

# Subclinical Pellagra: Its Diagnosis and Treatment

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## Definition

*Subclinical pellagra is a deficiency syndrome characterized by the presence of perceptual changes, affecting any or all of the five senses, associated with neurasthenia. It is due to the deficiency of, or an increased demand for, niacin; the administration of which causes prompt disappearance of the symptom complex.*

## Summary

*In a seven month period, since November, 1968, I have diagnosed well over 100 cases of subclinical pellagra; 65% of the cases were under 16 years of age. They all responded to vitamin B<sub>3</sub> which is niacin or its amide, within a few days or weeks. The chief criterion for diagnosis of this disease is the presence or absence of perceptual*

*changes. All the senses are involved in these dysperceptions to a greater or lesser degree. The other symptoms, which are common to almost any disease, are fatigue, depression, anorexia, headache, dizziness, weakness and various aches and pains. Woods<sup>1</sup> described the disinclination to work which is common to all and which is important clinically and socially. None of these patients had a symmetrical skin rash involving the exposed parts, although a few did have a chronic dermatitis of one kind or another. Stomatitis, esophagitis, gastritis, diarrhea, etc., were not of any consequence. Poverty and pellagra are hand maidens and ignorance is their boon companion. The exception to this rule is the teenager—who wont eat properly.*

## Introduction

All doctors have patients who do not seem to measure up to expectations. The child does not do well in school or finds it more difficult than before. With present day report cards, not even the teacher will tell how a child is doing, but the child has a good idea. The mother will mention the child is not normal, will lie down after school, is cranky, easily upset and tired. Adult patients find it hard to do their work, they feel and *are* miserable.

They complain of fatigue, malaise, headache or any sort of pain—seemingly to get attention. If in physical examinations we do find injected pharyngeal lymphoid tissue, or diagnose a mesenteric adenitis, we are happy and so are the patients but for the time being only. The patients will return with the same or other complaints in spite of the most careful explanation of their ills.

X-rays and laboratory tests show nothing abnormal, still the patients complain. For the past 20 years I have been diagnosing them as neurotic, having flu, neurasthenia, sore throat, backache, etc., etc., for want of something better. It is certainly true that patients have suffered perceptual changes in the past 20 years.

I spent a week with Dr. Abram Hoffer in Saskatoon, Saskatchewan, in October, 1968. After this I began to realize the basic problem. I have now discovered many of my patients have dysperception. Their pain sense is distorted, their thinking is not clear and their senses—perhaps all five of them—relay false information or information that is interpreted falsely. They have hallucinations involving all their senses—yet they never complain or mention these to a doctor. The only way to discover these dysperceptions is to ask direct questions. If you ask a direct question—you will get a direct answer. If you do not ask direct questions you will not get direct

answers. This simple statement is as true now as it was 50 years ago—**Scoring Perceptual Changes**

Questions regarding perceptual changes are no more leading than questions about bowel habits or weight loss. Patients regard perceptual changes as less important than their physical complaint. They do not try to rationalize nor to understand; their neurasthenia is more to the fore. This trait was first mentioned by Spies<sup>2</sup> in 1939.

To discover perceptual changes you have to be specific and ask questions that will fit the problem. The most pertinent questions are as follows:

1. Does your face seem to change when you look in a mirror?
2. Do words move when you try to read?
3. Does the ground move when you walk?
4. Do you feel you walk on the ground or off the ground?
5. Do pictures move when you look at them?
6. Do you hear someone calling your name when you are alone?

Each of these questions can be asked directly—if the patient denies it—add the word "sometimes," i.e., "Sometimes does your face seem to change when you look in a mirror?" If patients admit to some or all of these—I have them take the Hoffer-Osmond Diagnostic (HOD) test.<sup>3</sup>

Dr. Abram Hoffer and Dr. Humphry Osmond spent many months talking with schizophrenic patients to learn exactly what these people saw, heard, felt, tasted and touched. They questioned their fears and feelings, their thoughts and their emotions and moods. The HOD test consists of 145 questions—answered *true or false*. There are some questions added to catch the person who is trying to fool the tester.

### Scoring the HOD Test

In the scoring some questions have no value, some are valued at 1, others at 2, others at 5. The score is broken down into various categories. The total score is important and is called Total Score (TS), the lowest score you can obtain is 0, the highest 246.

