

Brilliant Green and Crystal Violet in the Treatment of Leprosy.

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WHILE preparing for the opening of a Leprosy Clinic on 1st April, 1932, I came upon an article by L. P. Garrod, published in the *British Medical Journal*, in which he shows that Brilliant Green destroys streptococci, even in the presence of blood, at a dilution of 1 in 10,000. In strong solutions it is entirely without irritant action. The same writer also refers to the "blue paint" advocated by Victor Bonney and C. H. Browning, known as "Bonney's Blue," which is composed of Brilliant Green and Crystal Violet in equal parts, as being an even more powerful disinfectant than Brilliant Green alone.

In order to study the possibilities of making some use of the ultra-violet rays so bountifully provided in the Indian sun, I obtained a book on Radiation Therapy by E. H. and W. K. Russell, which emphasizes the sensitising action of the aniline dyes on the skin tissues, so that the effects of ultra-violet rays are enhanced.

About this time I had the opportunity of discussing the question of treatment, as well as the general organisation of a clinic, with Dr. E. Muir, Dr. G. R. Rao, of Purulia, and Dr. Ryrie, of the Federated Malay States, who happened to be here on a visit, all of whom helped with advice and some of whom thought that the aniline dyes might be useful in the treatment of leprosy.

For the first three months after the clinic was opened, the specific treatment consisted entirely of intradermal injections of creosoted hydnocarpus oil and intramuscular injections of its ethyl esters. By this time we had engaged two skilled operators, dressers trained at the Purulia Leprosy Asylum.

In the earliest days, Brilliant Green, 1 in 10,000, was used for spraying an ulcer on the shin, with marvellous effect, this encouraged us to use it for all ulcers (except the purely trophic) external as well as in the nose, and for leprotic conditions of the palate and tongue. I have not, so far, found it necessary to use anything else, though the strength we now use is 1 in 2,500.

In June, 1932, intradermal injection of Brilliant Green was begun, 1 in 10,000 in normal saline being used, and, as no harmful results followed, the treatment was extended to many other patients, the strength being gradually

increased to 1 in 3,000. During the winter months a strength of 1 in 2,500 was used, but, as the local reaction to intradermal injection appears to be more severe on exposed parts of the body, and as this may be due to the action of the sun's rays, it is possible that this summer we shall have to revert to the lesser strength.

Twenty patients, of both C and N type, were chosen because they had bilateral lesions; on one side of the body Brilliant Green was injected, and oil on the other. Later, half the number of new patients presenting themselves were put on Brilliant Green and half on oil. Finally, nearly all have been given nothing but Brilliant Green. There are a sufficient number on oil to act as controls.

Up to 10th March, 1933, 1,054 patients had passed through our hands. Of these, 599 attended so seldom or so irregularly that they are not included in the following figures, though some of them, with single, small patches, may have absented themselves because they felt they had been "cured." The remaining 455 patients were classified as follows:—

N1	N2	N3	C1	C2	C3	Mixed N & C	N3 N1 or 2
104	60	19	62	68	23	102	17

Of these 455 patients, 76 were on oil throughout (intra-dermal oil with intra-muscular ethyl esters). These did well on oil. To those may be added a further 19 who had both oil and Brilliant Green at different times, and were definitely better on the former than on the latter.

All patients except the 76 on oil throughout, and 168 who had Brilliant Green throughout, began on oil and were later changed to Brilliant Green. Of these 211 patients, 135 were definitely better on Brilliant Green than on oil; 19 were better on oil than on Brilliant Green; 29 were about equally benefitted by each, while 28 were not improved by either. Thus 303 were improved by Brilliant Green treatment out of the 455 under consideration, or two-thirds.

On oil only.	On B.G. only.	On both. B.G.	On both. oil.	Benefit from equally	Benefit from neither.
76	168	135	19	29	28

Methods of Treatment.—*Intradermal injections* are carried out in the same way as with warm hydnocarpus oil, a fine intradermal needle being used. The solution of Brilliant Green is made in normal saline, 1 in 2,500. We have given up to 12 c.c. in one dose, but our dosage is limited by the small size of our staff, and the dose is usually 5–8 c.c.

The injections are no more painful than those of hydnocarpus oil, but for children and for those adults who are

unduly sensitive, we have combined Novocaine, in a strength of 1%, with the usual Brilliant Green solution. The injections are done slowly, with considerable diminution in pain. Nineteen children have been so treated, and two adults.

The immediate effects of Brilliant Green injections are much the same as those of oil. Seen three days after injection, the area of skin treated is slightly though definitely inflamed in most cases. A week after injection the skin has resumed the appearance it had before treatment. Some patients have tolerated weekly injections thrice repeated over the same skin area, though the majority must have at least a fortnight's rest. Here again, exposure to the sun's rays appears to have some effect.

In most cases Brilliant Green seems to aid the return of pigment to the de-pigmented skin, though not in all. I have not been able to determine the deciding factor, though it is not the normal colour of the patient, for dark skins benefit as much, or as little, as fair. Our short experience of Bonney's Blue suggests that it will be more valuable in this direction than Brilliant Green. Other factors being favourable, there is some return of sensation to anaesthetic areas.

