIMENT No. 1.		EXPERIMENT No. 2.		EXPERIMENT No. 3.	
	Izal oil, 20 m.	Izal oil, 42 m.	Izal oil, 50 m.	Izal oil, 78 m.	32 hours without Izal.	Izal oil, 36 minims.
Conditions after.						
Time since experiment began ...	24 hours	48 hours	48 hours	Sixth day	Eighth day	Fourth day
Motion since experiment began ...	Third	Fifth	Second	Sixth	Ninth	Fourth
Reduction of organisms at 37° C. on agar ...	68 %	86 %	Nil; increase of 24 %	90 %	Increase 300 %	60 %
Reduction of organisms at 22° C. on agar ...	73 %	78 %	10 %	91 %	Increase, 200 %	40 %

Experiments 1 and 2 were made on the same subject, a pause of ten days being allowed between the end of experiment, 1 and the beginning of experiment 2, and experiment 3 was tried on another subject. Both subjects were normal adult males.

In experiment 2 no reduction but an actual increase of blood heat organisms was noted, but this was only the second motion after the experiment began; later on in the same case after the aggregate administration of izal had by the sixth day reached a total of 78 minims, the reduction in micro-organisms was very marked. In this same experiment, further, by the eighth day and the ninth motion there was, 32 hours after stoppage of izal, an increase of no less than 300% of blood-heat organisms and 200% of others, on the amount to which they had been reduced to by the izal taken. These figures speak for themselves and shew clearly how very great is the resulting reduction of micro-organisms in the intestine consequent on the administration of izal by the mouth, and in this connection let me point out that a reduction of 90% of blood-heat organisms was effected by 78 minims of

ulcers and sloughs caused by the primary virus of dysentery are invaded by other microbes present in the intestine promoting putrefaction inside the intestine and aggravating the patient's general condition. Johnson, writing in 1818, says truly—Nature, to say the truth, is but a sorry Physician in dysentery. *In hoc enim corporis affectu aliquod certe in medicina opus est, haud multum in naturæ beneficio*, and that the "opus in medicina" has been recognized is abundantly shewn in the history of the treatment of this condition ever since Johnson's time. Quite recently izal has been used in this connection. Its properties, as above noted, render it peculiarly suitable for use as an intestinal antiseptic, but its scope and value as such can only be tested clinically, and I trust the record given in this communication may prove useful.

In the table appended I have summarized the results of treatment of 242 cases, all treated in the Police Hospital in Calcutta. Besides these there were three others admitted to hospital which died, making in all 245 hospital cases with three deaths. These three last were all of the severest possible type, and one died within 24

hours of admission, and their detail would scarcely alter the figures in the table. Besides these 245, my experience of izal in dysentery covers another 200 cases and more, making in all about 445 cases, but I regret the figures for the 200 odd last referred to are not obtainable as they are mostly cases occurring in practice, but there was not a single death among them. In further explanation of the table I may say that in the matter of arranging the cases, I have adopted a classification necessarily arbitrary, but based purely on a clinical appreciation of the gravity of certain symptoms or groups of symptoms. Thus of the three groups in the table, Type I is what is usually regarded by practitioners as mild, and of this class of cases the main feature is that there is only moderate, or at any rate no great, prostration, and no marked fever, although there may be considerable abdominal pain and tenesmus. The stools in this type are for the most part diarrhœic at first, but soon assume a distinct dysenteric character. Attacks of this kind are sometimes first attacks or instances of mild cases of recurrence of the disease and usually yield to appropriate treatment.

