Orthomolecular Therapy Review of the Literature

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An increasing number of research studies point to a biochemical etiology of mental illness in which transient factors, like history, and experience, play much the same role as in other physical disorders. This paper will review such research.

DEFICIENCY DISEASES

Mental illness, associated with physical disease, results from a low concentration in the brain of any one of the following vitamins: thiamine (B1), niacin (B3), Pyridoxine (B6), cyanocobalamin (B12), pantothenic acid, folic acid, and ascorbic acid (C). Mental function and Behavior may also be affected by changes in the concentration in the brain of other substances that are normally present, such as the amino acids and various minerals (Pauling, 1968; Cott, 1970).

Vitamins

Vitamin B1 (thiamine). Thiamine deficiency causes loss of appetite, generated by cell malnutrition in the hypothalamus (Williams, 1971). Other symptoms include depression, irritability, confusion, loss of memory, inability to concentrate, fear of impending doom, and sensitivity to noise. These symptoms, related to mild mental disease, disappear when thiamine is administered (Williams, 1971; Bruno, 1973).

Vitamin B3 (niacin) The earliest manifestations of pellagra, created by a severe deficiency of niacin, are anxiety, depression, fatigue, and vague somatic complaints (Joliffe, 1939; Joliffe et al., 1940; Frostig and Spies, 1940; Hoffer, 1973a). Frostig and Spies (1940) examined 60 patients with subclinical and mild pellagra, with an initial syndrome of hyperesthesia, hyperactivity, depression, apprehension, fatigue, headache, and insomnia. This pattern readily fits into the standard classification of anxiety neuroses (Hoffer, 1973a).

As the disease progresses, patients often complain of failing vision, hypersensitivity to light, illusions, vertigo, visual and auditory hallucinations, hyperacute sense of smell, dulled sense of taste, and persistent salty taste. These perceptual changes are, of course, very similar to those produced by schizophrenia and by the hallucinogens (Hoffer and Osmond, 1966).

Acute cases of pellagra quickly respond to 0.5 to 1.0 g of niacin per day, but chronic cases respond very slowly (Aring and Spies, 1939; Aring et al., 1939; Gillman and Gillman, 1951; Hoffer, 1973b).

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Vitamin B6 (Pyridoxine). Of the 12 known disorders involving genetic vitamin dependency, Pyridoxine is involved in five (Rosenberg, 1970). This vitamin is a precursor to 50 enzymes, necessary for the metabolism of all amino acids and required for the maintenance of a stable immunologic system (Axelrod and Trakatellis, 1964; Davis et al., 1970; Ellis, 1973; Philpott, 1974).

Vitamin B-12 (cyanocobalamine). A higher incidence of low B12 concentrations has been found in mental patients than in the population as a whole. Deficiencies of vitamin B12 can cause pernicious anemia, with mental symptoms ranging from poor concentration to stuporous depression, severe agitation, and hallucinations. Administration of vitamin B-12 sometimes corrects the mental symptoms only slowly and, occasionally, incompletely (Hart, 1971).

Pantothenic acid. Both animals and humans withstand stress better after receiving large doses of pantothenic acid (Williams, 1971). Volunteers fed a diet deficient in pantothenic acid became easily upset, irritable, quarrelsome, sullen, depressed, tense, dizzy, and numb (Wormsley and Darragh, 1955; Eiduson et al., 1964). The wide variance observed in reactions of the subjects suggests that requirements for pantothenic acid vary greatly (Williams, 1971).

Folic acid. Several surveys revealed low folic acid levels in the blood of 40 to 80 percent of elderly psychiatric patients. A significant number of subjects were benefited by folic acid administration (Williams, 1971). However, deficiency reappeared unless sufficient vitamin C was supplied to convert folic acid into a usable form (Scheid, 1952; Greenberg, 1957; Herbert, 1963).

Vitamin C (ascorbic acid). Ascorbic acid is present in all tissues of higher animals during development and occurs in greater concentrations in the tissues of higher metabolic activity (Martin, 1961). Research indicates that almost any physical or mental stress significantly lowers vitamin C levels in plasma (Urbach et al., 1952; Maas et al., 1961; Baker, 1967). Deficiencies of the vitamin can cause listlessness, decreased epinephrine response, and increased susceptibility to vascular stress (Dayton and Weiner, 1961).

The amount of ascorbic acid, 20 mg a day, necessary to prevent scurvy is well established for man. How much beyond this minimum is necessary for optimal functioning is still controversial. The unstressed normal rat synthesizes ascorbic acid at the rate of 70 mg/kg of body weight per day, and the stressed rat increases this to 215 mg/kg per day (Conney et al., 1961). This is equivalent to the production of 4.9 to 15.0 g of ascorbic acid per day calculated to the 70 kg weight of an adult human (Herjanic, 1973).

Minerals

Potassium. In a single week, healthy volunteers fed a refined diet developed muscle weakness, extreme fatigue, indifference, and lack of feeling. All symptoms quickly disappeared following administration of 10 g potassium chloride (Black, 1952; Wormsley and Darragh, 1955).

Magnesium. Persons deficient in magnesium are nervous, irritable, quarrelsome, and apathetic (Shils, 1964). In one reported case, magnesium deficiency accompanied severe paranoid psychosis, which was remitted when magnesium was administered (Williams, 1971). Magnesium plus salt and water has been successfully used to treat delirium tremens (Goodhart, 1957).

Zinc. Normally found in all human tissues, zinc is essential for the synthesis of protein and the action of more than 30 enzymes (Wohl and Goodhart, 1968; Hurley, 1969; Rodale, 1973b). It helps the body use up lactic acid developed during exercise (Mayer, 1972). Zinc deficiency affects taste, smell, and appetite and may cause lethargy and apathy (Rodale, 1973c, 1974).

