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# PENICILLIN AND ESSENTIAL FATTY ACID SUPPLEMENTATION IN SCHIZOPHRENIA

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## ABSTRACT

There is evidence of a prostaglandin deficiency in schizophrenia, possibly particularly of the 1 series. Treatment of neuroleptic-resistant schizophrenics with essential fatty acids and penicillin in an attempt to increase synthesis of 1 series prostaglandins had a therapeutic effect in six severely ill patients. Two detailed case histories are described.

## INTRODUCTION

There may be a deficiency of prostaglandins, possibly specific to the 1 series, in schizophrenia (1,2). Penicillin which has actions compatible with stimulation of synthesis of 1 series prostaglandins (3) prevented relapse in severe chronic phenothiazine-dependent schizophrenics withdrawn from neuroleptic therapy but did not cause significant improvement (4). In animal behavioral studies prostaglandins had effects very similar to those of clozapine, a drug regarded as highly successful in the treatment of schizophrenia (5). Clozapine and the prostaglandins had behavioral effects different from traditional neuroleptics (5). Clozapine is similar in structure to the prostaglandin antagonist SC19220 and in some in vitro test systems behaves as a prostaglandin analogue (2). Prostaglandins are made from essential fatty acids and an alternative approach to increasing prostaglandin biosynthesis in schizophrenia is to administer these acids (3). The richest available natural source is evening primrose oil which contains about 72% of linoleic acid and 9% of gammalinolenic acid. The gammalinolenic acid may be important because the conversion of linoleic to gamma-linolenic acid may be rate limiting and susceptible to inhibition in a variety of situations (6,7). Preliminary studies with the oil suggested that like penicillin it could prevent relapse but not cause improvement. We have therefore administered the oil together with penicillin to six severe chronic schizophrenics inadequately controlled by phenothiazines; in all cases all other drug therapy was withdrawn. No patient has become worse during a 16 week period and in some the improvement has been striking.

## CASE REPORTS

1. A divorced woman with two children was admitted to hospital at the age of 21 in 1957 with a diagnosis of schizophrenia. There was no evidence of alcoholism, epilepsy or organic brain disease. She was withdrawn, made monosyllabic replies and had neglected to care for herself or her home. She exhibited marked incongruity of affect and had paranoid and hypochondriac delusions. She was treated with chlorpromazine (100 mg tds) and trifluoperazine (10 mg bd) with only moderate success. In 1968 she developed catatonic features and she was given a course of electro-convulsive therapy (ECT) and fluphenazine enanthate (25 mg every 15 days). Her response was poor and over the next few years she became aggressive and unco-operative. She repeatedly accused the staff of trying to poison her or to kill her in other ways. She wrote numerous letters to the Duke of Edinburgh and to Scotland Yard giving ample evidence of paranoid delusions and disordered thinking of a schizophrenic type. She telephoned the local police station about once per week to make accusations about the behaviour of staff and other patients. She was markedly incongruous in affect. She took no interest in personal appearance and had poor personal hygiene. She ate meals irregularly but in spite of this was markedly overweight. She smoked heavily (40/day) and spent much time collecting cigarette ends. She developed a prolapsed uterus in 1966 for which she had surgery. Stress incontinence developed in the last five years; weight reduction and pelvic floor exercises were prescribed but she failed to co-operate. Various treatment regimes for her schizophrenia were tried without any substantial effect. Immediately before the present trial she was on haloperidol (10 mg tds) plus flupenthixol decanoate (40 mg/month).