II. The second type is one usually at once recognized as distinctly severe, and of which the main features are a sharp or fairly sharp onset, often ushered in by a sharp rise of temperature. Systemic depression and prostration are well marked and characteristic, and the stools, though the first few may be mainly or entirely diarrhœic, rapidly assume marked dysenteric characters and very often for a variable time consist of nothing but mucus and blood, the latter varying in amount, from being only enough to give the mucus a rosy tint to being present in large clots, while shreds of necrosed mucous membrane are passed in varying quantities. Obviously a large area of bowel is affected, and as much as from 18 to 20 oz. of typically dysenteric discharges *apart from feces* may be passed in the 24 hours. The abdominal symptoms are very distressing and acute, and this type of case not infrequently ends fatally or passes into a chronic condition, and is responsible for a large number of men being either invalided from the services or sent home on sick leave. From the first type of mild case this type is at once distinct, not pathologically, but in its degree of severity.

III. The third type is one which, when it occurs, is at once from the outset unmistakably a most grave and dangerous one. The acute symptoms supervene as a hurricane, and a fatal ending may ensue in from 48 to 72 hours, the bowel *post-mortem* shewing an uninterrupted or scarcely interrupted mass of ulceration and acute inflammation of even the entire large intestine from cæcum to anus. Such cases are usually ushered in by sharp fever, sometimes by a rigor, often followed by a fall in temperature. From the very first blood is passed in large quantities mixed or unmixed with mucus, and

shreds of necrosed mucous membrane occur in the discharges very early, and these last, at first very small, appear later in large pieces.

In one of these cases—and fortunately he was one that recovered—I measured the discharges passed between 3 P.M. and 9 P.M. of the same day, and found that in these six hours he had passed no less than 28 oz. of almost entirely blood and mucus with scarcely any fecal matter, and needless to say, in that period he was thoroughly collapsed. Indeed, it is characteristic that systemic depression and prostration in all of this type of cases are profound. Fortunately even among such cases recoveries are not uncommon, but clearly from the outset, prognosis can only be uncertain, guarded and grave.

It will be at once seen that in presenting these three clinical types there is no attempt at any differentiation into pathological groups or varieties, but only a more or less arbitrary division into groups according to degrees of severity, and to shew the various kinds of cases which have been treated with izal, and the results. The grouping was done after the cases had left hospital, that is, when one was fully able to review their character as a whole and, as far as is possible, the grouping of cases for the table follows faithfully the types outlined in the above remarks.

A further word of explanation is necessary. The period noted for the disappearance finally of blood and mucus from the stools includes the last days when their presence was noted even in the smallest visible quantity, and often enough there was scarcely any to speak of for a day or two or three days, before in some cases they finally disappeared. The maximum period for their disappearance noted under type II is entered as 22 and 42 days respectively. This is absolutely correct, but it occurred in a man who persistently broke hospital rules as to diet, and in whose bedding we repeatedly found parched pulse, salt, lemons and chillies (all of which are often eaten together) and whose feces repeatedly shewed the undigested remains of parched pulse and peas. Naturally he suffered from relapses and of course spoiled the average, and he was by no means the only man who did so. Indeed, this smuggling in of forbidden articles of diet was not infrequently a course of trouble. It is, however, significant that in the detailed records of cases of the second type, which are too long for publication, the next longest case shews 22 days' duration of mucus, and he also was an offender as regards diet. And a comparison of the figures in columns 2, 5 and 8 with those in 4, 7 and 10, especially in the first two types of cases, will shew that the maximum figures can only be referred to a few exceptional cases, and these were undoubtedly mostly like the two above quoted—offenders as regard diet. The period of establishing of healthy stool characters refers to the time from which normal formed stools came to be the rule. In some cases, after

the disappearance of dysenteric characters, stools were semi-solid or thin for a day or two, and then ceased for a day or two altogether, and then healthy stools followed. The whole of such periods are included in column 10.