The high-phosphorus diet consumed by many Americans may produce zinc deficiency and thus interfere with the nucleus formation of each cell in the body (Wohl and Goodhart, 1968). Animals lacking sufficient zinc during early brain formation made more errors during experimental tests than normal

controls (Rodale, 1973a). Deficiencies of zinc and the amino acid taurine have been linked to epileptic seizures (Barbeau in Rodale, 1974).

Chromium. Biochemically, chromium is an active compound that forms many complexes with protein, stimulates several enzyme systems, and may stabilize certain nucleic acid structures. It is present in exceptionally high concentrations in brain tissue, particularly in the caudate nuclei (Mayer, 1971).

Chromium is essential for the body to utilize sugar properly. Diabetes may be caused, in part, by a deficiency of this trace metal. Hypoglycemia has been corrected by daily administration of 250 mcg of chromium (Mayer, 1971, 1972; Schroeder, 1973).

Manganese. This trace metal activates numerous enzymes and aids in fat utilization. A high-phosphorus diet reduces the absorption of manganese (Pfeiffer, 1973).

Animals deficient in manganese show retarded growth, hyperactivity, abnormal bone structure, joint deformities, poor equilibrium, and uncoordinated movements. In some animals, choline and inositol supplements prevent the deficiency symptoms (Josephson, 1961).

Amino Acids

The dry material in the brain is over one-third protein; thus, brain function depends upon the amino acids. Stress so increases the demand for protein that it becomes difficult for the body to produce sufficient amounts of the nonessential amino acids (Tui, 1953).

A protein deficiency or an imbalance of amino acids can cause mental depression, apathy, peevishness, irritability, and a desire to be left alone (Knox, 1960; Williams, 1971).

In animals fed diets lacking any of the essential amino acids, production of uric acid increases (Bicknell and Prescott, 1953). Uric acid levels in children appear to be associated with self-mutilating behavior (Cott, 1971).

DEPENDENCY DISEASES

Vitamin deficiencies are acquired and respond to usual physiological doses. In contrast, vitamin dependencies reflect genetic disturbance, leading to specific biochemical abnormalities affecting only one reaction catalyzed by a vitamin. Such dependencies respond only to large, pharmacologic doses (Hoffer, 1973b).

SCHIZOPHRENIA

Genetic Transmission

Huxley (1964) suggested that schizophrenia is caused by a dominant gene with an incomplete penetrance of about 25 percent, determined in some cases by other genes and by the environment. Pauling (1973) suggested that the other genes may be those that regulate the metabolism of vital substances and that cause the development of brain cell membranes with a decreased permeability for the passage of essential nutrilites from the blood.

Karlsson (1966) proposed a two-independent-gene theory. The dominant gene predisposes toward thought disorder and occurs in one out of 15 people, and the recessive gene occurs homozygous in one out of six people. Hoffer (1973b) suggested that the dominant gene controls the formation of adrenolutin and is related to perceptual changes plus thought disorders and that the recessive gene controls conversion of tryptophan to nicotinamide adenine dinucleotide (NAD) by some unknown mechanism.

According to Karlsson (1966), his theory accounts for the known distribution of schizophrenia in the population. A breakdown is as follows: (1) 75 percent SSPp or SSPP; normal production of adrenolutin and adequate NAD, (2) 15 percent SSpp; normal production of adrenolutin with a dependency of niacin, creating a vulnerability to alcohol and to drug-induced psychosis, thus accounting for the success of niacin in treatment of alcoholics (Hawkins, 1968; Smith in Cheraskin and Ringsdorf, 1971; Hoffer, 1973b), (3) 5 percent SsPP or SsPp; excessive adrenolutin with normal NAD, creating susceptibility to schizophrenia induced by a decreased consumption of niacin, (4) 1 percent Sspp; too much adrenolutin and too little NAD, creating schizophrenia, (5) 0.1 percent SsPp or ssPp; double dose of adrenolutin in the

presence of normal NAD and niacin, possibly representing autism, thus accounting for the non-response of autistic children to niacin (Rimland, 1968) and suggesting treatment which decreases production of adrenochrome using glutathione, vitamin C, and other reducing agents, or penicillamine and other substances which divert adrenochrome into the inert indole leuco-adrenochrome rather than into the hallucinogen adrenolutin (Hoffer, 1973b), (6) 0.01 percent sspp; lethal condition of inadequate NAD plus double-dose adrenolutin. These are, of course, hypotheses, useful principally in directing further research.

Biochemical Defects

Research indicates that schizophrenia is not a single disease resulting from a single biochemical disorder, but more probably a constellation resulting from many biochemical disorders (Cott, 1970).

Methylation. One of the most likely biochemical defects is an overactive methylation process. Methylation of any biogenic amine results in a compound with greater lipid solubility and greater brain stimulant effect (Pfeiffer et al., 1973), creating overarousal. Goldstein and Beck (1965) and Kornetsky and Mirsky (1966) agree that overstimulation is inherent in schizophrenia.

Nicotinamide adenine dinucleotide (NAD). In schizophrenia, there appears to be an endogenous failure to deliver enough NAD to vital areas of the brain (Hoffer, 1973b). Nicotinic acid but not nicotinamide elevates blood NAD levels in animals and in humans (Altschule, 1964; Burton et al., 1962).