C type cases benefit even more than those of N type; where there are definite hard nodules, it is sometimes necessary to use a hypodermic needle and get well into them, and even then results are disappointing, probably because of the large amount of fibrous tissue in the nodules. We have had no more than half-a-dozen "accidents" with Brilliant Green—fewer, in fact, than with oil. The swelling subsided within two or three weeks on the usual treatment.

There are no contra-indications to the use of Brilliant Green. It may be used on seborrhoeic skins and all others.

The cost of Brilliant Green solution (made from Merck's product) is one thirty-sixth of the cost of oil obtained from Ernakulum, not taking into account the freight on the oil. There is no difficulty in obtaining Brilliant Green powder, nor in its carriage or in making up the solution.

Intramuscular injections into the buttock produce a slight burning sensation for a few minutes, which passes off and, as a rule, leaves no reminders. We have given up to 10 c.c. without harm.

Subcutaneously Brilliant Green can be given in massive doses without ill effect, and *intravenously* I have given half a pint without apparent damage to the renal epithelium or elsewhere but, without an adequate hospital at our disposal,

we have been unable to extend our experience in this direction. Dr. G. R. Rao confirms our finding. It is to be hoped that Brilliant Green is partly excreted by the skin.

The use of Brilliant Green as a spray has already been mentioned. From ulcers we do not remove scabs or bits of adherent cotton-wool but spray freely over the ulcer. For the nose and palate we have found it very useful. Brilliant Green may also be given by the mouth. If the stools are coloured green there is hope that the intestinal complications in leprosy will be benefitted, and one possible channel for spreading infection checked. I have not tried it for the eyes but, as it has little, if any, irritant action, it should be useful in suitable dilution. Thus Brilliant Green alone may furnish almost the whole pharmacopœa of a leprosy clinic.

BONNEY'S BLUE.

We use the following prescription :—

Brilliant Green powder ...	0.5 grammes.
Crystal Violet powder ...	0.5 "
Absolute Alcohol ...	25 c.c.
Distilled Water to 2,500 c.c.

The crystal violet is dissolved in the absolute alcohol (rectified spirit will do) and added to the rest.

It is an improvement on Brilliant Green alone.

SUMMARY.

The advantages claimed for Brilliant Green are :—

1. It is at least as efficacious as hydnocarpus oil and its derivatives.
2. There are no contra-indications to its use.
3. It is safe to use, *i.e.*, there are few accidents from its administration.
4. It is not unduly painful on injection and, for children, it can be combined with Novocaine.
5. It is cheap.
6. It is easily obtained, carried, made up and administered.

I am aware of most of the limitations of our work and of this article. It is written in the hope that others will be tempted to try Brilliant Green and other aniline dyes, so that our knowledge will be extended of their uses.

Further Information on Brilliant Green

Extracted from the Extra-Pharmacopœia (Martindale).

Brilliant Green.—Syn Tetra—Ethyl—Diamido—Triphenyl—Carbinol in form of either Sulphate or Zinc Double Chloride (discovered 1879). In medicine the Sulphate $C_{27}H_{34}N_2O_4S$ is to be used. Yellow crystals,

soluble in water and in Normal Saline and in Alcohol, forming a green solution.

Chemical Examination.—Samples which we have examined were mostly the zinc double salt, and probably much of the dye that is sold as Brilliant Green is in reality Malachite Green, the latter being in the form of Oxalate. Fuse with fusion mixture to liberate zinc, if present, before employing usual tests.

Antiseptic Power.—C. H. Browning and his co-workers found this substance to compare favourably with Acriflavine (q.v.), though the latter is more rapid.

Uses.—The dye was much used initially on their recommendation as a substitute for the yellow dye, and is still used, solution of strength 1 in 1,000 being employed. As a dressing it is painless.

Septic Conditions of the ears have been treated with Brilliant Green $\frac{1}{2}\%$, Mercuric Chloride $\frac{1}{2}\%$ in 90% Alcohol.

Bonney and Browning's Violet and Green Solution.—Syn. Blue Paint, Brilliant Green and Crystal Violet (Hexa or Penta-Methyl Violet or a mixture of these), 1% each in a mixture of rectified spirit and water equal parts used to sterilise the skin.—V. Bonney and C. H. Browning, B.M.J., i./18, 562.

Stains on the Skin can be removed with spirit, those on clothes by spirit or washing with soap.

Brilliant Green Ointment.—Brilliant Green 1 or 2% in twice the amount of Alcohol 90% and incorporated with Soft Paraffin.

Epithelial stimulant in various minor injuries and affections, e.g., impetigo, indolent ulcers of various kinds, superficial shell wounds involving only the skin, blisters, etc.—R. W. Hodgson-Jones, B.M.J., i./17, 455.

Sycosis.—Remove crusts with 5% Salicylic Ointment, followed by epilation of loose pustule-encircled hairs and daily painting with 1% Alcoholic solution of Brilliant Green in 70% Alcohol. 53 cases cured after 12 to 25 applications, with no relapses.—L. i./32, 202.

Brilliant Green Paste (Hey's).—Brilliant Green 1, Boric Acid 275, French Chalk 25, Liquid Paraffin 200. The Green is incorporated, dissolved in a little spirit. For filling wound cavities.—Wilson H. Hey, B.M.J. ii./17, 445.