A Case of Down Syndrome with Tourette Syndrome

Henry Turkel, M.A., M.D. and Ilse Nusbaum, M.A.[1]

Background

Tourette syndrome, first described in 1885, is a tic disorder differentiated from other movement disorders, such as myoclonic movements or transient tics of childhood. The median age at onset is seven years. In some cases, remissions occur or symptoms diminish. In other cases, the condition is lifelong. DSM-III-R diagnostic criteria are: multiple motor and one or more vocal tics present at some time; tics that occur many times a day (usually in bouts), nearly every day or intermittently throughout a period of more than one year; the anatomic location, number frequency, complexity, and severity of the tics change over time; onset before age 21; occurrence not exclusively during psychoactive substance intoxication or known central nervous system disease.

Since identical twins tend to be concordant, while siblings and fraternal twins are usually discordant for the syndrome, the hypothesis that the disorder has a genetic basis has been examined. Pauls and Leckman (1986) suggest that Tourette syndrome is etiologically related to chronic tics and also to obsessive-compulsive disorder, and is inherited as a "highly penetrant, sex-influenced, autosomal dominant trait." Donnai (1987) has presented evidence that the gene location suggested by Comings (Comings et al, 1986), 18q22.1, is correct. Her patient's karyotype revealed a deletion at 18q22.2. Prevalence of Tourette has been estimated at 1/2000 for total manifestations of the syndrome to 1/200 or 1/300 for multiple tics (Licamele and Goldberg, 1988).

Treatment of genetic disease that corrects the abnormal gene or introduces the lacking enzyme constitutes a cure and may be possible in certain inborn errors of blood formation by means of bone marrow transplant. Organ transplants have also been attempted in mucopolysaccharide storage diseases with little success. Specific but noncurative treatment of genetic diseases may involve withholding the substrate that accumulates, as in PKU, administration of a lacking end product, as in diabetes, or other supplementation, as in vitamin-dependency diseases. Ameliorative but non-specific therapy permits symptom reduction. The "U" Series, an Orthomolecular treatment modality (fig. 1), is a method of reducing metabolic accumulations associated with many genetic diseases and of supplying necessary nutrients. Prenatal, or even presymptomatic diagnosis is not available for Tourette syndrome; the syndrome is diagnosed only as it unfolds (Licamele and Goldberg, 1988).

By contrast, a third copy of chromosome 21 is diagnostic of Down syndrome prena-tally as well as postnatally. The relationship between aneuploidy and Down syndrome was established in 1959 (Lejeune et al). Jacobs' (1959) research led to the suggestion that "mongols are trisomic for one of the smallest acrocentric autosomes." Discovery of the chromosomal basis of Down syndrome has furthered the view that it is an untreatable as well as incurable disorder. Since the risk factor increases from 1/3000 at maternal ages 20 to 24 to 1/38 at maternal ages >45, the only accepted "treatment" at this time is to offer prenatal screening and elective abortion to women above the age of 35. No other medical treatment is considered scientific or standard. Nevertheless, the "U" Series has benefited patients with Down syndrome for more than 40 years (Turkel, 1975). The US Food and Drug Administration, though refusing to approve a New Drug Application for the "U" Series, has specifically stated that the "U" Series may be used to treat patients with Down syndrome in the state of Michigan. The Michigan board of medicine has investigated the "U" Series and has found no

1. US For DS. 9700 Cresta Dr., Los Angeles, CA 90035.

Figure 1.
ADULT DOSAGE OF THE "U" SERIES
PER CAPSULE OR TABLET

UMORPHOID - A & B	**BREAKFAST**
Thyreoglobulin	66 mg.
L. Triiodothyronine	25 meg.
Organic Iodide	66 mg.
Vit. A (water dispersible)	25,000 LU.
Vit. E as d-Alpha-tocopherol Acid Succinate, N.F.	10 LU.

UPNEOID	**B.L.D.**
Phenylpropanolamine Hydrochloride	20 mg.
Pyrilamine Maleate	25 mg.
Rutin	20 mg.
Ascorbic Acid t	100 mg.
Theophylline Magnesium (or Sodium) Glycinatel	OO mg.
t ascorbic acid to be individually	supplemented.

