Down Syndrome and Alzheimer's Disease Contrasted

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Abstract

All adults with Down syndrome above the age of 30 or 35 are believed to have the neuropathologic and biochemical changes diagnostic of Alzheimer's disease. During the past 35 - 40 years, hundreds of patients with Down syndrome and patients with several other disorders associated with mental retardation, but not dementia, have been treated at the Turkel Clinic with the "U" Series (Fig. 1, pre-1984 and European formulation of the "U" Series; Fig. 2, U.S. formulation of the "U" Series), and thousands more have been treated in other countries. Some of these patients are now in their 40s and 50s; they have not developed Alzheimer's disease. Alzheimer's disease and Down syndrome have been linked in the lay and professional press because of comparable structural and chemical alterations of the brain, and dermatoglyphic similarities. Although the gene that causes Alzheimer's disease is located on chromosome 21, the presumed excess of Down syndrome cases in families with familial Alzheimer's disease has not been corroborated by a three-year investigation by the Italian National Research Council and the U.S. National Institutes of Health (Wyngaarden, 1986). Down syndrome or trisomy 21 (Jacobs, 1959; Lejeune, 1959) is associated with underdevelopment of structures, including myelin, and soft-tissue accumulations of fats, amino acids, and calcium that, if untreated, can account for mental and physical retardation. Alzheimer's disease is associated with some demyelination and other brain changes that "can account for the dementia." (Sinex and Myers, 1982). This distinction is important to families who have a member with Down syndrome. Despite structural and biochemical similarities, there is a 70-80% probability that the untreated person with Down syndrome will not experience the devastating behavioral changes of Alzheimer's disease by age 40, Evelyn, the first "U" Series-treated patient with Down syndrome whose progress has been extensively recorded, has not received therapy for more than 20 years. She is 41 years old (Fig. 3, photographs at start of and during treatment; Fig. 4, photograph of Evelyn and her father at her 40th birthday party, 2/13/85). She has not experienced memory or intellectual loss consistent with the diagnosis of Alzheimer's disease. All tissues of the person with Down syndrome treated with the "U" Series are expected to develop more normally, as indicated by improved function. As a group, untreated persons with Down syndrome do experience a decline in intellectual power with advancing age, without dementia. Until sufficient numbers of elderly patients with Down syndrome are studied, the effect of Alzheimerlike neurological changes on quality of life will not be known.

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The Human Element

"After spending so many years treating and educating Pam, to give her an independent lifestyle, I now read in the paper that she will soon develop Alzheimer's disease."

When Pam, now 34 years old, was born, the doctor told her mother, "There is something wrong with your baby."

She replied, "I know she is a mongoloid, but what is *wrong* with her?"

The list of things "wrong" with Pam grew. She was a "blue baby," with three holes in her enlarged heart. She suffered from psoriasis. Chronic pulmonary infections scarred her lungs. Her blood was unusually thick, rupturing blood vessels.

Despite these disabilities, Pam's mother provided the academic training that was unavailable to "mongoloids" in special education classes of those days. She was treated medically for her separate illnesses. It would be an exaggeration, however, to say that Pam was thriving. Pam was 26 years old before her mother learned about the Turkel "U" Series. She was able to bring Pam to

Michigan from Hawaii one time only, for a year's course of treatment. During the year, Pam grew slimmer, easing the strain on her heart. Loss of fluids (including cerebral edema) and other accumulations made it easier for her to learn. Her concurrent illnesses, including psoriasis, lessened in severity. After treatment ended, Pam was placed on a good nutritional program, and after 1981, on the GTC Formula with thyroid (Harrelletal. 1981).

Then, in 1985, came a concerned letter, together with a clipping from the Honolulu press. The article stated flatly that all patients with Down syndrome develop Alzheimer's disease after the age of 35. Was it inevitable that all her mother's efforts to assure Pam's independence were about to go down the drain? The answer was unequivocally "no."

Background

The most common disease related to mental retardation, Down syndrome, elicited surprisingly little public concern until interest was aroused by its apparent connection with Alzheimer's disease. The latter, according to Sackler (1986), "afflicts over 15% of our elderly, is reportedly the fourth leading cause of death, and is expected to double or treble in incidence in the decades ahead." However, the neuropathological similarities between the two diseases should not be misinterpreted, undermining advances in the treatment and education of the patient with Down syndrome. On the contrary, amelioration of Down syndrome should provide hope for the patient with Alzheimer's disease. The patient whose myelin develops following "U" Series or GTC therapy, as evidenced by improved sympathetic and parasympathetic nervous system function, and who, unlike the untreated persons with Down syndrome (Oster, 1953), maintains intellectual ability, may be less likely to develop Alzheimer's dementia.

