Editorial

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THE WITTENBORN STUDY

Wittenborn et al. (1973) reported that 3 grams per day of nicotinic acid given to newly admitted schizophrenic men in addition to tranquilizers failed to show any advantage over those given 6 mg per day, i.e., over the control group. In fact their findings suggested "that the home and community adjustment had become more favorable in the control group." They also reported that a large proportion of their patients developed a brown hyperpigmentation which they labeled keratosis.

What they did not make clear is that the term "newly admitted" is not synonymous with acute or early and that on the average their patients had been sick many years. This should not be surprising. Generally in an area where there are many psychiatrists and psychiatric facilities, as in Montreal, only the very poor or very chronic non-responders appear in the mental hospital systems. The words newly admitted, by conjuring up an image of an early or acute schizophrenic, are imprecise and erroneous, but have also been used in this way by others.

In a more recent report Wittenborn (1974) found that about one-third of the total group had a premorbid history with relatively strong interpersonally oriented commitments. In this subgroup of 12 who were on 3 g per day, 10 achieved good outpatient adjustment scores while only five out of 12 who were on 6 mg per day achieved a comparable good score. It seems obvious to me that these patients with a good premorbid history were in fact not as sick or had not been sick as long and had not yet been alienated by their illness from their families. In other words early cases respond better, something we have been claiming since 1957.

De Liz (1973) criticized the first report on the grounds that to his personal knowledge (he was one of the psychiatrists involved in diagnosing patients for the study) a few patients were aware they were not receiving adequate quantities of nicotinic acid, i.e., the patients broke the double-blind code.

Since the double-blind was considered absolutely essential, it is important that everyone be aware of this fact. Dr. Wittenborn denies this happened and states: "The pharmacist provided assurance that treatment information had

not been and would not be given to anyone." But this begs the issue since Dr. De Liz had not accused any of the research group of deliberately breaking the code.

In the first report it was clearly stated that when the skin pigmentation became very obvious the code was broken in order to determine whether it was due to the vitamin. Some were off treatment for one month. However, the importance of this is that for these the side effect forced the code to be broken. Out of 47 patients who completed 24 months on vitamins 23 were pigmented, but Wittenborn does not outline for how many the code was broken. Once broken there was no way staff could again be ignorant that these subjects were on vitamin therapy. So I must conclude that the code was broken, but that-this was not due to anyone's fault. I doubt there are many double-blinds where the code does remain wholly unbroken.

The breaking of the double-blind code was particularly unfortunate in this study for two reasons. The first reaction of the group was that they had discovered a very serious toxic effect erroneously labeled acanthosis nigricans. No doctor or nurse would relish working with a drug which would disfigure the patient. This would be an additional set against the use of nicotinic acid in a situation where, according to De Liz, there already was a heavy bias against megavitamin therapy. The obecalp (placebo backwards) environment would be tremendously enhanced. Only later did the group discover that the pigmentation, so unusually frequent in their unique sample, was benign, and that patients reassured the staff they could easily rub off the pigment from their skin. This is of course the treatment. After a while pigment formation ceases.

Dr. Wittenborn leaves the impression that hyperpigmentation is common generally, as it was in his sample. On the contrary, it is extremely rare. I have not seen a single new case in nearly five years. There is something very odd about the New Jersey sample of patients. This should provide caution about drawing general conclusions from such a unique sample.

I do not think one should quibble about whether the control medication was a placebo or not. As far as schizophrenia is concerned 6 mg tablets are equivalent to placebo tablets.

I would also like to point out that it is impossible to double-blind an experiment using nicotinic acid. Even when a patient has become adjusted to the flush and no longer suffers any flush throughout the course of treatment it is impossible to prevent this completely and now and then throughout treatment that patient will suffer a flush. This is easily obvious to the patient and, of course, to anyone who happens to be by and watches it. For this reason, to maintain that any experiment with nicotinic acid can be double-blind is erroneous.

The only double-blind experiment was the one that we did ourselves in 1952 when we had three treatments, placebo, nicotinamide, and nicotinic acid. The clinical and nursing staff were not aware of the fact that nicotinamide was used which was a hidden control, and this is why this can be considered truly a double-blind experiment.

Recently Dr. Wittenborn submitted a correction to Dr. De Liz's criticism and I requested Dr. De Liz to prepare his comments on this. Both these communications are published here.

REFERENCES

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