There is a score for changes in perception; this is Perceptual Score (PerS), and can vary from 0-53. For paranoid changes there is the Paranoid Score (PS); this score can vary from 0-15. To measure depression there is a Depression Score (DS) which varies from 0-18. There is also a ratio score which is not important to this study and a short form score that does not concern us at the moment.

A Total Score of 40 or more is thought to be suggestive of schizophrenia. In adapting this test to my practice, a score of 40 or more is indicative of subclinical pellagra.

When I find these perceptual changes I start the patient on vitamin B<sub>3</sub>, usually niacinamide, in doses of 1.5 to 3 gm. a day. It is not uncommon for the illusions to be gone in 1-3 weeks. Should they last longer than 6-8 weeks on full doses, the possibility of schizophrenia must be entertained. The following three cases will demonstrate many of these points:

### Case Reports

Case No. 1: A.M.T.-Born August, 1959. A.M.T. is a white child, one of eight, whose father is permanently employed. I delivered the child and in 1963 did a tonsillectomy. I did not see her again until March 31, 1969. Her mother sent her to me because the child complained bitterly of daily attacks of abdominal pains, nausea and vomiting, and leg pain. She was not doing well in school; she now found learning difficult. Previously she had been in the top third of her class, now she was worried about passing her grade. She would spend her time in bed and would fight with her brothers and sisters. Her mother said she used to be an active and happy child and now she was miserable and unhappy.

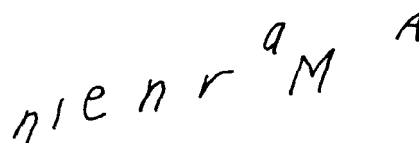
Physical examination revealed a short, well-nourished girl of 10 who wore glasses. I could find no reason whatsoever for her complaints on physical examination.

The perceptual examination revealed many dysperceptions.

*Vision:* When she looked in the mirror her face was blurred and got bigger. Her mother's face was blurred. When she looked at the blackboard it would seem foggy, the letters would move in all directions and made reading almost impossible (see Fig. 1). The ground would move up and down like waves, buildings would lean; she felt as if she was walking off the ground.



The above was written by me and I asked A.M.T. to depict it as it appeared to her on April 1, 1969.



This is what A.M.T. felt her name looked like. It is little wonder she had trouble reading.

Fig. 1

*Hearing:* At the beginning of September, 1968, she heard voices asking her to come out and play. She often heard her name called when no one was present.

*Touch:* The blackboard eraser felt fuzzy all over.

*Taste and smell* were both disturbed.

*Mood:* The child was depressed and felt afraid. She did not know the reason for this.

When the ground would move and the words would move and so on, she would get dizzy and develop severe headaches and become nauseated.

On April 1, 1969, I gave her the HOD test— Total Score was 107; Perceptual Score (PerS) 21; Paranoid Score (PS) 9; Depression Score (DS) 10. I started her on 1 gm. nicotinamide, three times a day. On April 16, 1969, she looked and felt better and thought she was getting better. She still had her dysperceptions.

By April 30, 1969, her hallucinations were all gone, she could read without trouble, she could watch television, the ground stopped moving, she heard no voices and so on. Her mood was happy, her fears evaporated. She had only two attacks of abdominal pain in the month and they were not bothersome. She looked and acted like a different girl.

I was unable to get another HOD Score until July 2, 1969, at which time her TS was 37; PerS 6; PS 6; DS 2.

I checked two of her sisters and found them suffering from the same disease. K. had a HOD Score of 77; L. was 95. They both responded to nicotinamide, 1 gm. three times a day. Their Total Scores on July 2 were 10 and 5. They had been on the vitamins for three months.

Case No. 2: W.R.-Born December, 1959. She is one of eight children of an Indian family living on a reserve. During the school year she resides at the Prince Albert Indian Residential School (P.A.R.S.) and has done so since 1966. The family history is non-contributory except the family is extremely poor and lives a sub-marginal existence.

I saw the child first on November 15, 1968.

The housemother who brought her in told me the child wet her bed every night and she was always vomiting in school and complaining of abdominal cramps. The child was demanding, told lies, was always fighting and would not or could not do her schoolwork. The child herself admitted only to enuresis and abdominal cramps. Physical examination revealed a well-nourished little girl who was sad and very quiet and had a small bruise on her right cheek.