Senility is not a normal feature of aging; however, the incidence of Alzheimer's increases greatly with advancing age. Early impairment occurs in memory skills, followed by decline in language and motor skills. Neuropathologic changes are evident, including the characteristic physical and biochemical changes, namely, plaques, neurofibrillary tangles, and reduction in the activity of choline acetyl transferase.

The nerves of the patient with trisomy 21, on the other hand, are incompletely myelinated as a result of delayed development (amyelination). This deficit, together with hypotonic muscles, manifests itself in characteristic functional difficulties, such as incomplete digestion of foods and elimination of wastes, strabismus, or mental impairment. Deposits in soft tissue and delayed development of structures were observed by Benda (1969). On post-mortem examination of stillborn infants with Down syndrome, he noted their thin skulls, lack of myelination, and deposits of calcium, edema, and lipids in their brains.

Gene-product Imbalance and Delayed Development

The current medical model of trisomy 21, for all its precision in assigning the Down phenotype to "trisomy for the q22 band of chromosome 21 and, more specifically, to q22.1 and possibly q22.2" (Summitt, 1981), has almost entirely failed to account for the disorder at the *physical* level: the level at which present therapeutic interventions succeed. Whatever else its function, the extra genetic material of trisomy 21 leads to a 50% excess of gene products (primary accumulations), which take up space within the developing organism, interfering with the delivery of nutrients and removal of wastes. The gene-dosage imbalance and lack of homeostasis (Shapiro, 1983) are also likely to interfere with the nutritional status of the patient. Malnutrition results, retarding development.

Malnourished organs of waste excretion and elimination function inefficiently. Retained waste products (secondary accumulations) further interfere with development. In untreated Down syndrome, structural and functional "malformations" are, to some extent, the result of malnutrition-induced retarded development that has become fixed. Many normal fetal characteristics (Smith and Jones, 1982) are present at birth, including the intraventricular septal defect, patent ductus arteriosus, depressed nasal bridge, epicanthal folds, hypotonicity (Turkel, 1961), and arrested neurogenesis (Wisniewski et al., 1984). Development of some of these features (e.g., the nasal bridge), proceeds rapidly following start of "U" Series therapy.

In Down syndrome, the muscles, bones, liver, kidneys, myelin are underdeveloped; indeed, every structure, tissue, and function is retarded. Calcium metabolism is disturbed. Incidence of atherosclerosis and dental plaque is reduced; the low levels in serum, hair, and saliva, and the thin calvaria, may indicate that calcium is stored abnormally in brain and other soft tissues instead of being eliminated normally or deposited properly in bones. Radiologists have been unable to detect this phenomenon to its fullest extent with currently available equipment. According to Wisniewski et al. (1982), basal ganglia calcification (BGC) "is a frequent finding in many disorders that are associated with hypocalcemia... The frequency of CTT-detected BGC in 100 post-mortem DS brains was 11%, whereas the histologically detected rate was 100%." In addition to problems of malnutrition, accumulations, and abnormal metabolism, oxidative damage has been suggested, including "clinical and biological signs of rapid aging with brain lesions similar to those observed in Alzheimer's disease." (Sinet, 1982).

Alzheimer's Disease as a Genetic Disorder Related to Down Syndrome

Defect of one gene on chromosome 21. In some families, Alzheimer's disease "appears to have an autosomal dominant inheritance...though only 10 percent of those siblings (of probands) had symptoms by age 70...(and) age of onset in...identical twins (has) occurred 13 years apart." (Katzman, 1986). Sinex and Myers (1982) calculate that 12 percent of the population carry an autosomal dominant gene for Alzheimer's. In a study of 56 probands, secondary cases were found in 42.9% of their families: "The findings related to Alzheimer's disease are analogous to findings related to many other diseases that begin in adult life and have a genetic component" (Cutler et al., 1985).

