BREAHTHROUGH CONCEPT FOR TREATMENT OF DOWN'S SYNDROME

A TREAMENT BY THE USE OF HERBAL NUTRITIONAL SUPPLEMENT

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Synonym's:

Trisomy 21:Mongol child: Mongolian idiocy

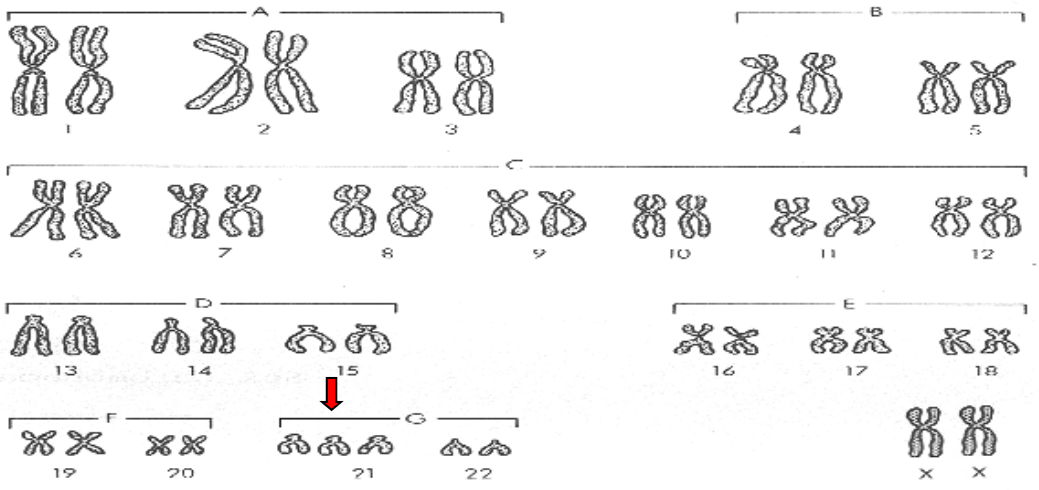
Introduction:

A chromosome is a rod-like structure present in the nucleus of all body cells, with the exception of the red blood cells, and which stores genetic information. Normally humans have 23 pairs of chromosomes, the unfertilized ova and each sperm carrying a set of 23 chromosomes. On fertilization the chromosomes combine to give a total of 46 (23 pairs). A normal female has an XX pair and a normal male an XY pair.

Chromosome abnormalities give rise to specific physical features. The problem varies from a range of cognitive disabilities as well as other attributes. Out of the so many genetic abnormalities one of the most common abnormality is **Down's syndrome.**

What is Down's syndrome:

Down syndrome, a chromosomal disorder, occurs when, instead of the normal complement of 2 copies of chromosome 21, there is a whole, or sometimes part of an, additional chromosome 21.



Down Syndrome

Incidences:

Approximately 1:700 live births (Recently reported as 1:1000 or 1:1100)

Causes:

Down's syndrome is caused by an error that occurs during the formation of the twenty-first chromosome. Its occurrence is sporadic and the parents are usually unaffected. The factors, which adds to the increasing incidence of this disorder are

- use of various approaches for prevention of pregnancies
- Amniotic fluid examination
- ***Elderly mother***, though the majority of children with Down syndrome are born to younger mothers.

However, in a minority of cases (3-4 per cent) a mother may have a balanced translocation of chromosome 21. In these cases the condition is inheritable.

Clinical features: (The details of characteristics are given in annexure 1)

Early Presentations in new born:

Apathy with feeding difficulties, prolonged physiologic jaundice, profound diffuse hypotonia, hyperextensibility of joints, and slowed response of neonatal reflexes are evident symptoms. Generally, children with Down syndrome are maladroit, move slowly, and have an unsteady, wide-based gait. Seizures, including infantile spasms, occur in approximately 2% to 9% of the patients. Some of the facial features, which identify an individual as having Down's syndrome include:

- Low set ears
- Up slanting palpebral fissures
- Low nasal bridge and dorsum
- Abnormal and excessive facial fat distribution
- Protruding, enlarged tongue
- Both prenatal and postnatal growth deficiencies can exist in the Down's patients. They often exhibit a short stocky stature and also have delayed growth of the brain resulting in a reduced mental capacity.

The extent to which they are intellectually deficient varies from patient to patient.

Neuropathology

- Pronounced and distinctive deceleration of nervous system development manifests
- Mild reduction of brain size and weight occurs. Mainly frontal lobe, brain stem and particularly the cerebellum is affected. Abnormality in cerebellum explains the generalized hypotonia in these children
- Myelination is incomplete or delayed in some cerebro cortical areas, such as the frontotemporal lobe and especially in the U fibers and the cerebello cortex

- The gross cortical convolution patterns are embryonic. A narrow superior temporal gyrus, an exposed insula resulting from lack of development of third frontal gyrus, and a short fronto occipital diameter with steep inclination of both occipital lobes
- Hippocampal dysgenesis discernible prenatally
- Histopathologically there is reduction in number of spines along with the apical dendrite of pyramidal neurons. A lack of granular cells and decreased aspinous stellate cells

Biological studies

- **An overall decrease in the efficiency of cellular metabolism, especially of brain.**
- Thyroid dysfunction
- Immune system derangements

Dermatoglyphics:

Displacement of the palmar triradius distally to the centre of the palm (ATD angle, formed between line drawn from the triradii at the bases of the index and little fingers to the axial triradius, greater then 45 degrees), a tibial arch on the hallucal areas of the sole, an unusual finger print pattern, including ulnar loops on all 10 digits.