UTEPTOID A	**BREAKFAST-DINNER**
Betaine-Choline Tartrate	100 mg.
Choline-Methionine Tartrate	100 mg.
Inositol	**50** mg.
Unsaturated Fatty Acids (linoleic-linolenic-sitosterol)	100 mg.
Desiccated Liver	150 mg.

UPEPTOID B	**DINNER**
Betaine HCL	66 mg.
Papain	66 mg.
Pepsin	66 mg.
Pancreatin	66 mg.
Diastase	3.3 mg.
Ketocholanic Acid	66 mg.
Desoxycholic Acid	66 mg.

UNOID	**B.L.D.**
Pentylenetetrazol	50 mg.
L. Glutamic acid	200 mg.
Nicotinic acid	50 mg.

Full dosage ..... ten years and over
Half dosage..... ages 5-10 years
One-third dosage ..... ages 2-5 years
One-fifth dosage..... ages 1-2 years
One-tenth dosage..... under one year old

UTROPHOID B	**LUNCH**
Thiamin Mononitrate	20 mg.
Riboflavin	20 mg.
Calcium Pantothenate	20 mg.
Para Aminobenzoic Acid	20 mg.
Pyridoxine	20 mg.
Niacin	20 mg.

UTROPHOID C	**DINNER**
Cyanocobalamin	25 meg.
Folic Acid	5 mg.
Calcium (Calcium citrate)	30 mg.
Cobalt (Cobalt Chloride)	0.1 mg.
Copper (Copper Sulfate)	1 mg.
Iodine (from Potassium Iodide)	0.15 mg.
Iron (ferrous gluconate)	10 mg.
Magnesium (from Magnesium Sulfate)	1 mg.
Manganese (from Manganese Sulfate)	1.25 mg.
Molybdenum (from Sodium Molybdate)	0.1 mg.
Zinc (from Zinc Sulfate)	1mg.

SUPPLEMENTS	
Zinc gluconate	31.5 mg.
Calcium Pantothenate	50 mg.
Pyridoxine	50 mg.
Potassium Gluconate	50 mg.
Magnesium	50 mg.
Niacinamide	15 mg.
Thiamin	2.2 mg.
Riboflavin	2.2 mg.

UPNEOID C	**PRN**
Naphazoline HCL	0.025%
Pyrilamine Maleate	0.250%
Chlorpheniramine maleate	0.125%
Methyl Paraben	0.005%
Propyl Paraben	0.010%

DENTAL ANESTHETIC	**PRN**
Benzocaine U5P	16%
Chlorobutanol USP	5%

DIURETIC

Furosemide 40 mg. - two days per week (e.g. Sundays and Thursdays) with breakfast only.

BREAKFAST-LUNCH

Bone meal contains: Phosphorus 300 mg.
contains: Calcium 600 mg.
contains: Vitamin D-3 (natural)* 100-200 LU.
Calcium 130 mg./Magnesium 60 m_K. from Dolomite 200 mg.

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objections regarding safety and efficacy. Patients treated with the "U" Series number well over 5000 to date, including those treated abroad by their own physicians.

We present a case of Down syndrome with Tourette syndrome in which treatment with the "U" Series for Down syndrome may have delayed the onset of the tic disorder. Resumption of treatment with the "U" Series has reduced the effective dosage level of haloperidol required to control the tics.