*Perceptual examination:* As the child sat at her desk she felt the lower part of her body was not there. She would put her head in her arms on the desk and retch. Her bed would rock like a boat and she could not sleep.

*Vision:* When she looked at the board the words would get smaller and would move back and forth. She felt the ground moved when she walked and felt as if she walked off the ground and she got smaller and smaller. She walked into a tree and this is how she bruised her cheek.

Her HOD Score was 41; PerS 8; PS 3; DS 5. I put her on 1 gm. nicotinamide three times a day, 1 gm. vitamin C three times a day and Tofranil® 25 mgm., q.h.s.

Seven days later she bounced into my office and said she was all better but still had some vomiting. On December 4, 1968, she was a happy, normal child with no perceptual changes and felt like playing instead of fighting with her friends. By January 14, 1969, her HOD Score was TS 9; PerS 2; PS 1; DS 0.

She told me she was going to stay on her pills. She did not take her pills home with her at Easter in April and in two weeks had recurrence of her abdominal pain. She saw another doctor in the outpatient department who could find nothing.

I restarted her on nicotinamide and vitamin C but not the Tofranil®. By May 30,

1969, she appeared to be an active, cheerful little girl with no problems and did well in school. Her enuresis had left her.

She had two sisters at school: C, age 14, who had a HOD Score total of 94, and A., age 13, with a Total Score of 90. They were both put on nicotinamide, 1 gm. three times a day with excellent results.

I saw the mother on April 3, 1969, who complained of abdominal pains but no perceptual changes. I could find nothing. On May 1, 1969, she still had abdominal pains and had developed perceptual changes. She too was given nicotinamide, 1 gm. three times a day and is now well. I have not been able to repeat the HOD test on the sisters.

Case No. 3: C.B.-Born January, 1955. This Indian girl had been attending the P.A.R.S. since 1963. She has averaged six admissions to the school sick bay each year, complaining usually of sore throat. From the sick bay records I could find no evidence of disease.

I saw her first in October, 1968, complaining of a sore throat—I found nothing and gave her aspirin. On November 27, 1968, she complained of a sore throat; again I found nothing and had her do the HOD test. Her TS was 126; PerS 29; PS 5; DS 12.

She was a grumpy, quiet little girl who would only answer questions after a good deal of persuasion. She admitted to hearing voices, her face changed in the mirror and the ground moved. She was depressed and fearful and she would not play with the other children.

I started her on nicotinamide, 1 gm. three times a day and did not see her again until March 5, 1969. She had taken her vitamins for only two weeks in November and then quit. She was still unhappy and would not talk but agreed to try the vitamins again. I gave her vitamin B<sub>3</sub> and C,

1/2 gm. of each three times a day, and Valium® 2.5 mgm. t.i.d.

One week later she saw another doctor who stopped all her medications and gave her Donnagel® for abdominal pains. On April 8, 1969, she admitted feeling better when she took her vitamins. She still had perceptual changes; her face got small when she looked in the mirror; she felt her feet got small. Potatoes tasted bad; her boots felt hot. When she looked in the mirror all she could see were her eyes. She also told me she could see no one else in the mirror even if someone was standing beside her. She heard voices day and night; she felt tired all the time. She agreed to restart her vitamins.

When I saw her April 30, 1969, the ground still moved but not so much; words stopped moving the week before; she could see her face in the mirror. On May 28, 1969, her condition was very good, she was now the pitcher on her ball team. Her hallucinations were all gone and she would talk freely to me. She was no longer frightened; she thought she was better and said she would continue her medications for the summer. I do not know the family history in this case.

### Methods and Materials

I have practiced in Prince Albert since 1948. Canadian Indians constitute about 70% of my practice, the balance being white people as may be seen in any rural-urban center. The income level of the Indians is extremely low—under \$1,200 per annum, the average of the non-Indians would be about \$5,000. My practice is stable, yet never did I diagnose pellagra until November, 1968.