Inheritance of a "dementing" gene located on chromosome 21 does not completely explain the 100% incidence of Alzheimer-like brain changes in Down syndrome. A normal gene on one of three copies of the trisomy should be partially protective. However, excesses of normal gene products cause harm. For example, an excess of antiviral protein originating from trisomy 21 sadly fails to protect these patients against infectious diseases, even though "cells... trisomic for chromosome 21 were three to seven times more sensitive to protection by human interferon than the normal diploid or trisomic 18 or 13 fibroblasts. The differential response...is consistent with the known assignment of the human antiviral gene to chromosome 21." (Tan et al. 1974). Similarly, the person with Down syndrome is obviously not protected by the excess of SOD-1, which has been assigned to band q22.1 of chromosome 21.

Possible mosaicism. Like Down syndrome, Alzheimer's disease is not associated with a specific characteristic universally present, and "there is no single feature exclusively limited to Alzheimer's disease." (Sinex and Myers, 1982). Dermal ridges are an example of nonspecific changes that appear to be similar in the two disorders. If a relationship between Alzheimer's disease and Down syndrome does exist, mosaicism may be involved. Genetic, environmental, and chromosomal factors are involved in the formation of dermal ridges. They are "determined by the fourth month of fetal life." (McKusick, ed. 1973). Penrose (1963) cited Cummins' 1936 research in his presentation of dermatoglyphic features in "mongolism" and compared these features in trisomy 21 and in mosaicism. In his latter illustration, Penrose pointed out that the radical loops on digits IV suggested trisomy 21.

The assumption that mosaicism is rare in Down syndrome is supported by banding techniques that clarify the origin of the trisomy during nondisjunction (Magenis and Chamberlin, 1981; Mikkelsen, 1984). However, if nondisjunction (Fig. 5) occurs toward the end of the first trimester of development and the 45-cell line dies out, late-forming structures would most likely reveal Down-like anomalies of dermal ridges and amyelination of the nerves. There would be slow retention of calcium and other wastes, as the ever-increasing quantities of the implicated gene products began to interfere with proper utilization of nutrients and with excretion or elimination of wastes. At the same time, the diagnosis of mosaicism with few 47-chromosome cell lines is often difficult to establish, especially in a phenotypically normal person. The trisomic cell line may appear in unexamined cells. Hook (1981) discusses a case of 47, XYY/48, XYY,

"U" Series

FULL DOSAGE SIZE - European formulation

Brand / Generic Name	dosage per tab / cap
UMORPHOID	
one with breakfast	
Thyroglobulin	66 mg.
Cytomel	25 mcg.
Organic Iodide	33 mg.
Vitamin A (Acetate)	25000 IU
Vitamin E Palmitate	10 IU
UTROPHOID	
one with breakfast	
Thiamin HC1 as Mononitrate	20 mg
Riboflavin	20 mg.
Methionine	100 mg.
Calcium Pantothenate	20 mg.
Para Aminobenzoic Acid	20 mg.
Pyridoxine HC1	20 mg.
Niacin	20 mg.
Folic Acid	5 mg.
Cyanocobalamin (B-12) mcg.	25 mg.
Calcium as citrate or phos.	30 mg.
Cobalt as chloride	.1 mg.
Copper as sulfate	1 mg.
Iodine as calcium iodate	.15 mg.
Iron from reduced iron	10 mg.
Magnesium as sulfate	1 mg.
Manganese from sulfate	1.25 mg.
Molybdenum	.1 mg.
Zinc from zinc sulfate	1 mg.
UNOID	
one with breakfast, lunch, dinner	
Pentylenetetrazole	20 mg.
L-glutamic acid	200 mg.
Nicotinic Acid	50 mg.
UPNEOID	
one with breakfast, lunch, dinner	
Pentylenetetrazole HC1.	20 mg.
Ascorbic Acid*	100 mg.
Pyrilamine Maleate	25 mg.
Rutin	20 mg.
Aminophylline Na. Glycinate	100 mg.
Diuretic	
one with breakfast Wednesday & Saturday	
either Lasix (furosemide)	40 mg.
or Hydrochlorothiazide	50 mg.