First Treatment Period

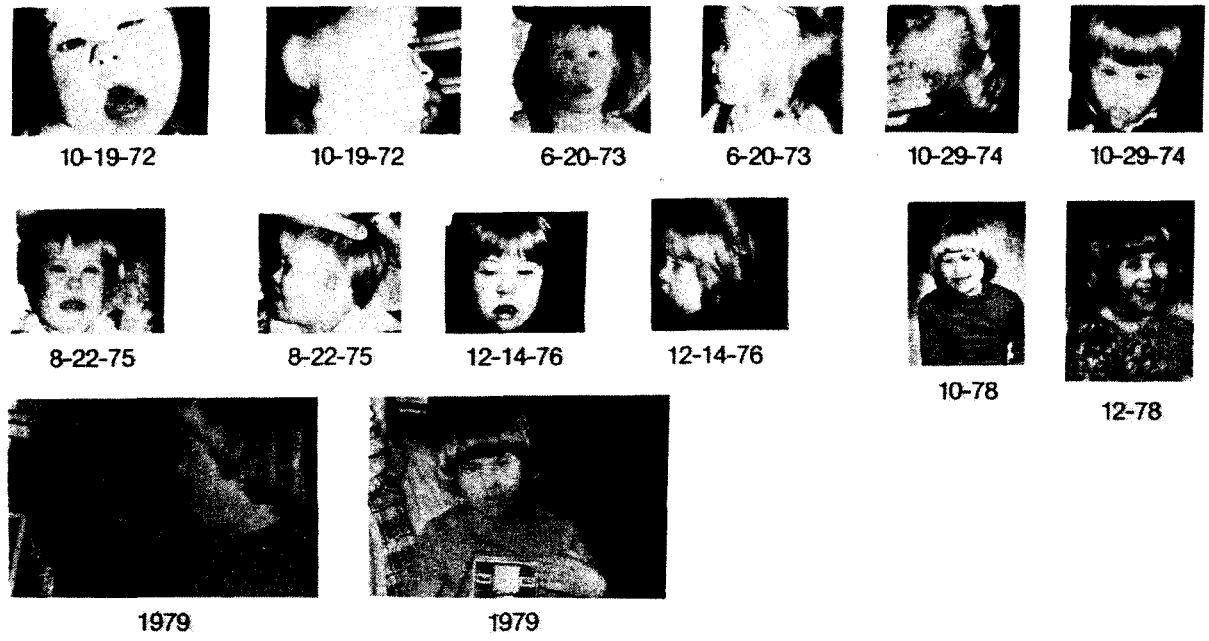
RT, born 8/20/71, was referred for treatment with the "U" Series at the age of 14 months (10/19/72). The diagnosis of Down syndrome was confirmed by chromosome analysis. As an infant, she had been treated for six weeks with ACTH for infantile myoclonic seizures, unrelated to Down syndrome. At the age of six-and-a-half months, her motor development was at the four-to-five month level, and other skills were at the two-to-three month level. At the age of 11 months, with her seizure disorder under control, her developmental level, by her pediatrician's report, was approximately two months behind her chronological age although she was not yet sitting or crawling.

X-rays taken when R was 14 months old demonstrated several skeletal anomalies compatible with Down syndrome including flaring of the iliac wings and slight flattening of the acetabular angles. The skeletal system is delayed in prenatal and postnatal development in Down syndrome. As a result, these patients may have single palmar lines, incurved fifth fingers, delayed bone age, and pelvic abnormalities. Other aspects of this pattern include delayed development of the nasal bridge, which in turn, produces the typical epicanthal eye-folds. In addition to developmental delay, the accumulations of the trisomy result in other specific characteristic features, such as macroglossy and thick gums with narrow palate. Moreover, Down syndrome is associated with close to *5%* of the cases of mental retardation (Steele, 1982). In untreated individuals with Down syndrome, there is an uneven but inexorable decline in the IQ with advancing age (Lott, 1986).

The goal of ameliorative therapy of
Down syndrome is to reduce the accumulations, accelerate physical and mental development, and to improve general health. Some treatments have accelerated skeletal development (Anneren, 1984) without improving mental development or general health; others have raised IQ scores (Harrell, 1981) without accelerating physical development or improving general health. The "U" Series therapy leads to improvements in the areas of physical growth and development, general health (Turkel, 1975); improved intellectual ability (Turkel, Nusbaum, Baker, 1984); and prevention of the decline in IQ scores with advancing age. In a random sample (n = 31) of the 209 patients treated with the MD "U" Series, IQ scores increased while the scores of untreated children declined (Iida and Kurita, 1969; Tomoda, 1975). In our sample, IQ scores of patients treated with the "U" Series likewise increased; scores of untreated children declined with advancing age (Turkel and Nusbaum, 1985).

At the time of R's first examination, her mother stated that R was a fitful sleeper, awake most of the night, and an irritable baby. Her hands and feet were cold; her skin was dry. These behavioural and physiological features are not typical of Down syndrome. After six months of treatment, she began to sleep through the night, her hands and feet were warmer, and her skin was less dry. At her two-year developmental evaluation, her motor development was at the 20-month level, and language, adaptive, and social development were at the 16-to-18 month level.