At the beginning of the year the haloperidol and flupenthixol were withdrawn and on 20th January 1978 she was put on penicillin V (250 mg qds). In the first week she became less aggressive, paranoid and hypochondriacal. The moderate improvement was maintained at a steady level until mid-May when she was withdrawn from penicillin. By the third week after drug withdrawal she had again become markedly aggressive, paranoid and unco-operative with incongruous affect. On 20th June 1978 treatment was started with a combination of penicillin (250 mg qds) and evening primrose oil (2 x 0.6 ml capsules qds). She initially complained of some nausea and headache but these passed off. Within two weeks she no longer had hypochondriacal delusions and by the end of July the paranoid delusions and incongruity of affect had disappeared. When shown letters written to the Duke of Edinburgh and Scotland Yard she was amused and said "I certainly would not write such things now". The calls to the local police station have stopped completely. She writes regular sensible letters to her family and makes spontaneous reasonable conversation with the staff. Her personal hygiene has improved dramatically, her stress incontinence has disappeared, she has bought new clothes and has started saving regularly. Her smoking has been reduced to 10/day and she is eating regularly yet has nevertheless lost about 6 kg in weight.

Her total brief psychiatric rating scores were as follows:

| Date | Drug Regime | Total BPRS Score |
|---|---|---|
| 1 Jan. 1978 | Off all drugs | 64 |
| 20 Jan. 1978 | Penicillin V commenced | -- |
| 1 March 1978 | Penicillin V continued | 38 |
| 15 May 1978 | Penicillin V stopped | -- |
| 10 June 1978 | Still off penicillin V | 48 |
| 20 June 1978 | Penicillin V plus evening primrose commenced | -- |
| 1 August 1978 | Improvement maintained | 21 |

2. A male patient aged thirty-one years, of above average intelligence, asocial and introverted, was admitted to the hospital in June 1966. At that time he reported hearing voices of God speaking to him and claimed to be Jesus Christ. He exhibited marked incongruity of affect and disturbances in the form and content of his thinking. He was diagnosed as suffering from a schizophrenic illness and was treated with ECT, trifluoperazine 15 mg bd, and benzhexol 5 mg daily and was discharged in November 1966. In the next five years he was admitted to hospital three times due to acute relapses of the schizophrenic illness. His last admission was in October 1971 and he has been an in-patient ever since. During this period in hospital he has been on several different drug regimes with large doses of chlorpromazine, haloperidol, trifluoperazine and also depot injections of fluphenazine decanoate 25 mg every two weeks. In spite of the different drugs employed in various dosages, ECT and rehabilitation programmes he has presented an unchanging psychotic picture most of the time.In April 1978 it was decided to withdrawn all neuroleptic therapy and to treat him with oil of evening primrose and phenoxy methyl penicillin (penicillin V). At this time his thought disorder was severe; he did not speak spontaneously to others; he would stand in front of a mirror and laugh and talk to himself; his affect was markedly incongruous and his face had a wild staring appearance. He complained frequently of hearing voices and was aggressive to fellow patients. It was extremely difficult to make him participate in any of the ward's rehabilitation activities. He had been receiving fluphenazine decanoate 75 mg every two weeks, benzhexol 5 mg tds and supplementary chlorpromazine as required. He was taken off all this medication and treated with oil of evening primrose 2 capsules qds and phenoxy methyl penicillin 250 mg qds.

His total BPRS score at this time was 44. It was expected from his previous history that his schizophrenic illness would become worse after withdrawing drugs. However within the first month he became more co-operative and rather more spontaneous in speech. At this time the primrose oil treatment was increased to 3 capsules qds. He stopped hallucinating and his thinking became clearer. He gradually became very co-operative on the ward and was not easily upset by fellow patients. By the end of the second month the incongruous affect had cleared almost completely. After five months he did not show any further aggressive behaviour. His speech to others was spontaneous and appropriate and affect almost normal. His BPRS scores for each month are given below. During treatment he lost about 4 kg in weight.

| Month 1978 | April | May | June | July | Aug. | Sept. |
|---|---|---|---|---|---|---|
| BPRS Score | 44 | 38 | 30 | 24 | 23 | 21 |

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In summary, two schizophrenic patients who had been severely ill for twelve and twenty one years in spite of treatment with several different phenothiazine regimes showed a dramatic improvement when oral penicillin was administered in combination with evening primrose oil. This treatment warrants careful and extended trial especially since it seems to cause no serious side effects.

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