Brand / Generic Name	dosage per tab / cap
Bone Meal one with breakfast, lunch dinner	
Phosphorus (bone meal)	300 mg.
Calcium (bone meal)	660 mg.
Vitamin D (Fish Liver Oil)	300 IU
UPEPTOIDA	
one with dinner	
Betaine HC1	66 mg.
Ketocholanic Acid	132 mg.
Pancreatin	66 mg.
Papain	66 mg.
Pepsin	66 mg.
Diastase	3.3 mg.
UPEPTOID B	
one with breakfast & dinner	
Methionine	100 mg.
Betaine HC1	100 mg.
Choline Bitartrate	200 mg.
* Inositol	100 mg.
Unsaturated Fatty Acids	100 mg.
Liver, desiccated	150 mg.
SUPPLEMENTS one with lunch	
Pantothenic Acid	50 mg.
Pyridoxine	50 mg.
Potassium	50 mg.
Magnesium	50 mg.
Niacinamide	15 mg.
Thiamin	2.2 mg.
Zinc gluconate	31.5 mg.
Riboflavin	2.2 mg.
one with breakfast, lunch, dinner	
Calcium	260mg.
Magnesium	120 mg.
UPNEOID C NASAL SPRAY	
Chlorpheniramine maleate	.125 %
Pyrilamine maleate	.25%
Naphazoline HC1	.025%
DENTAL ANESTHETIC	
Benzocaine	16%
Chlorobutanol	5%

* Additional vitamins C and E may be added at the physician's discretion
Lecithin may be supplemented except in infant size

Figure

"U" SERIES

FULL DOSAGE SIZE - U.S. Formulation

dosage code	Brand / Generic Name	per tab / cap
UMORPHOID one with breakfast		
1	Thyroglobulin	66 mg.
2	Cytomel	25 mcg.
3	Organic Iodine	33 mg.
6	Vitamin A (Acetate)	25000 IU
7	Vitamin E Palmitate	10 IU
UTROPHOID one with breakfast		
	Riboflavin	20 mg.
	Thiamin HC1. as mononitrate	20 mg.
	Calcium Pantothenate	20 mg.
4	Niacin	20 mg.
	Para Aminobenzoic Acid	20 mg.
	Pyridoxine HC /	20 mg.
	Cyanocobalamin	25 mcg.
	Folic Acid	5 mg.
	Calcium as citrate or phosphate	30 mg.
5	Cobalt as chloride	. 1 mg.
	Copper as sulfate	1 mg.
	Iodine as calcium iodate	.15 mg.
	Iron from reduced iron	10 mg.
	Magnesium as sulfate	1 mg.
	Manganese from sulfate	1.25 mg.
	Molybdenum	.1 mg.
	Zinc from zinc sulfate	1 mg.
UNOID one with breakfast, lunch, dinner		
	L-glutamic acid	200 mg.
7	Rutin	20 mg.
	Nicotinic Acid	100 mg.
UPNEOID one with breakfast, lunch, dinner		
	Phenylpropanolamine HC1	20 mg.
	Ascorbic Acid*	300 mg.
8	Pyrilamine Maleate	25 mg.
	Theophylline Na. Glycinate in a base containing calc. carb.	100 mg.
DIURETIC one with breakfast Wednesday & Saturday		
150	Furosemideor	40 mg.
15x	Hydrochlorothiazide	50 mg.
UPEPTOID A one with breakfast and dinner		
	Betaine HC1	66 mg.
	Ketocholanic Acid	132 mg.
11	Pancreatin	66 mg.
	Papain	66 mg.
	Pepsin	66 mg.
	Diastase	3.3 mg.
UPEPTOID B one with breakfast and dinner		
	Methionine	100 mg.
	Betaine HC1	100 mg.
	Choline Bitartrate	200 mg.
12	Inositol	100 mg.
	Unsaturated Fatty Acids	200 mg.
	Liver, desiccated	150 mg.
SUPPLEMENTS one with lunch		
	Zinc gluconate	50 mg.
17	Calcium pantothenate	50 mg.
18	Pyridoxine HCI	50 mg.
27	Potassium gluconate	50 mg.
	Magnesium gluconate	100 mg.
one with breakfast		
	25D Calcium	260 mg.
	Magnesium	120 mg.
	Cholecalciferol	400 IU
one with breakfast, lunch, dinner		
25	Calcium	260 mg.
	Magnesium	120 mg.
one with dinner		
26	Zinc	30 mg.
UPNEOID C nasal spray, daily as needed		
	Pyrilamine maleate	.25 %
	Chlorpheniramine	.125%
	Naphazoline HCI	.025%
DENTAL ANESTHETIC		
	Xylocaine topical sol. (Astra)	49b

•Additional vitamins C and E may be added at the physician's discretion. Adults may use lecithin.