During the course of treatment, school evaluations noted improvement in all areas, including attention span, a specific problem for her. At the age of four, her social age was three years eight months. She was still hyperactive. However, when the "U" Series was withheld, she became listless. Six months later, her behaviour was aggressive and disruptive during three days out of every two weeks, on the average. Her short attention span continued to interfere with cognitive development. Because of aggression and attention deficit disorder, partly controlled by the ,"U" Series (though atypical of Down syn-drome), R remained on treatment for 10 years and on maintenance dosage for two



additional years. "U" Series treatment ended December 1984, with a two-month supply of medication remaining on hand for emergency use. The usual course of "U" Series therapy is four to six years. Improvements in Rachel's appearance over the treatment period are evident (fig. 2).

In March 1985, three months after treatment was discontinued, attention deficit disorder recurred and tics first appeared, starting with inattentiveness at school, slight head and shoulder movements, and facial grimaces. Within two weeks, the severity of motor and vocal tics increased, becoming uncontrollable when R was under stress. At the same time, she claimed to see things that were not there. Similarly, Donnai's (1987) patient presented with obsessive-compulsive behaviour, had panic attacks, and reported visual hallucinations.

On June 6, 1985 the diagnosis of Tourette syndrome was made, and R was placed on haloperidol, 1 mg per day, increased after 10 days to 2 mg per day. Compulsive inappropriate touching of others, increased fears, and incontinence were other effects of the syndrome or treatment. Her appetite was ravenous; she gained almost 20 pounds in three months. Attempts to reduce the dosage of haloperidol had resulted in the recurrence of motor and vocal tics and insomnia. To treat attention span deficit, not unusual in patients with Tourette syndrome, pemoline, a central nervous system stimulant, was prescribed for a trial period of 10 days. However, R became extremely agitated, and this treatment was discontinued. Thyroxine was prescribed, and R's obsessive fears diminished. Adverse effects of thyroxine included heart palpitations, constipation, and pre-esophageal dysphagia. Her mother reported that the appearance (facial edema) and behaviours (tongue thrusting) of Down syndrome were returning.

In December 1985, Mrs. T began to dispense the remaining maintenance dosage of the "U" Series. Noticing improvement in attitude, behaviour, awareness, alertness, and appearance, she returned with R for further treatment with the "U" Series March 1986.

Skeletal Changes

X-rays were taken. There was neither flaring of the iliac wings nor flattening of the acetabular angles. These results correspond to the findings in Japan. Tomoda (1975) reported improvements toward the norm in four types of anomalies of Down syndrome over eight years of treatment with the modified "U" (MD) Series: retarded skeletal development; brain-wave abnormalities; biochemical abnormalities; mental retardation. The study of skeletal abnormalities included measurement of the ilium index. Normal children show more than 60 in the index. Tomoda examined 80 untreated children with Down syndrome aged newborn to six, with the following results:

age	number	percentage with ilium index <60
0	8/8	100%
2	13/13	100%
3	15/15	100%
4	15/15	100%
5	12/13	92%
6	14/16	83%

He then examined 30 randomly selected children treated continuously from 1968 to 1974, with the following results:

age	**number**	**percentage with ilium index <60**
0	30/30	100%
2	26/30	87%
3	26/30	87%
4	18/30	60%
5	12/30	40%
6	8/30	27%

According to Tomoda, normalization of development of the wrist bone and second lumbar vertebra was even greater than that of the pelvis. Ten of 16 (63%) of the untreated children at the age of six retained the wrist features of underdeveloped bone age as compared with five of 30 (17%) of the treated children. Abnormalities of a recess on the front edge of the second lumbar vertebra were retained by eight of 16 untreated children and none of 30 (0%) of the treated children, all of whom had displayed this abnormality at the start of treatment. R's bone age at 14 months was nine-to-12 months. At the age of 14!/2 years, her bone age was 14 1/2-to-15 years. The latter X-rays revealed very slight scoliosis of the lumbar spine. Positive results in IQ scores and skeletal development of patients treated with the "U" Series at the Turkel Clinic, together with reports by Iida and Kurita (1969) and Kurita (1977) will be supplemented by data from the 1981 -1987 experience of the Japanese with the "U" Series when these become available, as well as the results of an ongoing cross-over, double-blind study in Europe. Davis (1988) has recommended that since the "extensive and long-term Japanese experience with the "U" Series in Down syndrome ... has not been adequately reported," concise summaries of all patients be prepared. This work is in progress.