Tryptophan. Tryptophan, niacin, and Pyridoxine are essential precursors of NAD. The body is unable to quickly metabolize tryptophan, the most toxic of the essential amino acids (Cullino et al., 1956). When amine oxidase, one of the enzymes which helps destroy tryptophan, is blocked, tryptophan becomes more toxic. Overloading with tryptophan is harmful, because it increases the psychologically powerful indoles (Hoffer, 1973b). Olson et al. (1960) found that 10 g of L-tryptophan caused perceptual and mood changes in 16 normal subjects but not in chronic alcoholics.

Indoles. When indole derivatives polymerize in vitro to melanins, hydrogen peroxide is generated. The brain is deficient in enzymes to destroy hydrogen peroxide (Cohen and Hochstein, 1963), and thus cell membranes and other lipid-containing cellular components may be damaged (Altschule and Hegedus, 1973).

Adrenolutin. Adrenochrome may be produced from adrenaline and non-adrenaline substances made in the body from tyrosine and possibly serotonin (Altschule and Hegedus, 1973). In schizophrenia, adrenochrome is converted to toxic adrenolutin. In non-schizophrenia, adrenochrome is converted into nontoxic leucoadrenochrome. This change is facilitated by the presence of sufficient amounts of vitamin C and the amino acids, glutathione and cysteine (Cott, 1972; Hawkins, 1973).

Adrenochrome is a potent inhibitor of glutamic acid decarboxylase (Osmond and Hoffer, 1966), which assists synaptic transmission. Thus, inhibition of glutamic acid decarboxylase disrupts transmission of neural impulses, producing abnormal neurophysiological activity (Krippner, 1972).

Ceruloplasmin, a protein present in normal blood, can combine with and remove adrenolutin. The blood of some schizophrenics has more Ceruloplasmin than others, and Heath (1966) found that these were more often the ones who recovered.

Taraxein. The brain of schizophrenics may be sensitized to substances like adrenolutin by the toxic protein taraxein. Taraxein, which Heath (1966) isolated in Ceruloplasmin from the blood of schizophrenics, made monkeys psychotic and produced EEC tracings like those found in chronic schizophrenics. Human subjects, injected with taraxein, showed behavior similar to that seen in schizophrenic patients.

Glutamic acid. Glutamic acid removes intracellular ammonia and other toxic wastes in the brain. The metabolite of glutamic acid, glutamine, is involved in the maintenance of cerebral tissues. Glutamic acid is metabolized, in part, into the amine gamma amino butyric acid (GABA), which is believed to coordinate and regulate electrical activity

at postsynaptic junctions and to aid the depolarized nerve to recover and fire once more. Thus, GABA inhibits neural fatigue and, conversely, enables the neural fibers to be receptive to continuous stimulation. This may underlie the increased attention, persistence, and ability to perform simple repetitive tasks reported to follow administration of glutamic acid (Vogel et al., 1966).

Vitamins B3 and B6. A deficiency of vitamin B6 interferes with the metabolism of amino acids, proteins, and biogenic amines. L-dopa may induce Pyridoxine deficiency (Golden et al., 1970). Some psychotic symptoms caused by L-dopa administration to psychiatric patients are blocked by administration of nicotinic acid (Yaryura-Tobias, 1973). The action of nicotinic acid is potentiated by Pyridoxine, possibly by opening up the kynurenine cycle of tryptophan metabolism and thereby decreasing the formation of indoles (Ananth et al., in Hawkins, 1973).

Alpha-2-globulin. Studies in molecular biology indicate that the function of the molecule depends on its geometry, symmetry, and other three-dimensional attributes. All forms of chronic schizophrenia may be associated with an abnormal molecular conformation of the alpha-2-globulin. Increased metabolic activity in 60 percent of the subjects in a study by Gottlieb et al. (1971) was associated with preponderance of the alpha-helix form of this protein, while in normal controls the beta-conformation predominated. Such increased activity altered intracellular levels of tryptophan and affected catecholamine ratios. In the 40 percent of the patients lacking the alpha-helix and the beta-conformation forms of the alpha-2-globulin, the molecule had a unique shape, which could be artificially reproduced in the laboratory only by exposure to a "leaked" intracellular protein destroying all alpha-helix forms (Lucas et al., 1971; Hawkins, 1973).

Catecholamine. A survey of psychiatric patients indicated that urinary catecholamine levels tended to increase in acute but not in chronic schizophrenics. It appeared that excretion of catecholamines may be modified by emotional and physical factors, but that overall metabolism of catecholamines is normal in schizophrenics (Ridges, 1973).

Kryptopyrrole (mauve factor). The EEGs of kryptopyrrole excretors were more frequently abnormal or borderline abnormal, showing low alpha content, high beta content, and sometimes delta activity, but no paroxysmal response to photic stimulation. Large excesses of beta waves have been associated with kryptopyrrole (Irvine, 1973).

Infections

Papez (1952, 1954), in studies of brain cultures, reported the consistent presence of a pleomorphic organism in the brains of schizophrenics. Philpott (1974) found bacterial infections in the urine of a majority of 30 schizophrenics. Ten of these showed progenitor cryptocides, a pleomorphic organism.

Orthomolecular Treatment

Symptomatology. The early stages of schizophrenia are marked by perceptual distortions resulting in altered subjective experiences of the self and the world. The illness may remain mild and never progress beyond this stage, aptly termed "metabolic dysperception" (Kowalson, 1973).

Posthypnotic suggestions to normal subjects indicated some of the profound effects which altered perceptions have on the human mind (Aaronson, 1967). Induced alterations of time and space resulted in elation or dysphoria, catatonia or hypomania. Suggesting that the world appeared two-dimensional resulted in depression and flattening of affect. Suggestions of altered perception of depth, size, constancy, and time rates produced paranoid reactions, schizoid behavior, and proprioceptive changes with alterations of posture, speech, and gait (Fogel and Hoffer, 1962; Aaronson, 1967).