Figure 2

+ 21 mosaicism "detected only because over several hundred cells were counted." Whalley (1982) reports that females with Alzheimer's disease display an increase in aneuploid cells, but not specifically involving chromosome 21. Katzman (1986) states that "the presence of trisomy 21 in the cells of patients with Down's syndrome appears to be a sufficient (although not a necessary) cause of Alzheimer's disease."

Metabolic processes in trisomy 21 are altered, probably to a greater extent than diagnosed by conventional testing. Plasma analyses are often unreliable because of tissue storage problems, when the subject is malnourished (Baron, 1969). Fewer deviations from the norm may lead to deterioration rather than retardation in the mosaic individual. Metabolic idiosyncrasies of the trisomic patient may reduce intellectual powers instead of (or preceding) dementia; the opposite clinical course occurs in the Alzheimer's patient.

Prejudging the Patient with Down Syndrome

By the sixth through ninth decades of life, Alzheimer's disease begins to affect individuals in the general population as frequently as heart attacks or strokes (Katzman, 1986). Some investigators believe that of the relatively few individuals with Down syndrome who survive beyond the age of 60, "many" develop dementia (Patterson et al., 1962). Nevertheless, it is important to point out that other people are not given the diagnosis of Alzheimer's disease unless clinical symptoms appear. Despite similarities between the two diseases, Cutler et al. (1985) state that "...older adults with Down's syndrome are rarely judged to be clinically demented..." Since trisomy 21 produces changes characteristic of Alzheimer's disease without necessarily leading to dementia at the early age of 35 or 40, individuals with Down syndrome, like others, should not be given the diagnosis of Alzheimer's until and unless behaviors diagnostic of the disease, such as memory loss, occur. Structural and biochemical changes in the brains of patients with Alzheimer's disease cause the loss of memory and social skills. Deterioration in the patient with Alzheimer's disease differs from that in the adult with Down syndrome. By the end of post-mortem examination, the brain tissues may look similar, but the process may have been different.

All genetic or chromosomal disorders produce accumulations of some unmetabolized substrate along a metabolic pathway. Eventually, these diseases cause degeneration of structures. Like patients with other genetic diseases, patients with Alzheimer's disease of the familial type may benefit from "nutritional teamwork" therapies (Heffley and Williams, 1974), the "U" Series for reduction of accumulations and provision of nutrients (Turkel, 1981), or specific nutritional supplements. Stone (1984) has recommended high doses of vitamin C to help prevent the onset of senility. Vitamin C dosages for patients with genetic diseases may be determined in accordance with the Cathcart (1981) bowel tolerance procedure (Turkel, 1983). Burns and Holland (1986) report that "nearly 60% of patients with dementia had serum vitamin E levels below the accepted normal range." Other potential therapies have been suggested, such as an anticholinesterase (Summers et al., 1986) to prolong the effect of acetylcholine, or "various vitamins [B12, folate], choline, and coenzyme Q" (Roberts 1982).

Pentylenetetrazole, used in the United States for many decades and a component of the "U" Series until the Food and Drug Administration took it off the market, may prevent some of the brain changes seen in Alzheimer's disease. According to Landfield and his coworkers, "long-term treatment of rats with a neural stimulant, pentylenetetrazole (PTZ)...can retard the development of both some neuromorphologic and some behavioral correlates of brain aging in rats." They further report that long-term drug treatment seems to have induced a prolonged change in the structure or physiology of the brain (or both), allowing aged rats to perform more like the young" (Landfield et al., 1981).

Loss of Intellectual Abilities as Opposed to Dementia After Age 35

Forty years ago, parents were advised to institutionalize their "mongoloid" infants at birth because, their doctors predicted, they would never learn to walk, talk, or be toilet trained, and their presence would destroy the family. Twenty years ago, when the majority of doctors were still warning parents that

their children with Down syndrome would be severely retarded; our testing indicated that of those brought to this clinic, most functioned at or near the level of mild retardation before treatment. Most of these children do not lag far behind in attaining basic skills, especially if they participate in infant stimulation and medical programs. "It is increasingly recognized that the lives of children with Down syndrome can be happy," (Steinbock, 1986). However, linking Down syndrome to dementia has alarmed parents, who have coped with retardation but are faced with the threat that their children will develop Alzheimer's disease almost as soon as they have developed a semi-independent lifestyle.