Second Treatment Period

When "U" Series treatment resumed, R lost 10 pounds in four months. To supplement the "U" Series, another physician prescribed 5 mg diazepam and .1 mg thyroxine. These supplements were discontinued in June 1986 because of tachycardia. Decreased fluid accumulations — puffiness of the eyelids, macroglossy — and decreased tongue thrusting were early results of resumed "U" Series therapy. Interestingly, the symptoms of Tourette syndrome also diminished, and the effective daily dosage of haloperidol was reduced to .3 mg. Animal studies have suggested that "megavitamin therapy, which includes pharmacological doses of [ascorbic acid], has been successful in treating certain forms of schizophrenia" (Rebec et al, 1985), and that haloperidol, given with ascorbic acid in their study, provided significantly greater improvement than haloperidol alone.

Summary

R**,** a patient with Down syndrome, was treated with ACTH to control infantile myoclonic seizures. Treatment with the "U" Series was instituted when she was 14 months old and continued for 13 years. Although previous attempts to terminate "U" Series therapy resulted in attention span deficit, a non-treatment period began December 1984. Three months later, R developed a movement disorder diagnosed as Tourette syndrome. Haloperidol failed to control the most disturbing behaviours, such as compulsive touching of others in inappropriate places. Either termination of the "U" Series or the administration of haloperidol led to rapid weight gain, lethargy, and sedation that prevented further academic progress. "U" Series therapy was reinstituted in March 1986. New X-rays demonstrated that a previous abnormality of skeletal development had normalized. R's general health remained excellent, as anticipated in a patient treated with the "U" Series. Her academic ability has deteriorated following the onset of Tourette syndrome. She continues to receive the "U" Series and a reduced dosage of haloperidol.

Discussion

The presence of trisomy 21 does not preclude development of any other syndrome,

disease, or disorder. When a child with Down syndrome displays disturbing behaviours, the cause should be investigated just as in any other person. A patient with Down syndrome is too often stereotyped as atypical in all aspects. In the case of R, agitation, hyperactivity, and motor disorders were attributed to the primary diagnosis. During her years of treatment with the "U" Series, these separate problems were more or less under control, possibly as an effect of the medication and necessary nutritional supplementation.

Since the "U" Series has benefited patients with other genetic disorders (Turkel, 1981), and since Tourette syndrome may be a genetic disorder involving the backup of a substrate behind an enzymatic block, it may be that the "U" Series reduced the abnormal metabolites. Almost as soon as "U" Series therapy was discontinued, the movement disorder manifested itself. Within three months, in March 1985, the tics of Tourette syndrome became evident, and a firm diagnosis was established in June 1985. We suggest that the "U" Series may have delayed the onset of the movement disorder. Whether as a result of therapy with haloperidol or discontinuation of the "U" Series, R promptly gained 20 pounds, and the features of Down syndrome became increasingly prominent. Fourteen months following termination of the maintenance dosage of the "U" Series, treatment was resumed. The puffy facial features and excessive weight were lost within weeks. Tourette syndrome remains overwhelmingly stressful to this moderately retarded patient and her family. However, several symptoms of both syndromes have been alleviated by the second course of treatment with the "U" Series, which has also permitted reduction of the effective dosage level of haloperidol.

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Book Reviews

Reducing the Risk of Alzheimer's *by Michael A. Weiner, Ph.D.* Quantum Books, Box 2056, San Rafael, CA 94912-2056,1987.176 pages, $17.95 US

This book treats Alzheimer's disease primarily as a toxic psychosis due to the accumulation of aluminum in the brain. It follows that eliminating aluminum from our diet will prevent Alzheimer's or reduce the risk that it will develop.

Alzheimer's disease was a rare problem when it was first described in 1906. Now it is present in half of all seniles in the U.S.A. and i n 5 to 15 percent of al 1 people over age sixty-five. It begins around age fifty and can come on at any age thereafter.

The first symptoms are insidious and not disabling. There is a decrease in drive, in initiative and energy. The person gradually withdraws from engaging in new activities. The first clear clinical stage is characterized by forgetfulness: first for short-term memory, later for long-term memory. Into the second stage confusion and disorientation are added. During this phase the victim may still live at home if supported by a loyal and devoted spouse or other relative. In the last stage, deterioration is marked and all intellectual activity is lost. By this time they must be in special institutions. It is finally diagnosed after death at pathological examination of the brain.