The perceptual distortions in schizophrenia appear to occur independently of their subjective meaning to the patient. The disease process seems independent of the patient's personality and psychological type, although the patient's stability and psychological strengths determine to some degree at which point in the illness he becomes incapacitated (Hawkins, 1973).

Diagnosis. Perceptual disorders and the degree of schizophrenia can be measured by the Hoffer-Osmond Diagnostic Test (HOD) and the Experiential World Inventory (EWI). The HOD consists of 145 true-false statements, read and answered by the patient, which are designed to measure visual, auditory, olfactory, touch, taste, and time dysperceptions, as well as thought and mood disturbances (Hoffer and Osmond, 1961a, 1961b, 1966; Kelm, 1967). The EWI consists of 400 true-false statements measuring perceptual, affective, and ideational components and determining the relative contribution of perceptual and non-perceptual phenomena to each category of disturbance (El-Meligi and Osmond, 1973).

Prognosis. In general, the higher the HOD or EWI score, the greater the likelihood of response to Orthomolecular therapy. The grown-up childhood schizophrenic, with the low score, postural stigmata of proprioceptive deficit, and primarily visual perceptual distortions, in particular the loss of depth, is the least likely to benefit. This type of patient appears to belong to a different biochemical category of the subtypes of the schizophrenias (Hawkins, 1973).

Treatment with vitamins. Appreciable drops in HOD or EWI scores and/or obvious clinical improvement have been seen following regular, daily treatment with combinations of the following: 20 mg to 1 g B-|, 20 mg B2, 1 to 4 g B3, 75 to 200 mg B6, 15 mg pantothenic acid, 3 to 4 g C, 600 to 1,200 I.U.E (Hoffer, 1962; Le Clair, 1972; Adams, 1973; Hawkins, 1968, 1973; Robie, 1973).

Interference with absorption of medications taken orally is, in some cases, a significant factor in those patients who respond poorly to treatment or who do not respond at all. Improvement can be speeded up by parenteral injections of the megavitamin (Cott, 1967, 1971).

A 48-week double-blind controlled study demonstrated the significant therapeutic effect of Pyridoxine alone, nicotinic acid alone, and the two together. The effect of nicotinic acid was found to be potentiated by Pyridoxine (Ananth et al., in Hawkins, 1973).

However, another double-blind study failed to demonstrate any therapeutic effect of the oral administration of nicotinamide (3 grams daily for one year) in the treatment of a consecutive series of 265 schizophrenic patients (McGrath et al., 1972).

Side effects observed in treating over 5,000 patients with megavitamins have been minimal and minor. Vitamins B6, C, and E produced no side effects, although vitamin C may reputedly cause diarrhea. Niacinamide in a dosage of 4 g a day can produce nausea, particularly in adolescent girls. Niacin produces occasional nausea and an initial flush due to the release of histamine from the mast cells. The main contraindications to niacin are peptic ulcer, hypertension, diabetes, and gout (Hawkins, 1973).

Treatment with trace minerals. Many elements, needed by the body in trace amounts for specific enzyme action (Pfeiffer et al., 1973), compete with each other in biological systems, so an excess of one can block other minerals from an active enzyme site (Nicolson et al., 1966). Trace element levels in the body may be determined by testing such tissues as hair, nails, skin, and leukocytes (Pfeiffer et al., 1973).

Brain autopsies of schizophrenics revealed less zinc than brains of other patients. Offspring born of zinc-deficient rats and mice have learning deficits. Rats on a zinc-free diet have a 38 percent drop in serum zinc levels within 24 hours, indicating a lack of easily mobilized zinc reserves in body tissues. Zinc is necessary for RNA synthesis and for adrenal corticoid action involving protein synthesis (Pfeiffer et al., 1973).

Manganese, like reserpine, increases the activity of acetylcholine acetylase. In 1929, English (in Pfeiffer et al., 1973) treated 181 schizophrenic patients with intravenous injections of manganese chloride and found that half showed improvement.

Copper is high in the blood serum of some schizophrenics (Angel et al., 1957; Horwitt et al., 1957). Hypercupremia can aggravate depression and other symptoms

toms in the schizophrenic. In one study, approximately 20 percent of 240 schizophrenic outpatients had elevated copper levels, 11 percent had low serum zinc levels, 12 percent had high iron levels, and 8 percent had low iron levels (Pfeiffer et al., 1973).

High serum copper levels, tremor of the hands, ataxia, and intermittent schizophrenic symptoms with wide mood swings may indicate mercury poisoning. In a group of 200 outpatient schizophrenics, four suffered from mercury poisoning. This may mean that 2 or more percent of mental patients are suffering from mercury poisoning (Pfeiffer et al., 1973).

Histamine levels. Pfeiffer et al. (1973) found that 50 percent of a group of schizophrenic patients had low blood histamine (H-) with a rise as they improved, while 20 percent had high blood histamine (H +) with a decrease as they improved. The H- group was characterized by a low incidence of allergies, a low basophil count, freedom from head colds, and slowness in achieving ejaculation or orgasm. Their main psychiatric symptoms were thought disorder, paranoia, and sometimes hallucinations. These patients generally responded to the usual antischizophrenic therapies and sometimes responded dramatically to folic acid therapy plus vitamin B12. Dilantin, a folate antagonist, made them worse. H+ schizophrenics were characterized by a normal or high incidence of allergies and a basophil count above 0.6 percent. These patients were obsessed with suicidal depression and did not respond to the usual antischizophrenic therapies. They did respond to zinc and manganese and to histamine-releasing methadone.