We do not claim that the untreated patient with Down syndrome retains all intellectual ability with advancing age. In their study of the MD "U" Series, Iida and Kurita (1974) of the Japanese National Institute of Mental Health adjusted for the well-known phenomenon of the decline of I.Q. with advancing chronological age in Down syndrome. They demonstrated that the MD formulation was effective in preventing the decline in I.Q. However, because of the greater benefits obtained in the areas of physical development and general health with the Turkel formulation, the Japanese began to import the European formulation of the "U" Series in 1981. In the Japanese study, none of the untreated children improved, but significant improvement was seen in 39% of the MD-"U"-Series-treated males and 67% of the treated females. In our (1985) study of 14 individuals with Down syndrome, aged 14 months to 19 years, before-treatment testing revealed a decline in I.Q. scores that correlated with advancing age ($r = .69$). Fishier (1975) noted a similar decline in the developmental curve for (untreated) children with mosaic Down syndrome.

Despite the decline in I.Q. scores before treatment, family members marvel at older patients' excellent memories for people, places, and events. For example, Patient Mike V., born December 2, 1957, started treatment October 16, 1985. Before treatment, he was routinely evaluated. February 10, 1983, tested with the Stanford-Binet Intelligence Scale, Form L-M, he obtained a mental age equivalent of 3 years 5 months. On the Peabody Picture Vocabulary Test-Revised, he obtained a mental-age equivalent of 2 years 6 months. He was reevaluated in Georgia before starting the "U" Series. On the Stanford-Binet, he obtained a mental age equivalent of 3 years 2 months, I.Q. 16. Although his language skills declined to the one-year level, his self-help skills remained at the 4 year 4 month level (Vineland Adaptive Behavior Scales, Expanded). This pattern of intellectual and behavioral impairments differs from those described in Alzheimer's disease. Memory loss is an early clinical feature of Alzheimer's disease. In the patient with Alzheimer's disease evaluated by Cutler, the decline in I.Q. scores was less evident, at least until after the patient's fifth year into the disease, than the deterioration of memory.

Preventing intellectual deterioration

As a group, patients treated with the "U" Series do not experience the characteristic decline in I.Q. scores with advancing age. Born February 4, 1966, Jimmy H. was a typical patient with trisomy 21. He was functioning in the mildly retarded range, with a maturity quotient of approximately 60, at the age of 2 years 7 months. Treatment started September 7, 1977. His I.Q. score was 41. The age-related decline gradually began to reverse. The following year, he obtained an I.Q. of 48 on the Stanford Binet. When last examined at this clinic February 5, 1981, his I.Q. was 59. Treatment ended six months later. When reevaluated by his school district January 1985, he obtained a Full Scale I.Q. of 57 on the WAIS-R.

A study (1985) of 31 Turkel-"U"-Series-treated patients (1/7 of the current patient population; 15 females and 16 males) was made in order to compare treatment results with Japanese (MD "U" Series) findings. As in the Japanese study, the mean score did not decline, but in fact increased slightly. At the start of treatment, the mean age was 8 years (range 4 months to 20 years). The mean score was 61.8 (standard deviation = 8.3); range 110 (3 year 2 month old female) to 19 (15 year 9 month old female). The mean score of 63.3 after two years of treatment contrasts with declining scores in untreated groups. These findings support the claim that the "U" Series, at the least, delays or prevents the decline in I.Q. scores, and probably accelerates the process of myelination, reducing the risk of early-onset Alzheimer's disease in