The usual course taken by cases treated with izal was much as follows: Blood usually disappeared rapidly, and very often never reappeared after 24 hours' treatment, more often the decrease was very rapid within the first 24 or 48 hours, and after that only very small amounts were passed. In a few cases there was scarcely any diminution in the amount of blood passed—even when in fairly large amount, for the first 24 hours, but after that it rapidly decreased, and in some of these instances was reduced on the second or third day to about a tenth part of what it was on the first day. Usually it disappeared before the mucus did. In a few cases where the last days of dysentery shewed but very small amounts of both, it disappeared with the mucus and at the same time. Mucus usually followed the same course. When blood ceased very early, mucus sometimes was passed in very large quantities as clear jelly-like matter, often several ounces in the day and often unmixed with fæces. Fæces, after the typical dysenteric discharges were no longer in evidence, were often thin or semi solid for anything up to three or four days before they were fully formed, and were sometimes fully formed at once on blood and mucus disappearing, or even for a day or two before these latter finally disappeared.

ted, and I used Mellin's Food largely, and I was always satisfied with the result.

Lastly, as to the use of izal. Most officers of the I. M. S. will remember a circular issued in 1901 asking us to make a trial of izal in dysentery and recommending a dose of m. 3 thrice daily or so in adults. This dosage proved to be absolutely useless or nearly so, and this has also been the experience of most officers of the I. M. S., to whom I have spoken on the subject. Arguing from the facts noted in the earlier part of this paper, I pushed izal considerably. I had adopted three standards of dosage in treating the above cases, *viz.*, preparations containing ʒiiss, ʒii and ʒiiss of izal emulsion in the eight-ounce mixture of eight doses, averaging thus, $10\frac{1}{2}$, 15 and $26\frac{1}{4}$ minims of izal emulsion per dose respectively. Of these the last two were the most serviceable. Doses were given about every three hours while awake, thus averaging, say, six doses from 6 A.M. to 9 P.M., and usually a seventh dose about midnight. The mixture may be made up to suit the taste, and usually chloric ether, tinct. cardam. co. and glycerine combined make a good vehicle, diluted suitably with water. Another good combination is with spt. chloroformi, syrup of tolu, glycerine and ether cinnamon, ol. anethi or peppermint. Some patients prefer diluting the mixture with milk.

In seven cases, especially where abdominal pain and tenesmus were very distressing, opium stupes to the abdomen or morphia by mouth

Table classifying results of treatment of Dysentery with Izal.

TYPE OF CASE.	NUMBER OF DAYS TAKEN FROM COMMENCEMENT OF IZAL TREATMENT FOR FÆCES TO BE FINALLY FREE OF DYSENTERIC CHARACTERS.						Number of days taken from commencement of izal treatment to establishing of healthy character of stools.		
	Free from Blood.			Free from mucus, shreds of slough of mucous membrane, &c.					
	Maximum number of days.	Minimum number of days.	Average number of days.	Maximum number of days.	Minimum number of days.	Average number of days.	Maximum number of days.	Minimum number of days.	Average number of days.
Columns 1	2	3	4	5	6	7	8	9	10
TYPE NO. I.									
145 Cases	8	1	1.64	10	1	3.18	19	2	4.55
TYPE NO. II.									
87 Severe cases	22	1	4.31	42	3	6.65	48	4	8.60
TYPE NO. III.									
10 Extremely severe cases	16	3	7.40	22	7	8.80	23	8	13.30
AVERAGES OF ABOVE.									
242 Cases in one series	22	1	2.83	42	1	4.66	48	2	6.35

Next as to the detail of treatment. The diet was as is usually prescribed in dysentery, but I preferred a plain meat broth (not jugged) to milk where the patient's caste prejudices permit-

or preferably hypodermically—or laudanum by the mouth were resorted to, but opiates were sparingly used, the idea being to use them only enough to allay pain and to allow the

bowel a little rest and to give the izal opportunity to exert its germicidal powers in *vitro* and then trust to natural healing in the gut.

In many cases in which very satisfactory results followed, the faeces smelt of izal, and in at least one such case izal was passed apparently unchanged through the bowel.

In conclusion, I may say that in dysentery of the very worst as well as of the milder types I have found this drug *facile princeps* the most reliable remedy, but I cannot too strongly insist on the fact that small doses are useless, and the drug must be pushed to doses of the kind recommended. It is quite useless to play about with doses of three to five minims. I have two or three times been pulled up by dispensing chemists, and once by a well-known European firm, and my dosage criticized and objected to, and one of my assistants who had the temerity to follow my example and prescribe doses of m. 15, was once promptly ordered out of a chemist's establishment in Calcutta, and his prescription was rejected by the dispenser who flatly refused to make it up for him.