Pfeiffer et al. (1973) suggested the following daily vitamin and mineral supplements for an adult histapenic (H-): 3 g vitamin C, 200 I.U. vitamin E, 3 g vitamin B3, 200 mg vitamin B6, 2 mg folic acid, 100 mg rutin, a multivitamin without minerals plus 1 mg B12 by injection each week; for an adult histadelic (H +): 2 g vitamin C, 200 I.U.
vitamin E, 1 g calcium lactate, 200 mg niacin.

Oxidation levels. Watson and Currier (1960) and Watson (1965, 1972), studying over 200 mentally ill persons exhibiting a wide range of psychological disorders, established two basic types of subjects and two basic classes of vitamins and minerals for treatment. Blood studies showed significant differences between the group means of plasma pH, plasma bicarbonate, dissolved carbon dioxide plus carbonic acid, while the blood sugar difference was not quite significant at the 0.05 level.

Biochemical differences between groups disappeared and every subject showed psychological improvement when treated daily with the following supplements:

Type 1: 30 mg vitamin B1, 30 mg vitamin B2, 30 mg vitamin B6, 75 mg niacin, 75 mg para-aminobenzoic acid, 900 mg vitamin C, 7,500 I.U. vitamin D, 900 mg potassium citrate, 300 mg magnesium chloride, 0.6 mg copper gluconate, 30 mg manganese oxide, 200 mg ferrous sulfate.

Type 2: 50,000 I.U. vitamin A, 200 I.U. vitamin E, 20 mcg vitamin B12, 400 mg niacinamide, 100 mg calcium pantothenate, 100 mg choline, 180 mg inositol, 100 mg vitamin G, 100 mg bioflavonoids, 660 mg calcium, 500 mg phosphorus, 0.45 mg iodine, 20 mg zinc sulfate.

Type 1 subjects were, on the whole, made more ill by administration of Type 2 vitamins, and the contrary was true of Type 2 subjects.

A consideration of the metabolic roles of the vitamins suggested. two major types of disturbances in intermediary metabolism, (1) slow oxidation of carbohydrates and glucogenic amino acids, resulting in a slow but preferential utilization of fats and ketogenic amino acids (Type 1 subjects), and (2) fast oxidation of carbohydrates and glucogenic amino acids, together with a slower but still more rapid than normal oxidation of fats and ketogenic amino acids (Type 2 subjects). Intense psychological stress resulted in decreases in the

oxidation rates of Type 1 slow oxidizers and increases in the oxidation rates of Type 2 fast oxidizers (Watson, 1965, 1972).

Other studies of metabolism in schizophrenia (Kety et al., 1948; Cordon et al., 1955) have not found oxidation variations. However, representative samples were not tested, according to Watson (1972). In Watson's terms, 20 of Kety's 22 subjects were fast oxidizers, and 21 of Cordon's 24 subjects were slow oxidizers. **Fasting.**

Fasting has been successfully used to treat seriously disabled schizophrenics who have not responded to other means of treatment (Nickolayev in Cott, 1969; Lilliston, 1972; Meiers, 1973). Acidosis provoked by fasting and its compensation reflect a mobilization of detoxifying defense mechanisms, which may neutralize toxins associated with the schizophrenic process. As the acidosis decreases, the blood sugar level rises. The pH and other blood parameters remain constant after acidosis decreases. Fasting mobilizes the proteins in the body, which are higher in schizophrenics than in nonschizophrenics. After fasting, the protein level becomes normal, but tends to rise to the prefast level after three to six months, even when patients eat a meat-free diet. Therefore, recurrent short fasts are necessary to maintain non-schizophrenic protein levels (Nickolayev in Cott, 1969).

The presence of neurological allergies may also explain the benefits derived from fasts. Abstention from food and drink permits the withdrawal of allergens from the patient's internal environment, creating improved mental and physical functioning. Over 90 percent of the schizophrenics studied by Philpott (1973) displayed neurological reactions to common foods.

Gluten. Hoffer (1973b) believes the gluten in wheat and other grains may decrease absorption of niacin. A high association has been found between gluten enteropathy (celiac disease) and schizophrenia (Dohan, 1969).

Dohan et al. (1969) found a significant relationship between wheat consumption and hospitalization of schizophrenics. In Norway, Finland, Sweden, and Canada, consumption of wheat decreased by 30 percent from 1936 to 1939 and likewise the mean annual hospital admissions decreased by about 30 percent. In Canada, in 1943, wheat consumption rose and hospital admissions again increased.

In a controlled study by Dohan et al. (1969), a milk and cereal-free diet (CF) or a somewhat high-cereal diet (HC) were fed all men admitted to a locked psychiatric ward. Of the 47 CF relapsed schizophrenics, 62 percent were released from the ward to full privileges before the end of the median day, compared to 36 percent of the HC patients. The CF schizophrenics were discharged from the hospital significantly sooner than the HC group. When wheat gluten was secretly added to the CF diet, the difference in release rates disappeared. Such dietary changes had no effect on non-schizophrenics.

CHILDHOOD SCHIZOPHRENIA AND AUTISM

Although numbering only three or four per 10,000 among their age group, children afflicted with childhood schizophrenia and autism are victims of one of the most disabling illnesses known (Rimland, 1964). The most common means of treatment, based on psychoanalysis and related forms of psychotherapy, have been evaluated in numerous controlled studies and have invariably been shown to be of no discernible benefit. (For review, see Lewis, 1965.) Drugs have also been widely used in the treatment of such children, but few believe the drugs currently available provide more than stopgap assistance.