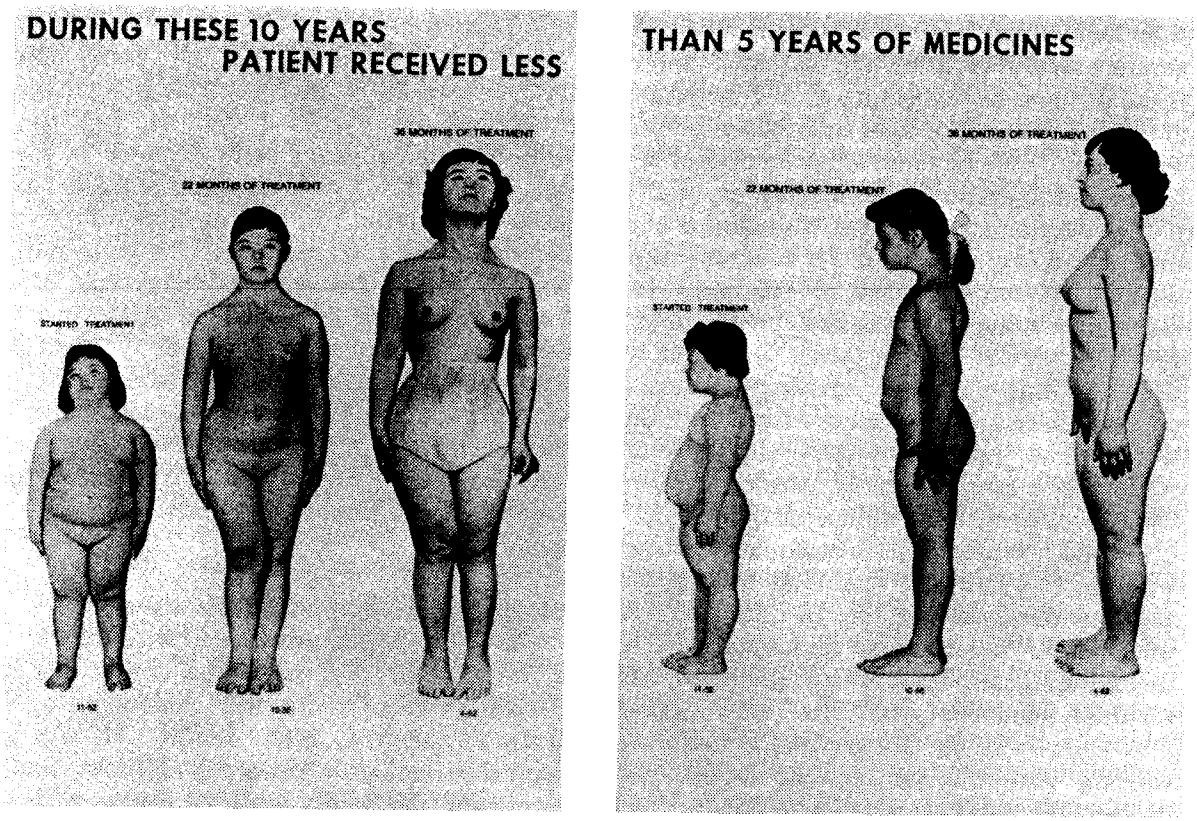

Figure 3

the individual with Down syndrome.

To date, reports indicate that *no patient treated with the "U" Series has developed Alzheimer's disease.* Evelyn (Figs. 3 and 4) is 41 years old. Her mother died of Alzheimer's disease at the age of 75. Evelyn's I.Q. score before treatment, at the chronological age of 7 years 9 months, was 46. It has not declined. More importantly, except for the effect of mild mental retardation, her memory and social skills are intact. She assumes full responsibility for her share of housework in a community home, with five other mildly retarded adults. She is the only one with Down syndrome.

Other patients have maintained their skills into their late 30s and 40s. Janie L. lives in Arizona in her own apartment. She walks to work, keeps her checkbook balanced, pays her rent, and treats her friends to meals at her home or at a restaurant. Elmer B. of Colorado works under supervision and travels alone on vacation. Roger R. works for the National Institutes of Health as a maintenance man; he lives in his own apartment. Jonathan lives with his wife in an apartment in Chicago. He supports the family as an employee of the post office. Patient S., whose father had Alzheimer's disease, was an "old man" of 40 when he started treatment. He became more vivacious, worked as a farm hand for his uncle, and took up horseback riding. Mike V. is learning new words and is speaking in three-word sentences. Pam herself is enjoying life in Hawaii, with no decline in her abilities and no deterioration in her behavior. Reports of other adults indicate similar retention of old skills and acquisition of new skills. They live semi-independently, are employed, and socialize actively. Dementia is an eventual possibility, as it is in the general population, but not at the early age of 30 or 35. Since 20% of previously normal adults develop senile dementia after the age of 80, the fear of Alzheimer's disease with Down syndrome should not provide an excuse for denying the child with Down syndrome treatment, education, and all civil liberties available to other members of society.

Summary and Conclusion

Down syndrome and Alzheimer's disease are associated with structural brain changes, deficiency of choline acetyl transferase, and abnormal amyloid protein. In untreated Down syndrome the development of all structures, including myelin, is delayed.

