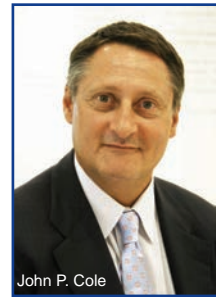


Cyberspace Chat

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John P. Cole



Bradley R. Wolf

To Dye or Not to Dye

Dyes, including gentian violet and methylene blue, have been used during hair transplant surgery for staining to facilitate microscopic dissection, recipient site creation, and graft placement. In patients with darkly pigmented skin, recipient incisions may be seen easier for graft placement after staining the recipient skin. Staining white or non-pigmented hair during strip dissection may help visualize the follicles and reduce transection. Staining the external shafts of white or non-pigmented hair can make them easier to visualize during the procedure.

In an internet communication, Melvin Mayer asked:

Are any of you aware of studies that have been done to evaluate graft production staining sites with gentian violet? Living in San Diego, I have many darker skinned patients. We are also using smaller recipient sites. These factors have led me along with my staff to use more staining. I don't think it is affecting my production, but occasionally a patient comes back not getting the production I would expect and I wonder if the staining has had a negative effect.

Bradley Wolf replied:

If you are experienced at placing and use high magnification (4.0 or greater), there is no need for staining. A slight alteration in the scalp surface, lack of resistance to the tip of the forceps, and knowledge of the incision pattern show you where the incisions are and aren't. I've never used any staining.

John Cole reported:

I agree with Brad Wolf. I believe that with high power magnification, staining the recipient sites is unnecessary for graft placing. I've never used any staining.

Bob Haber added:

I've been using 1% methylene blue in almost all my cases for several years. Occasionally, I use 5%. We generally enjoy excellent growth, so the occasional case of less than optimal growth I do not feel is related to the use of the stain. I used gentian violet for a year or so before switching to the methylene blue. While my staff appreciates the improved visibility of the sites with the stain, I find that applying stain when I have 500 or so sites left to make reveals many small gaps in my pattern, and allows me to refine my sites. I will then reapply the stain after all sites are made. I'm not aware of any studies looking at toxicity.

Bessam Farjo, Michael Beehner, Paul Rose, and Bob True added:

Bessam Farjo: I agree with Bob and share the same experience. Without a doubt, it speeds up the placing. I believe it's gentian violet rather than methylene blue that has toxicity question marks against it.

Michael Beehner: I've done around 30 cases with gentian violet, usually the full strength, and have had no problems with poor growth. I've used methylene blue around the same

number of times and again no problems. I dilute it usually 1:1 with saline.

Paul Rose: I would think that the gentian violet is toxic. It is used as an antiseptic. We use the methylene blue, as does Dr. Haber.

Bob True: I also use methylene blue, but only in very dark skinned patients. I have not observed this to reduce yield. Typically, the stain is washed away completely with spraying during the procedure. I use gentian violet rarely to control donor incision oozing.

Melvin Mayer followed up:

What I have been using is 1% gentian violet. I also use 2 drops in 30cc normal saline and place the "white hair" slivers in it. My techs think this is very helpful identifying the white hair. I also, as many of you do, dye the hair dark brown or black to better identify the external portion of the hair. Most seem to use methylene blue and I am going to switch because of occasional questionable production with gentian violet. It seems that none of us are aware of any comparative studies regarding production and the use of stain.

Comment

Gentian violet or crystal violet is a triarylmethane dye. The dye is used as a histological stain and in Gram's Method of classifying bacteria. Gentian violet has antibacterial, antifungal, and anthelmintic properties, and was formerly important as a topical antiseptic. The medical use of the dye has been largely superseded by more modern drugs, although it is still listed by the World Health Organization. The name "gentian violet" refers to its color, being like that of the petals of a gentian flower; it is not made from gentians or from violets.