Several psychiatrists have experienced encouraging results using megavitamins. Green (1969) has successfully used several grams each of niacinamide and ascorbic acid daily, along with a high-protein, low-fat diet. Bonisch (in Rimland, 1973) reported that 12 of 16

autistic children became more interested and accessible when treated with vitamin B6. Heeley and Roberts (in Cott, 1972) reported that 11 of a group of 19 psychotic children exhibited an abnormality of tryptophan metabolism, which responded to supplemental vitamin B6.

Cott (1972) successfully treated 500 children between 1966 and 1972 with 1 to 3 g niacinamide, 200 to 400 mg vitamin B6, 400 to 600 mg calcium pantothenate, and 1 to 3 g vitamin C. Frequently folic acid, vitamin B1, vitamin B2, vitamin E, and glutamic acid were added. Cott's records indicated that those beginning treatment early in life, between ages three and seven, responded better than those further advanced in age. Children 11 years and older had the dimmest prognosis.

Rimland (1968, 1973) treated 190 schizophrenic children in a controlled study, with daily administrations of two multiple vitamins plus 200 mg pantothenic acid, 1 to 3 g vitamin C, 1 to 3 g niacinamide, and 150 to 450 mg vitamin B6. Vitamin B6 brought the most obvious and dramatic changes. It not only seemed to stimulate speech but also to create a pressure to talk, a finding supported by Bonisch (in Rimland, 1973). Vitamin C seemed to increase alertness, social awareness, and sociability, a finding supported by Milner (1963) and VanderKamp (1966). Niacinamide seemed to quell bizarre behavior in some children but in others to produce irritability and hyperactivity. The children benefited by pantothenic acid seemed to become more alert, calmer, and more accessible, but the behavior of some children seemed to worsen with the addition of this vitamin (Rimland, 1968, 1973).

For a child to receive a "definite improvement" score, he not only had to improve during the three months of treatment but also to regress during the no-treatment period. Many children regressed within a matter of days, others took a month, and still others took longer. This suggested that the child who deteriorated very rapidly may have had a deficiency process quickly remedied or partially remedied by the added vitamins. In the slowly responding children, the process might instead have been one of gradual accretion of some toxic product of metabolism (Rimland, 1968, 1973).

Fifty-nine percent of the 37 autistic children showed definite improvement, as compared with 63 percent of the remainder of the sample. Among the children in the study showing the greatest improvement were six autistic children taking Dilantin along with the vitamins. Children taking Mellaril also showed unusually good improvement on the vitamins but unlike Dilantin, Mellaril showed no special interaction with autism. No other drugs seemed beneficial (Rimland, 1968, 1973).

LEARNING DISABILITIES

Genetic Transmission

Multiple occurrences in siblings and a history of familial psychiatric disorders point toward genetic transmission of learning disabilities (Wender, 1973). A high percentage of adults developing schizophrenia exhibited hyperactivity and/or learning disabilities as children (Cott, 1972). A study of 112 dyslexic children revealed that 90 percent had parents and/or siblings with similar problems, compared to 10 percent among the first-degree relatives of the control group (Hall green in Wender, 1973). Fifty percent of a small sample of fostered-away full sibs were hyperkinetic, whereas only 15 percent of the half sibs were so diagnosed (Safer in Wender, 1973). **Etiology**

Almost any insult to the nervous system at a critical point of maturation may result in poor development of motor control, perception, language, or impulse inhibition. However, research points to a biochemical rather than an anatomical defect in children with learning disabilities (Wender, 1973).

Allergic insults in early infancy may

impair some of the subtle interactions of the brain. Kittler (1970) reported that feeding difficulty, with repeated formula changes, is almost always part of the neonatal history of children with learning disabilities.

Characteristics

Clinically, children with learning disabilities appear to be hyperaroused, with high motor activity, sleep difficulties, poor attention span, and poor figure-ground discrimination. In many respects, they appear similar to children in early schizophrenic and manic excitement (Wender, 1973).

Children with learning disabilities and/or hyperkinesis were reported by Cott (1972) to eat a heavily salted diet high in cereals, carbohydrates, sweets, and sugary processed foods. Hypoglycemia occurred frequently. The glucose-tolerance test generally revealed either a flat curve, in which glucose levels showed little or no response to the ingestion of glucose, or a sawtooth profile. The flat curve is produced by an overproduction of insulin and the sawtooth curve by an erratic production of insulin (Shaw in Cott, 1972).

Lead and copper levels tend to be high in the hair of learning disabled children (Cott, 1972), while zinc, potassium, sodium, and manganese tend to be low (von Hilsheimer, 1971). This picture has frequently been reported for schizophrenics (Pfeiffer et al., 1973) and for allergic patients (Philpott, 1973, 1974).

Treatment

In a parental evaluation of the reactions of children with learning disabilities to various treatments, Mellaril, the drug with the best results, helped 15.8 percent. In a later study, parents indicated that 45 percent of the children taking high dosages of vitamins were definitely helped (Rimland in Lilliston, 1972J.

Other encouraging results have been reported using combinations of 1 to 3 g niacinamide or niacin, 1 to 3 g ascorbic acid, 50 to 60 mg calcium pantothenate, 50 to 400 mg vitamin B6, 300 to 600 LU. vitamin E, 250 to 500 mg calcium, 8 to 15 mg lecithin granules, plus a high-protein, low-carbohydrate diet accompanied by digestive enzymes (Hoffer, 1973b; Cott, 1972; Fredericks, 1972; Powers, 1973; Vogel, 1973; Green, 1969, 1974). Some children react unfavorably to vitamin B6, probably because it interacts with magnesium in such a way that it is removed from the body. Addition of 100 to 500 mg magnesium promptly corrects the deficiency (Martin, 1974).