For 20 years, if someone came in complaining of a sore throat I would eventually convince myself the lymphoid tissue was injected and agree with their diagnosis; or call them neurotic and start treatment. Until

November, 1968, I had never asked about perceptual changes in this type of patient and therefore could not diagnose the condition. If you never ask about hallucinations you will never find out about them. I estimate 5-10% of the people I see in my office have subclinical pellagra.

### Recognition

In a busy practice you always watch for common signs and symptom complexes. Subclinical pellagrins show the following:

1. Complaints: Their complaints of physical disability are not supported in any way by the physical examination. A child may be crying because of joint pain yet we may not be able to find a sign of a local pathological process. If you do happen to find an infected throat or swollen knee—you are not inclined to question any further. It is when they keep returning that you finally "wake up."
2. Disproportionate Response: The patients hyper-react to the exam or treatment. If you touch them they may cry or scream, they are fearful and unhappy. They may also be too quiet. If these criterion are present, I look for the following points in spite of the fact they are such common findings:

(a) *Learning*: Children do not do well in school. The teachers, even in this day and age, suggest they are underachievers; very often the child will have failed a grade. The main difficulty appears with reading—they complain they cannot see the writing on the board and they get headaches. Very often they wear glasses of less than one diopter correction. Further questioning reveals that words move or blur and word reversal is often present. The words move so much that they can't read them. The teachers get exasperated

with their inability to learn.

(b) *Fatigue*: This is very common. The child will come home and sleep after school, the mother can't get her work done. The children are tired all the time and yet their sleep is often disturbed. The mothers do not complain of the child's fatigue although they certainly notice it.

(c) *Anorexia*: Close questioning about eating habits will often show that the patient eats almost nothing for breakfast and carbohydrates are what they do eat in the main. Girls are particularly bad in this respect. Many of these people get very little meat to eat. Even if there is meat they won't eat enough. They prefer to eat pop and potato chips.

(d) *Mood*: The patients will admit to being fearful and unhappy and depressed; they are quiet, non-committal, yet they get angry very easily and fight with their friends.

(e) *Thought*: They tend to be vague. They realize they are not well but they do not seem unduly disturbed by their hallucinations. They accept them as matter of fact. They know their hallucinations are false, they are not deluded in any way. They are not able to learn as they should.

(f) *Seeing*: The visual sense is the one most often involved and the easiest about which to question. A school child will readily admit that words move, a teenager that her face looks different, an adult that pictures seem to move. It is important not to be surprised or doubting as the patient knows these things are wrong—but he does see them. If you say these things are wrong they will not tell you any more.

One patient of mine never sees in the mirror the same reflection twice. With the visual sense I include the

fact the ground moves which means the trees move, buildings will lean over and the patients have difficulty walking—many actually fall down. Many of them feel they walk off the ground a few inches. (g) *Hearing*: The auditory sense is less often disturbed but it is still very common. The most common hallucination is to hear your name called when no one is there. Many of them hear voices or animals or music.

(h) *Other Changes*: The gustatory changes will sometimes cause them to stop eating meat or milk or almost anything. The olfactory and tactile senses also are changed but apparently less so. It may be I don't ask enough questions or the wrong questions to determine minor changes.

### Diagnosis

Many of the people I now diagnose as having subclinical pellagra have been coming to my office for years. Until the presence or absence of hallucinations are established, the diagnosis cannot be made with certainty.

### Laboratory Findings

The Clinical Nutrition Laboratory, Laboratory of Hygiene, Department of National Health and Welfare in Ottawa, Canada, has undertaken some screen tests for me— tests for

niacin; riboflavin; ascorbic acid.

They have also tested for NI methyl-nicotinamide (N<sup>1</sup>Me) and the pyridone of N<sup>1</sup>Me in the urine. If the excretion is more than 10 mgm. in 24 hours, the patient is considered not deficient. Pellagra is diagnosed if it is less than 3 mgm. in 24 hours.<sup>4</sup> The test is difficult, expensive and not particularly useful. Ten of my patients were tested and none excreted less than 10 mgm. of niacin in 24 hours, although one boy was low on riboflavin. In my opinion the limit is set too low to be of any use except in the third and fourth stages of pellagra.

### Nutrition

The nutritionist (Mrs. Lorraine Samborsky) from the Department of Public Health in Prince Albert made a study to determine the niacin content of the diets available. Niacin equivalents were not calculated but the amount of protein, including tryptophan, was checked.