One study in mice demonstrated dose-related carcinogenic potential at several different organ sites.^{1,2} The U.S. Food and Drug Administration has determined that gentian violet has not been shown by adequate scientific data to be safe for use in animal feed (to prevent mold). Use of gentian violet in animal feed causes the feed to be adulterated and is a violation of the U.S. Federal Food, Drug, and Cosmetic Act. On June 28, 2007, the U.S. Food and Drug Administration issued an "import alert" on farm raised seafood from China because unapproved antimicrobials, including gentian violet, had been consistently found in the products. The FDA report states: "Gentian violet is readily absorbed into fish tissue from water exposure and is reduced metabolically by fish to the leuco moiety, leucocrystal violet (LCV). Several studies by the National Toxicology Program reported that the carcinogenic and mutagenic effects of gentian violet in rodents. The leuco form induces renal, hepatic and lung tumor in mice."³ It has even been applied to the mouth

and lips of premature infants, and has a long history of safe use. La Leche League recommends gentian violet for thrush on the nipple.⁴ However, in large quantities, gentian violet may lead to ulceration of a baby's mouth and throat and is linked with mouth cancer.⁵ Gentian violet has also been linked to cancer in the digestive tract of other animals.⁶

Methylene blue (MB) is a heterocyclic aromatic chemical compound. It has many uses in a range of different fields, such as biology and chemistry. At room temperature, it appears as a solid, odorless, dark green powder that yields a blue solution when dissolved in water. Methylene blue is a remarkable compound in the history of pharmacology and chemotherapeutics. MB was the first phenothiazine compound developed and it has active biological properties that have been under investigation for over 120 years. Methylene blue was first prepared by Caro in 1876 as an aniline dye that became the first synthetic chemical tested in human patients, which Ehrlich demonstrated in 1891 as effective in malaria treatment. The early works of Ehrlich lead to a great interest in the use of methylene blue for numerous therapeutic applications, from microbiology to psychiatry. For example, methylene blue is a therapeutic dye with antimicrobial activity, supravital staining and diagnostic histopathological uses, blood staining activity, medicinal photosensitizer action, cancer chemotherapeutic uses, and psychoactive uses in dementia and psychosis. Currently, some of the most important clinical uses of methylene blue include the therapy of methemoglobinemia, septic shock, encephalopathy, and ischemia.⁷

In an interesting article in *Biochemical Pharmacology*, the authors propose the use of methylene blue as a means of suppressing the production of superoxide radicals O₂⁻ by acting as an alternative electron acceptor for xanthine oxidase. Accordingly, they propose that methylene blue may represent a new class of antioxidant drugs that competitively inhibit reduction of molecular oxygen to superoxide by acting as alternative electron acceptors for tissue oxidases.⁸

Summary

Dyes are used by some hair transplant physicians to stain the skin, helping to visualize incisions for recipient sites and to visualize white or non-pigmented hair during graft dissection and placement. This may speed up placing and decrease transection. Staining to identify where incisions have and have not been made allows additional incisions to be made to create greater density. Staining white or non-pigmented external shafts can make them easier to see during the procedure. Some physicians use high magnification to facilitate these tasks precluding the use of dyes. Some use commercial hair dyes to color external shafts. While no studies with respect to toxicity have been performed in the hair restoration field, studies described above have been performed on gentian violet and methylene blue stains. While methylene blue has been used extensively internally without toxicity at indicated doses, gentian violet has been shown to be carcinogenic in animal studies. While Melvin Mayer's original question as to whether staining recipient sites with gentian violet affects the growth of the transplanted hair has not been fully answered, it is our experience and opinion that staining of recipient sites is not necessary. However, if a surgeon chooses to use a dye, methylene blue should be used to stain skin or tissue rather than gentian violet. If it is necessary to dye the external hair shafts, a commercially available hair dye should be used. It is interesting

that methylene blue may reduce ischemia/reperfusion injury. Further studies using methylene blue in graft storage solution may be warranted and would be interesting.

Editors' Note: In the course of this discussion and investigation, there was an incidental revelation of possible further potential application of methylene blue in hair restoration surgery. So, we want to include this comment from Dr. John Cole:

"I think that it is important to encourage a study using methylene blue as an antioxidant to evaluate its potential role in hair restoration surgery beyond its function as a visual aide. The primary reason we use liposomal ATP (LATP) is to prohibit the production of ATP through anaerobic means. Of course, LATP is very expensive. Minimizing the production of ATP anaerobically limits the production of hypoxanthine. Hypoxanthine is subsequently converted to hydrogen peroxide, super oxide, and the most damaging of all free radicals, the hydroxyl free radical. Minimizing this conversion by xanthine oxidase has the potential to either augment the benefits of LATP or even replace LATP at a more economical price point. LATP may not be allowed or available in many countries as well. We should look more closely at methylene blue with a focus on its potential to improve yields due to its anti-oxidative properties. I think this is clearly far more interesting than its capacity to stain the skin."

References

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