Amyelination and the secondary (waste-product) accumulations typical of the disease most likely produce the post-mortem findings of accumulated metabolites — lipids, edema, calcium — "demyelination," undifferentiated fetal cells, and neuritic plaques and tangles described by Stephens and Menkes (1969). These brain changes do not produce dementia in 70-80% of *untreated* persons with Down syndrome in early midlife. Moreover, the normalization of functions (such as digestion and excretion) related to myelination of nerves suggests that the underdeveloped myelin begins to develop more normally in persons treated with the "U" Series.

It is incorrect to couple the diagnosis of Down syndrome with Alzheimer's disease unless the individual with Down syndrome is clinically demented. Few of these patients are severely retarded. Most have good potential for routine, supervised work and a fairly independent life as adults. Parents are alarmed by reports that the brain changes of Alzheimer's disease, seen in adults with Down syndrome, produce dementia in all patients at an early age. The behavioral changes associated with advancing age differ in the two diseases. In most cases, within the limitations of mental retardation, the memories of adults with Down syndrome remain excellent for concrete matters, and social skills are relatively unimpaired. Incomplete reports and conjectures linking the two diseases are likely to undermine progress in infant stimulation, training and treatment programs, and ultimately to endanger the life of the infant with Down syndrome (Turkel, 1985).

Figure 4

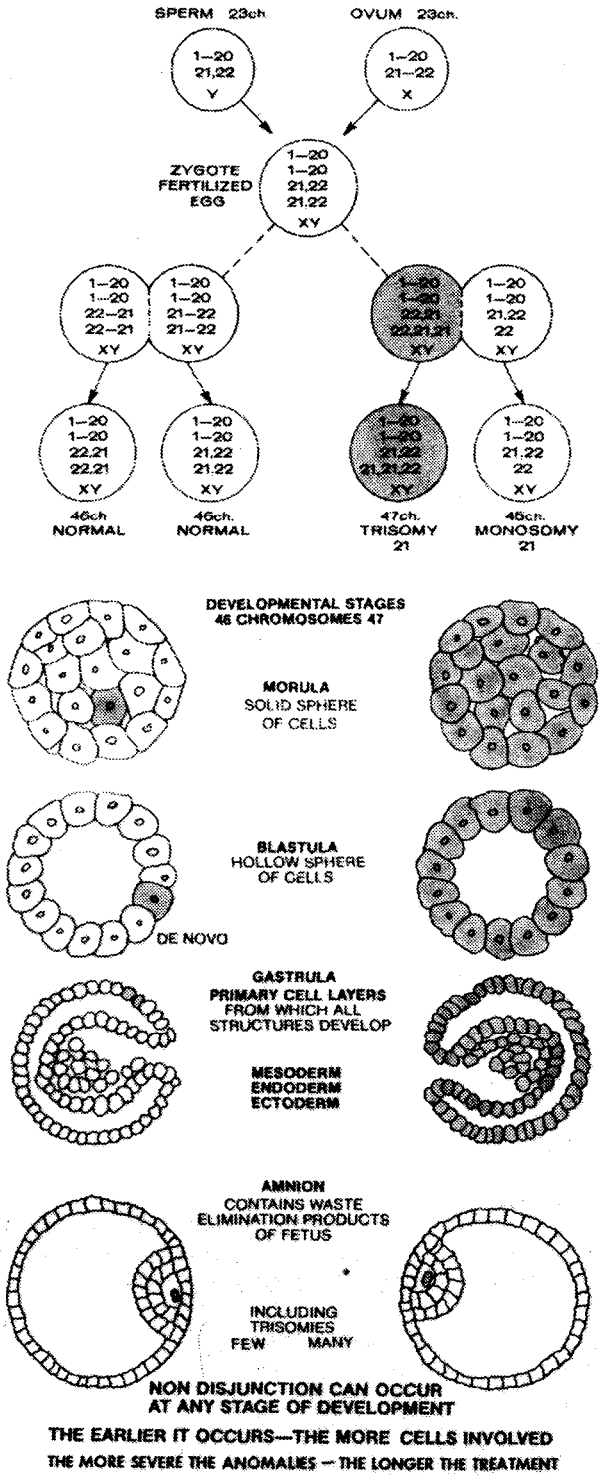

Figure 5

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