The P. A. Indian Residential School was the source of 27 cases and its administrator, Mr. David Lawson, agreed to the study. The *conclusions* reached by Mrs. Samborsky in her report are as follows:

1. The margarine used has no vitamin D added. Unless the children are receiving vitamin D supplement in their daily diet—they would be deficient in that vitamin.
2. The week's diet offers adequate niacin content for all age groups except the 16 to 17 year-old-boys on two days. It offers adequate vitamin C values except for one day for all age groups. The amount of protein offered in the meals is adequate except for the 13 to 15 year-old-boys and girls on two days. The calcium content was calculated for one day only but this day it was slightly inadequate and from the menu for the other six days it would seem that the calcium content was on the skimpy side.

A preliminary investigation of the A.M.T. family was done by the same nutritionist. A good diet was available but the members of the family who suffered subclinical pellagra were not eating properly. Their niacin intake was generally below the Canadian suggested levels and the protein too was low.

### Other Laboratory Investigations

Serum proteins were normal in the 10 cases tested. Many of the patients had an iron deficiency anemia which responded to ferrous sulphate. In the patients who had enuresis, a urinalysis was done; if it was normal no further testing was done until I observed their response to niacin. If the enuresis disappeared, which it often did, no further investigation was done.

Many had had previous investigations for epigastric pain, gallbladder pain and bowel pain. The findings were usually normal although gallstones are very common in this area. Those with joint pains had latex agglutination, sed. rate and so on— with normal findings. I did not check the urine for porphyrins.

### The HOD Test

This test as before mentioned was designed to help physicians discover what their patients feel and think, in a manner which offends neither their sensibilities nor their intellect. The test is particularly useful in adults and in children who read easily.

When the test has to be interpreted by an adult for a child, its value decreased but only by the degree of intelligence of the adult. When it has to be interpreted from English to Cree, its value is limited again, only by the wisdom of the interpreter. A common finding is for the patient to admit some perceptual changes on the test paper which he or she had previously denied. When confronted he readily admits the change. The HOD test is valuable both for diagnosis and for prognosis.

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The main usefulness of the test in the series thus far is as follows:

1. It elicits perceptual changes for which I haven't time to probe.
2. It is a good measure of the degree of dysperception.
3. It is a good measure of the results of treatment.
4. The patients on the whole do not mind doing the test and I can have them return at a more convenient time for discussion and treatment.
5. The very high scores—above 110—are more likely to be a combination of pellagra and schizophrenia; at least they take longer to respond to treatment.
6. The scoring is simple and my interpretation of the results improves with practice.

Dr. Hoffer feels a Total Score of 40 or more is suggestive of schizophrenia. This may well be true of the cases which are referred to him. The people I see in the main do not require referral because of their dysperception—they respond so readily to vitamin B<sub>3</sub> that their hallucinations would have disappeared before they got an appointment with the psychiatrist. I find that psychiatrists make little or no attempt to elicit hallucinations in children who are not overtly schizophrenic.



**Results**

The patients with subclinical pellagra (S.C.P.) come to their doctor as sick and unhappy individuals. They know or suspect some vague disease and I believe they are happy when the doctor assures them there is nothing to be found. They do, however, keep returning to your office or another doctor's in search of proper diagnosis and treatment. Once you discover metabolic dysperception, the way is clear—high doses of vitamin B<sub>3</sub>, niacin or its amide. Spies<sup>2</sup> was using 1500 mgm. a day in 1937; I have been using 1500-6000 mgm. I usually treat the patient for 2-6 months depending on the findings at examination and the change in the HOD Score. I allow the patients to stop the vitamins altogether with the admonition to return if there is a recurrence of symptoms. If there is no return, no further medication is given.

If the symptoms do recur, I follow the dictates of Hoffer and keep them on (at least a year and maybe more) 1-3 gm. a day. All patients are put on a high protein, low carbohydrate diet throughout the course of treatment. Because of the expense of protein and the general dietary habits, I continue

treatment for some considerable time. The patients begin to feel better within a day or two; within a week their hallucinations are much decreased; in two weeks they are gone as a rule. If they are still complaining of perceptual changes in eight weeks, the diagnosis is likely incorrect or they are not taking their vitamins.