There are many pathological changes:

1. Neurofibrillary tangles rich in aluminum silicates.
2. Senile plaques in the same areas.
3. Abnormal chemical changes in brain cells in the same areas.

A number of factors may be involved, but according to Dr. Weiner, the aluminum theory best explains all the findings.

The solution is to avoid aluminum. In modern society this may be very difficult. This is done: (1) by avoiding foods containing aluminum — the most common aluminum salt is sodium aluminum phosphate; Weiner provides a list of foods which contain aluminum; non-prescription drugs may contain aluminum — these too are listed; (2) by avoiding occupational sources of aluminum; (3) by eliminating aluminum in the kitchen, for example by never wrapping highly acid or alkaline foods with foil and by avoiding aluminum cookware.

Treatment is not very satisfactory. Aluminum may be removed by chelation. Nutrition is improved, a few drugs seem to be partially helpful, but very few recover. It is certain prevention would be more effective.

However, this book is not pessimistic by any means. There is no doubt that Alzheimer's is a nutritional disorder caused by the massive deterioration in the quality of our diet. It is a slowly developing, insidious disease which probably starts many years before the first symptoms become clear. This means that we are able, most of us, to cope with the slowly developing changes in our brains for many years. If we give up our modern, high-tech diet and follow a diet which is more similar in quality to the paleolithic diets we have adapted to, the prevalence of Alzheimer's would drop in a matter of several decades to its previous historically low levels.

I recommend that everyone not following these nutritional (Orthomolecular) principles — especially if there is a family history — should read this book and take its message very seriously. It is not too late, unless the brain has already been partially destroyed.

A. Hoffer, M.D., Ph.D.

The Paleolithic Prescription *by S. Boyd Eaton, M.D., Marjorie Shostak and Melvin Konner, M.D., Ph.D.* Harper & Row, Publishers, New York, 1988. Hardcover, 306 pages.

The plague of chronic disease in modern industrialized societies results from a major dysharmony between our genetic needs for food to which we have adapted, and the

foods we actually eat. This will not surprise readers of this journal, Hoffer and Walker (1978), Hoffer (1983). This is also the conclusion of Eaton, Shostak and Konner (1988). In this excellent book these authors have come to the same conclusion. They have examined the food and lifestyles of our ancestors relative to our modern society. There was a relatively stable relationship between the foods we had been forced to adapt to over many years, and the foods we continued to eat. But beginning about 10,000 years ago there began an ever-widening gulf between our genetic needs and the foods we provided. Our genetic requirements have altered little — our foods have been totally altered. It is this discrepancy which has created our present crisis of chronic disease, with nearly every second person suffering from one or more.

The authors recommend we try to restore the harmony. This, of course, is what Orthomolecular nutritionists have been recommending for the past twenty-five years. The authors suggest further that we re-create some of the other factors which shape our health and psychosocial culture, such as fitness and social organizations to which our genes had been tuned.

This is a very valuable book, providing a mass of detail about ancient diets, modern diets and how to re-create a diet much more like our ancestral diets. There are a few conclusions which are incorrect and which can be ascribed to the authors' unfamiliarity with Orthomolecular literature and with some of the standard literature. Thus they write about niacin that, "... it has recently been shown to be toxic in large amounts." This statement has no scientific meaning since *large* is not defined. They could mean one pound per day. I know of no recent evidence that niacin used in recommended doses is toxic. On the contrary, in doses of 3 to 9 grams per day it is one of the few nutrients to lower mortality and to increase longevity, Canner (1985). It is now a standard prescription for lowering cholesterol levels and in elevating high density lipoprotein cholesterol.

I do find it incredible that there is not a single literature reference to any of the Orthomolecular scientists, even though the word is mentioned once. Linus Pauling, Irwin Stone, Carl Pfeiffer, Roger Williams, Bernard Rimland, Donald Davis, Emmanuel Cheraskin, and a host of others, are totally ignored.

But it is a great book, and when future editions have corrected these errors, it will be even more valuable.

A. Hoffer, M.D., Ph.D.

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