One more point. The disinfectant preparation of izal sold in the markets is quite as effective for treatment of dysentery as the "medical" izal, and I have used it for over a hundred cases, the "medical" izal being not procurable in time. It is a little more inclined to produce a hot sensation in the mouth than the medical izal, and requires more careful combination in prescribing so as to cover the taste.

This paper deals only with dysentery, but I may add that I have used izal with success in diarrhoeas of various kinds, and in foetid discharges from the bowel in various conditions, in cholera and in acute croupous pneumonia. These last I hope to make the subject of a future note. Finally I must express my obligations to Assistant-Surgeon Bepin Bihari Sen Gupta and to Hospital Assistant Girish Chandra Bagechi for their very painstaking assistance in the trial of Izal, on which this communication has been based.

NOTES ON SOME CASES OF FROST-BITE.

BY F. POWELL CONNOR, F.R.C.S.,

LIEUT., I.M.S.

In a recent number of the *Indian Medical Gazette* (July, 1904) there appeared some observations on "Frost-bite in the Tibet Mission Force." We can derive from it considerable information as regards the aetiology and immediate treatment of such cases. Several patients representing a more chronic and advanced stage have been handed on to the Depôt Hospital of the 8th Gurkha Rifles at Shillong under my charge. A few words dealing with my experience of the treatment of such cases may not be amiss.

These cases came under the two headings of moist and dry gangrene, affecting generally the

fingers and toes, but sometimes half the foot, etc. Damp and wet clothing—as pointed out in the article abovementioned—was a predominant predisposing factor in their causation.

The cases of lesser severity involving fingers and toes, etc., only came under the heading of dry gangrene. The striking point in these was the importance of conservative surgery in the first instance. For, oftener than not they appeared more serious at first sight than was actually the case. Looking at such cases—I speak only of such as have come under my care weeks or months after being frost-bitten—the blackening of the skin may be found to extend much further back than the actual death of the part as regards its deeper and more important elements. In other words, much of the apparent gangrene involves merely the epidermis and therefore can be neglected. If operative treatment is precipitate more of the limb would be sacrificed than is justified by the condition of the parts.

Another point of importance, which bears on the operative treatment, is the excellent vitality of the adjacent tissues. This is to be expected considering the fact that the chronic inflammation of the part produces hypervascularity and therefore an increased power of healing. One is apt from text-book ideas, which are often so hard to shake off, to think of the process of gangrene as death of a part with much adjacent lowering of vitality. This is certainly so in the ordinary types of gangrene, for such depend essentially on gradual vascular degeneration. In frost-bite the case is entirely different—a part is struck dead, but the adjacent tissues after recovering from the first shock acquire if anything greater vitality, resenting as they do the presence of the neighbouring dead tissues. This fact is of obvious importance when performing an amputation. Much of the blackened parts can be spared, as it is only epidermis-deep, and the rest of the flap beneath it is of excellent quality.

Antisepsis here as in all branches of surgery occupies a prominent place, and it is a fortunate circumstance that in these cases it is comparatively easily attained. Every Surgeon knows how difficult it is to get healing by first intention in operations where chronic suppuration has been going on for some time. Yet, my experience has been much more favourable in dealing with this class of cases, because the suppuration is of a very inactive form (especially in dry gangrene), and because of the excellent vitality of the flaps. Thorough scraping of the wound, after removing all the obviously dead tissues, combined with the use of plenty of strong antiseptic such as 1 in 3000 Hydrarg. Perchlor. must be carried out. All dead bone should be carefully removed, if possible as far as the nearest healthy joint, and even the blackened epidermis carefully scraped throughout its extent. By employing this technique I obtained primary union in all cases—even some of moist gangrene.