The physical complaints such as joint pain, headache, fatigue and so on seem to take longer to go away. The frequency and duration of pain does decrease markedly however. Since you have cured their hallucinations, they will accept the fact that their pains will go away eventually if vitamins are continued. It is unusual for patients to stop taking vitamins if they feel their need. If they stop too soon hallucinations reappear and they will restart. If they stop taking vitamins, their hallucinations will remain until the niacin is again taken. Nicotinamide is much better for children and teenagers since it does not cause the marked flushing that niacin elicits. In older people the niacin is preferred because of its beneficial side effects.

**Discussion**

Here are the contents of a letter written by A.M.T. and given to me July 7, 1969, by her mother:

*before. I felt ill and couldn't get my work done—I didn't do what my mother told me to do. And I didn't listen to my teacher either. I got very mad at my friends and brothers and sisters. I was so mad because I had to stay in bed all day long, now. I feel better now. And I can get my work done in school and at home. Now I can do things without being told. I feel better because I took tablets. The tablets were called niacinamide tablets u.s.p. Now I feel real better.*

Mr. David Lawson, administrator of the Prince Albert Indian Student Residence, Saskatchewan, wrote me January 21, 1969, about W.R.:

I have checked with W.R. 's supervisor and teacher, both note a change in her attitude.

She has not been complaining of little aches

and pains. She has not been telling tales about other children either at school or in the dormitory. She is excitable but no more so than any child her age. It appears that she has improved in behavior and attitude.

This child knows the problem and now knows the solution. Even in her tender years she suggests that subclinical pellagra is a dreadful disease. You lose your ability to think, to make friends, to do your work, to enjoy life and to be a good member of society. Subclinical pellagra is a very real entity and causes untold miseries. The disabilities are soul destroying, they disrupt the family and society.

### Conclusion

In 1939, Spies<sup>2</sup> said that pellagra caused a rapid breakdown of personality and suggested that if a nation was nutritionally deficient, the population may not only be weak in strength but may also break down in morale. I venture to suggest our Canadian Indians bear out the truth of that statement.

The patients in the main are poor—they do not get enough protein to eat. The poor seem to think they are doing their children a favor by giving them candy instead of meat. The less protein—the greater the symptoms—so a vicious circle is established, one which can be broken very quickly with vitamin B<sub>3</sub> or very slowly by diet and education. The patients are almost unconcerned with their perceptual changes. This, combined with fatigue, the disinclination to work and poverty, provides an iron curtain within our society. I now suspect that at least 25% of the people with incomes below \$5,000 have at one time or another— sooner or later—dysperceptions that will

disappear with the administration of niacin. It is the poor that buy the multivitamin tablets from chain stores and the like. It is probably just as well—certainly we doctors would hesitate to prescribe them.

There is very likely a direct relationship between subclinical pellagra and schizophrenia. It is possible that recurrent S.C.P. over the years may result in more permanent hallucinations which are then diagnosed as schizophrenia. There is no seasonal variation to S.C.P.—I find as much now as in the fall and winter. The poor rarely have gardens and meat is always a problem.

About 30% of the children with pellagra suffer from enuresis. After B<sub>3</sub> administration their enuresis completely disappears in about 50% of the cases without any other treatment. I feel that enuresis may well be the response of the G.U. tract to a niacin deficiency. The patients are all told to eat a high protein—low carbohydrate diet.

Until some miracle food comes along—a protein which is both cheap and palatable, I very much fear we will need vitamin supplements for years to come. The diagnosis and treatment of subclinical pellagra is simplicity itself. The social significance of the untreated is overwhelming. The disinclination to work due to fatigue, insomnia and depression leads them deeper into the soul destroying poverty from which it sprang.

### REFERENCES

1. Wood, E. J.: A Treatise on Pellagra. N.Y., Appleton & Co., 1912.
2. Frostig, J. P. and Spies, T. D.: The initial nervous syndrome of pellagra and associated diseases. *Am. J. M. Sci.* 199:271-274, 1967.
3. Kelm, H., Hoffer, A. and Osmond, H.: Hoffer-Osmond Test Manual. Saskatoon, Modern Press, 1967.
4. Goldsmith, Grace A.: Diseases of Metabolism. Philadelphia, W. B. Saunders Co., 1964, p. 605.