Many children with learning disabilities respond to a rotation diet and allergy treatment, including 2 to 4 g ascorbic acid given immediately after exposure to a known allergen (Green, 1974). A well-established function of niacin in flushing histamine seems to have a long-term positive effect as an allergy treatment (von Hilsheimer, 1971).

As a pilot study, 20 children with abnormal electroencephalograms (EEGs) and a history suggestive of allergy were placed on a rotation diet free of foods to which they were sensitive. After six weeks, nine EEGs reverted to normal. Two more showed marked improvement. Scores on the Wechsler Intelligence Scale for Children (WISC) showed improvement following the dietary restrictions for those children initially scoring in the normal range. Those children with initial lower scores (50 to 80 I.Q.) showed no consistent change (Kittler, 1970).

MENTAL RETARDATION

Injections of vitamin B12 markedly enhanced learning in rats (Enesco et al. in Krippner, 1972). An absence of vitamins B3 and B12 has been identified as a possible cause of brain dysfunction and/or mental retardation in animals (Brozek, 1961a, 1961b; Brin, 1967).

Nearly half the retarded children in a London study had higher lead levels than the maximum found in the control group of normal children. It does not necessarily follow that lead caused the children's mental retardation, but it is a possibility that lead at levels too low to cause obvious poisoning might result in

mental retardation (Moncrieff, 1964). Animal studies revealed that any level of lead affects the functioning of the enzyme ALA dehydratase, in both the blood and the brain (Millar et al., 1970). A study by Careddu et al. (1963) indicated that mental retardates excreted slightly less N-methylnicotinamide than normal subjects, although mongoloids excreted over twice as much N-methyl-6-pyridone-5-carboxamide. When given 2 mg/kg of nicotinic acid intramuscularly, excretion of the 6-pyridone derivative increased slightly in mongoloids and in normal subjects and more than doubled in retardates.

Carter (1970) recommends treating various types of mental retardation with the following vitamins: cystathioninuria, vitamin B6; homocystinuria, choline and vitamin B6; hydroxykynureninuria, niacin; infantile spasms, vitamin B6; methylmalonic aciduria, low-protein diet and vitamin B12; hyper-B-alaninemia, vitamin B5; Lowe's syndrome, vitamin D, sodium, and calcium; Fanconi's syndrome, vitamin D, sodium, and potassium bicarbonate; hepatolenticular degeneration, low-copper diet. Potent concentrates of wheat germ oil have also been successfully used with retardates (Fredericks, 1972).

Perry et al. (1970) found that a deficiency of plasma glutamine was more characteristic of the degree of mental retardation in phenylketonuria than an excess of phenylalanine. Several investigators reported improvement in personality and an increase in intelligence of 5 to 20 I.Q. points for patients with mild to moderate deficiencies after administration of 10 to 20 mg daily of glutamic acid (Zimmerman and Ross, 1944) or glutamine (Vogel et al., 1966).

Turkel (1972) developed a formula of 50 different substances, including enzymes, hormones, vitamins, and minerals, which he successfully used to clear the mongoloid's blood and tissues of their excess metabolites. Retardation, he believes, is caused by accumulation of these metabolites, by-products of enzymes produced by genes contained in the extra chromosome in each cell. These aggregates cause water retention and calcification and prevent assimilation of nutrients and elimination of wastes.

In Russia, promising results in treating retardates have been obtained from vitamin B15, pangamic acid, which aids in respiration of brain tissue (Blumina in Cott, 1972). Adequate tissue respiration is required for proper brain function. Warburg (in Himwich, 1951) reported that vitamins B3 and C are important in respiration of all body tissues.

Fredericks (1974) reported that current, as yet unpublished, research indicates the megadoses of vitamin B6, manganese, and zinc may prove to be the bridge to normal function for some of the retarded.

ALCOHOLISM

Alcohol's primary metabolite, ace-taldehyde, competitively inhibits nico-tinamide-adenosine-dinucleotide-linked aldehyde dehydrogenase (NADase), which interferes with the metabolism of dopamine, producing aberrant metabolites. Prolonged consumption of alcohol enhances the activities of the enzyme-reduced NAD phosphate oxidase (Davis and Walsh, 1970; Lieber and DeCarli, 1970). Alcoholics have been found to have a lower level of leukocyte ascorbic acid than control groups (Goldberg in Hawkins, 1973).

In 1972, an estimated 20,000 to 25,000 alcoholics were taking megavitamins. Cure rates ranged from 50 to 80 percent for alcoholics and alcoholic-schizophrenics, with improvement generally appearing between the third and sixth months (Hawkins, 1968, 1973). Using vitamins B3, B6, and C, Hoffer and Osmond (in Cheraskin and Ringsdorf, 1971) obtained a cure rate of 75 percent, as compared with a cure rate of 30 percent of alcoholics not treated with megavitamins.

In curing alcoholism and in relieving the intoxicated crises in alcoholics (Smith in Hawkins, 1973) and in LSD psychosis (von Hilsheimer, 1971; von

Hilsheimer et al., 1967), niacin appears to be more effective than niacinamide. This may relate to the ability of niacin to release histamine from the mast cells, pointing to allergies, probably of grains (Cordas, 1975).

DRUG ADDICTION

Heroin addiction causes a considerable increase in the body's acid and also depletes the body's potassium and calcium. Blackman et al. (1973) used sodium bicarbonate to neutralize the acid, potassium bicarbonate to replace the lost potassium, and calcium carbonate to replace the lost calcium.

