A Note of Criticism Concerning Wittenborn's Paper on an Experimental Double-Blind Research Design Dealing with the Action of Nicotinic Acid on Schizophrenia

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1 was senior psychiatrist for the niacin research project and I sorted and clinically rated about 100 chronic schizophrenic patients. Most of these patients had been hospitalized in the ward of a state hospital where I was in charge. I did not remain an active member of the research project until its final conclusion and consequently cannot assume responsibility or make any statements related to the continuation of the work done after that. However, I spent about 1,000 hours interviewing and rating patients during approximately two years, and therefore had the opportunity to gain insight through direct acquaintance with some of the most decisive and representative stages of the research project. A sample of 100 patients was divided into two groups of 50 subjects — the members of one group being placed on 3,000 milligrams of nicotinic acid daily while the other half received placebo. Both groups of patients received also various types of neuroleptic drugs.

In a paper recently published by Wittenborn, Weber, and Brown (1973), we are informed that after elaborate statistical analysis of the differential response of the patient to nicotinic acid and placebo on a double-blind basis, no therapeutic difference in favor of the nicotinic acid was found.

However, the main conclusion of the Wittenborn paper becomes considerably weakened in the light of the following facts:

1. There was a great lack of stability in the psychosocial integration and cohesion of the small social group that constituted the staff.

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The concept was completely missed that such a working staff has to achieve the status of a structure and that the most pertinent premise is not the whole as such but the transformational interactions, entailing not only systems of relations and interactions (regarded as sufficient unto themselves) but also seeking to explain such empirical systems of social relations by postulating "deep structures from which those which meet the eye can be in part derived, that is, implicit or covert structures that may be postulated by reflective abstraction".

Since structures in general, and social structures in particular, are ultimately logico-mathematical models of the observed social relations, they do not themselves belong to the domain of directly objectifiable "fact". This signifies that the individual members of a group under study are generally unaware of the structural models in terms of which the anthropologist interprets constellations of social relations. As soon as, however, the anthropologist so becomes aware of them, he proceeds to search for laws regulating the transformational interactions obtaining between the participating individuals, much the same way the molecular biologist analyzes inter- and intramolecular transactions occurring inside the cells of a living organism.

2. My ascribed role in the project had been formally limited to psychiatrically evaluate the mental status of the patients by interviewing them and by using rating scales as well. As it follows, I was not consulted at any time about my deeper apperceptions by the Director of Research. In fact, he rather gathered general information about the way the research was moving from Brown, the
nurse in charge.

3. As an anthropological analyst, I discovered later on by reflective abstraction that most members of the staff had implicitly evolved covert feelings and a priori attitudes — although not verbalized —towards the action of nicotinic acid on schizophrenic patients. I detected that some members of the staff did not believe in the therapeutic action of nicotinic acid on schizophrenia. On the other hand, some of the patients had also evolved a feeling of uncertainty as to whether or not all of them were given nicotinic acid.

4. My suspicion that a break of the double-blind code had occurred had not been respected. No attempt was made to keep the double-blind code out of the hands of the research staff.

5. I discovered that one or more patients were taking nicotinic acid, not from the bottles given at the Clinic, but from bottles purchased in drug stores. These patients had, in fact, realized that they had not taken nicotinic acid during most of their participation in the project. For example, a young schizophrenic that I suspected of taking nicotinic acid admitted with a high sense of anxiety and bewilderment that he had been taking nicotinic acid which he had purchased in a local drug store. When he was further questioned why he had done so he answered that he had sensed, like many others, that the pill given to him as the drug of his expectation was not nicotinic acid at all but something else. Finally, he explained how he had confirmed his suspicions. He had learned that when a person takes nicotinic acid for the first time, face flushing occurs. Since he had experienced this face flushing only once at the beginning of his participation in the research project and never thereafter while he was continuously taking the alleged nicotinic acid, and he had re-experienced the flushing for the second time after taking the privately purchased vitamin,
he concluded — intelligent as he was — that he had been deceived. His father, who found out about the case, became very disturbed over his son's disappointment and tremendous increase in anxiety and tension. It required a great deal of work to placate him.
It was only logical to assume that this patient's self-discovery had implicitly or explicitly been conveyed to the other patients. It was also logical to assume that, once this fact had become part of the general con-

sensus of the whole sample of patients, these subjects would manifest secondary reactive symptoms. In fact, a massive alteration of their total personality profile in perception, in cognition, affect, imagery, thought processes, and behavior introduces alterations in the clinical picture already detected in previous ratings.

This means that the patient's sample had become strongly biased and, therefore, unrepresentative of all the cases concerned from which inferences were to be drawn. For, if in any pharmacological experimental procedure any set of factors pervasively introduces an unacknowledged error, this set of factors evidently causes this error to become a constant error to bias the whole gamut of operations and its final statistical conclusions.

Consequently, if this error has not been embedded in the statistical analysis of the differential responses to nicotinic acid and placebo, the conclusion that this differential response failed to reveal any therapeutic difference in favor of nicotinic acid cannot seriously be considered an empirically validated proposition. Conversely, if the error had been acknowledged, albeit in its irreversibility, and as such embedded in the final theoretical constructs as abstractions of the statistically identified empirical material, then logically the main author would have been, unable to draw his negative inference.

6. During the course of the nicotinic acid research, a number of patients, eight or 10 to the best of my recollection, belonging to the sample of subjects receiving nicotinic acid developed a curious and unpredictable skin reaction heralded by numerous and extensive patches of what was thought to be massive deposits of Melanin. These spots were black to brown in color and would start in the arm pits and then progressively spread to other parts of the body. These findings are most puzzling considering their statistical significance, and this because no such skin reactions have been, to my knowledge, ever found in literally thousands of schizophrenics who were treated with massive amounts of that vitamin continuously during many years. This sort of thing — I don't pretend to be facetious — might perhaps be said to be comparable to the occurrence of a white crow.

Appendix

Linus Pauling's main postulate concerning the therapeutic action of megavitamins in certain emotional and physical conditions is based on his conviction that these agents are effective only and if only administered in massive amounts.

Concerning the assumed therapeutic action of nicotinic acid in schizophrenia, the amounts of this vitamin have proven to be effective in the writer's experience and in certain classes of schizophrenias only if this vitamin is given in amounts far surpassing 3000 milligrams a day. As regards the action of vitamin C, although a paper published by scientists of the John Hopkins University refuted Pauling's views, more recent research on this matter carried by scientists at the University of Texas unquestionably proved Pauling's thesis: that vitamin C was in fact very effective in the treatment of infected rats but only when it was administered in tremendously high amounts.

Even assuming that the logical structure entailing basic rules of procedure, that is, the double-blind criterion, had been adhered to in Wittenborn's work, and therefore no placebo effects had interfered with the psychophysiological reactions of the patients, predicted from the very fact of being schizophrenics, the final conclusion of the paper would just indicate that, for the amount of nicotinic acid given, no therapeutic effects were detected when compared with the clinical picture of the group of 50 patients receiving placebos.