

Editorial

A Brief History of the Discovery of Kryptopyrrolle: A Diagnostic Test for a Subgroup of the Schizophrenias

Last November I received a telephone call from Mrs A.B. in Saskatchewan who reminded me that her mother, a chronic schizophrenic, had been under my care at University Hospital, (before it became Royal) in Saskatoon, Saskatchewan in 1960. This call re-awakened my interest in the history of the discovery of the mauve factor, which characterized a syndrome we called malvaria and which we later identified as kryptopyrrolle.

Before 1960 Humphry Osmond and I had been studying the psychological experience induced by hallucinogenic drugs such as mescaline and LSD so that we might better understand the experiential world of our patients. Our studies of this experience, then considered psychosis mimetic or psychotomimetic, led Humphry to conclude that the experience was mind-manifesting or "psychedelic" and he announced this word at the New York Academy of Sciences meeting in New York in 1957. Psychedelic is a Saskatchewan word! These experiences could be either beneficial or harmful depending upon the setting, the objective, the supports and many other factors which influence psychological reactions.

We began to use the psychedelic experiences to treat our alcoholic patients who were refractory to other treatment. In 1960 I thought that since LSD could induce an experience similar to that in schizophrenia cases, perhaps it might also produce in the body a chemical or chemicals that were similar to the ones naturally present in our patients. Like chemicals tend to have like physical and psychological properties. In other words, I hoped that under the influence of the LSD we might spot something in the urine of these alcoholic patients that was not present before they took the drug and that it might also be present in schizophrenia patients but not in normal people.

Our research biochemists were looking

at the urine using paper chromatography, a technique that had been recently developed which allowed one to separate a large variety of chemicals from the urine and which could lead to their identification. I therefore took a sample of urine from one of our alcoholic patients before he was given LSD and took another sample at the height of the experience, about two hours later. The laboratory was instructed to search the urine for any compound present during the experience that had not been present before. The next day our biochemists found a large mauve staining area on the paper chromatogram at location RF 0.80. We studied this chemical further and established that it was not LSD or some metabolite of it. Eventually I submitted to the laboratory 12 numbered urine specimens. Two were obtained from normal subjects. The remaining 10 were taken from schizophrenic and from non-schizophrenic patients. The laboratory did not know the code. The next day we examined the paper chromatograms and found to my surprise and delight that the mauve stain was present only in the urine of schizophrenics.

This was our incentive to pursue this most vigorously, but we needed large volumes of urine from patients who produced reliable large amounts of this factor. Luckily at this time Mrs A.B.'s mother arrived and when we tested her she had large amounts of the factor. We then collected as much urine as possible from this patient and this allowed us to proceed with further careful examination of this factor. Large scale studies at our research laboratories in Saskatoon, in Moose Jaw and in North Battleford soon showed that we had a test that correlated highly with schizophrenia.

We published our findings in a series of papers listed below. Briefly, about 90% of our early acute patients had this factor in their urine and it disappeared when they recovered. It was present in about half the chronic patients and also vanished when they became well. It was present in less

than 10% of non-schizophrenic patients and was present in 2% of normal controls but they were siblings of schizophrenic patients. We found that the presence of this factor correlated highly with the clinical picture, with the HOD test and with the prognosis for recovery. Since we did not know what that factor was, we called it mauve factor and we diagnosed everyone who had it, malvaria patients.

By then Dr. Osmond was Director of Research for the Neuropsychiatric Research Center near Princeton, New Jersey. Carl Pfeiffer was working with him and their biochemical team and we cooperated in trying to identify this substance. Dr. Pfeiffer's group discovered that this factor, which by then we had identified as kryptopyrrole, bound both pyridoxine and zinc producing a double deficiency. As a result all patients with this factor were given vitamin B₆ supplemented with zinc and this increased the recovery rate. Dr. Pfeiffer renamed mauve factor, calling it pyrroluria. It is one of the three subgroups of schizophrenia that he discussed subsequently in many reports. Dr. Pfeiffer developed an easy colorimetric method for measuring this compound in urine.

Mrs A.B's mother, therefore, made a major contribution to our research and I remain ever grateful to her. After I discharged her on the simple vitamin program we used at that time, she remained much improved and even spent a long time with her daughter then living in Mexico. But unfortunately she developed a blood condition and had her spleen removed. In hospital the doctors would not give her the vitamins and she no longer was allowed to continue on the program. She deteriorated and regressed and today, while still alive in a nursing home, she no longer recognizes her daughter. I am sorry she was not continued on the program because I have seen a few chronic patients show major improvement after 10 to 15 years of vitamin therapy. It would not have

hurt her to remain on the program and the therapeutic gain she had made under our program would have been beneficial to her family as well. At one time I considered calling kryptopyrrole the X factor, "X" standing for her name, but I could not break the confidentiality of the patient and we settled for the color term, mauve factor and later malvaria.

—A. Hoffer, M.D., Ph.D., FRCP (C)

Malvaria Literature

- Hoffer A, Mahon M: The presence of unidentified substances in the urine of psychiatric patients. *J Neuropsychiatry*, 2:331-362, 1961.
- Hoffer A, Osmond H: The relationship between an unknown factor (US) in the urine of subjects and HOD test results. *J Neuropsychiatry*, 2:363-368, 1961.
- Hoffer A, Osmond H: The association between schizophrenia and two objective tests. *Canadian Medical Association Journal*, 87:641-646, 1962.
- Hoffer A: The presence of malvaria in some mentally retarded children. *Am J Mental Deficiency*, 67:730-732, 1963.
- Hoffer A, Osmond H: Malvaria: a new psychiatric disease. *Acta Psychiatrica Scandinavica*, 39: 335-366, 1963.
- Hoffer A: Malvaria, schizophrenia and the HOD test. *Int J Neuropsychiatry*, 2:175-177, 1965.
- Hoffer A: Malvaria and the law. *Psychosomatics*, 7:303- 310, 1966.
- Hoffer A: Quantification of malvaria. *Int J Neuropsychiatry*, 2:559-561, 1966.
- Hoffer A: Families of malvarians. *J Schizophrenia*, 1:77- 89, 1967
- Hoffer A, Osmond H: The Hallucinogens. Academic Press, New York, 1967.