In a controlled study of 19 heroin addicts, Blackman et al. (1973) administered to each a salts mixture with a weight ratio of 6 NaHCC>3 to 3 KHCO3 to 1 CaC03. A dose of one-tenth gram of the mixture per kilogram of body weight was administered with an eight-ounce glass of water every half hour for a two-hour period. Following a two-hour break, the salts were again administered with water for two hours at half-hour intervals. When symptoms occurred, an additional dose of the salts was administered.

All volunteers said the salts either eliminated withdrawal symptoms or considerably alleviated those symptoms that appeared. In 16 of the 19 cases, the volunteers reported no severe withdrawal symptoms; minor symptoms did occur, but only of short duration. In the other three cases, most symptoms were relieved within 30 minutes by additional doses of salts, and no symptoms lasted more than four hours (Blackman et al., 1973).

NEUROSES

A biochemical basis apparently exists for at least some anxiety neuroses. This is underlined by a strong familial tendency toward anxiety neuroses. Inherited biochemical individuality may be a factor. Excessive metabolic lactate production or excessive adrenaline secretion may be the metabolic fault. Perhaps anxiety neurotics need far more calcium than others. The antifatigue characteristics of ascorbic acid may point to a greater need for this vitamin (Williams, 1971). Many neurotic patients are greatly helped by the hypoglycemic diet, particularly when the presenting symptoms are depression, anxiety, phobia, fatigue, irritability, or hypochrondia (Hawkins, 1973).

Mild or heavy exercise produced significantly higher levels of lactate in anxiety neurotics than in control groups (Wendel and Beebe, 1973). Anxiety attacks were precipitated in susceptible neurotics by the infusion of lactate into the blood. But when calcium ions were infused with the lactate, the subjects did not experience anxiety symptoms (Williams, 1971).

ALLERGIES

Although most allergy patients have multiple organ-specific reactions, some have central nervous system (CNS) reactions as the primary organ-specific target. In such cases, sensitivities to specific foods, chemicals, or inhalants may be responsible for emotional reactions, not unlike the symptomatology commonly labeled "neurotic" or "psychotic" (Campbell, 1970). Confusion, mental blocking, dullness, lethargy, tenseness, irritability, dissociation, and perceptual distortions are some of the more common CNS allergic responses (Rinkel et al., 1951; Randolph, 1962; Philpott, 1974).

Acetylcholine is thought to be a major factor in CNS allergic reactions and is one of the synaptic junction transmitters in tension states. Both carbon dioxide and sodium bicarbonate destroy acetylcholine (Speer, 1970). Alkaline therapy with sodium and potassium bicarbonate (2:1 ratio) also effectively treats the acidification characteristically occurring during an allergy reaction (Randolph, 1962; Philpott, 1974).

Maladaptive reactions to foods and chemicals can generally be relieved by the administration of appropriate nutrients. This reinforces the thesis that

enzyme deficiencies are involved in these reactions and that these nutrients are priming essential enzyme production (Philpott, 1974).

The most important nutrients for treatment are vitamins B^3, B^6, and C, calcium, magnesium, and manganese. Of lesser importance are vitamins A, B^1, B2, D, and E, pantothenate, and other essential minerals. However, doses of appropriate nutrients reduce but do not completely prevent maladaptive reactions. Nutritional treatment works best when combined with initial avoidance of incriminating substances and a four-day dietary rotation by food families (Philpott, 1974).

HYPOGLYCEMIA

Research indicates that some individuals are unable to tolerate the American diet with its heavy emphasis on sugar, coffee, cola, and alcohol. In response to such dietary stress, some persons develop hypoglycemia (Yudkin, 1963), with such symptoms as fatigue, apathy, tension, irritability, confusion, anxiety, listlessness, trembling, sweating, and headaches (Portis, 1950; Mason, 1958). In schizophrenics, the marked drop in blood sugar, indicative of hypoglycemia, may precipitate suicidal depression, rage, or catatonia (Buckley, 1969).

Research studies indicate that hypoglycemia occurs in 30 to 70 percent of psychiatric patients (Cott, 1967; Hawkins, 1973; Meiers, 1973) and in 90 percent of alcoholics and alcoholic-schizophrenics (Hoffer and Osmond, 1962; Meiers, 1973, Hawkins, 1973).

Hypoglycemia may be caused or aggravated by shortages of zinc and chromium, vital to insulin and pancreatic action but often dissipated by excess starch (Pfeiffer et al., 1973). Recent animal studies showed that a high-carbohydrate diet or an increase in blood insulin altered tryptophan and serotonin levels in the brain (Fernstrom and Wurtman, 1971).

Most hypoglycemics respond favorably to frequent feedings of a low- carbohydrate, high-protein diet lacking caffeine, alcohol, and cigarettes (Fredericks, 1972; Hawkins, 1973; Meiers, 1973).

PSYCHOTHERAPY

During the acute phases of a mental illness, when the patient's HOD score is elevated, the most effective psychotherapy is probably an educational approach, which benefits both the patient and his family. This may be followed by supportive practical advice as the patient recovers and goes through the successive stages of recovery, including changes which may lead the patient erroneously to conclude he is getting worse (Hawkins, 1973).

After the patient's HOD score has returned to normal, specific conflicts may be handled either by supportive, individual therapy or by group therapy. At this stage, recurrence of symptoms accompanied by elevated HOD scores indicates that the cause is biochemical and should be treated by a change in the medical regimen. Symptoms unaccompanied by a rise in the HOD score, on the other hand, probably stem from interpersonal or psychological conflicts and, therefore, may be treated psycho-therapeutically (Hawkins, 1973).

SUMMARY

Slight changes in molecular concentrations of common substances may affect the brain in such a way as to bring on major changes in behavior, mood, and perception. These phenomena can be commonly observed, easily demonstrated, experimentally induced, and therapeutically utilized.

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