Karyo typing

It may be of three types

1. 47 XX, +21 or 47XY, +21
2. t(14q 21q) ; t(21q 22q) ; t(21q 21q)
3. Mosiac pattern 46/47, +21

Prognosis and Life expectancy in children with Down's syndrome

1. One third of infants do not survive more than an year
2. One half dies during the first five years of life
3. Although there have been many advances in the medical care of these patients, the life expectancy of a patient with Down's syndrome may be up to 50-60 years
4. Cause of death is usually cardiac complications and respiratory infections

Future risk

The risk for future children conceived by the same couple is minimal.

Neuro imaging studies:

Reveal under development of the temporal lobes and calcium deposits within the basal ganglia and cerebellar folia, also indicated as poor cerebral perfusion.

Prenatal diagnosis

- Tripple Marker Test – Usually done Between the 15th and 20th weeks of pregnancy
    - hCG (human chorionic gonadotropin), which is made by the placenta
    - estriol, which is made by the placenta and the fetus
    - alpha-fetoprotein (AFP), which is made by the fetus
- level of inhibin-A, which is made by the placenta, also is measured – Increased in DS

Alfa Feto protein	**Estriol,**	**hCG (human chorionic gonadotropin),**	**Inhibin A**	**Expected associated conditions**
Low	Low	High	High	Down's syndrome
Low	Low	Low	Low	trisomy 18 (Edward's syndrome)
High	-	-	High	neural tube defects (e.g. spina bifida - may have associated increased levels of acetylcholinesterase in the amnionic fluid),omphalocele, gastroschisis,multiple gestation (like twins or triplets)

- Amniocentesis is usually offered at 16 weeks
- Chorionic villus sampling is usually available at ten to twelve weeks
- Fetal scans for 'neck translucency' are also used

Down's syndrome and Alzheimer disease

There is speculation that Alzheimer disease is a part of the pathological process of Down's syndrome. The following are the similar findings observed in both the diseases:

- Early appearance of neurofibrillary tangles, senile plaques or both, as well as strand like clusters of filamentous protein in the perikaryon
- High frequency of hematological cancers

- Decease in Choline acetyltransferase in the cortex
- Decrease in neurotransmitters (Dopamine, serotonin, nor epinephrine)
- Selective loss of cells in the nucleus basalis of meynert.

Treatment:

1. Treatment of decreased efficiency of brain

Biological studies in cases of down syndrome have revealed decrease in the efficiency of cellular metabolism, especially of brain. It have also been documented by reduced cerebral perfusion of brain. So far no way was there to improve cellular metabolism of brain, hence brain functioning. An effort by KRASS have come out with a **herbal supplement (Details about supplement and its mechanism of action is given in annexure 2)** which is very useful in improving the cellular metabolism of brain hence giving an improvement in functioning of brain. Two case studies have been narrated in Aneexure 3 and Annexure 4 for ready reference.

2. Treatment of complications

Treatment of the anomalies associated with this syndrome include a surgery to correct the eye slant and to remove the skin folds from the inner corners of the eyes. These patients usually require nasal surgery to augment and increase the projection of their nose. In addition, some of the fat in their cheek can be removed to reduce the fullness of their face. It may also be necessary to reduce the size of their tongue to increase its mobility.

3. Speech therapy for improve their speech.

4. Training – This includes school training and vocational trainings

Annexure 1

Detailed clinical features of Down Syndrome

Head: small brachycephalic head, large anterior fontanel and widely separated sutures, a flat facial profile with depressed nasal bridge; upward slanted palpebral fissures; epicanthi; narrow palate; loose skin folds on the posterior portion of a short neck; and low-set, small, and misshapen ears with a narrow auditory canal {Aase et al., 1973].

Hands and Foot: Incurvation of the fifth finger (bradyclinodactyly), which is usually short because of hypoplasia of the middle phalange; broad, short hands; solitary transverse palmar crease (simian line); and a wide gap between the first and the second toe are typically evident but are not of diagnostic value.

Skin: Cutaneous manifestations are variable and nonspecific [Colomb et al., 1977]. Hyperkeratotic lesions, alopecia areata, adenomas of the sweat glands (syringomas), psoriasis, although rare, may be present.

Eyes : Brushfield spots (circumferential specking of the iris resulting from a diminished amount of storma), squint, and lens opacities. Refractive error and senile cataracts may appear later. nystagmus and slowly reactive pupils. Blepharitis is also a disturbing feature.

Ear : congenital malformation of the bones of the middle ear, permanent fixation of the stepes, and shortening of the cochlear spiral. Hence an increased frequency of sensorineural hearing loss.

CVS : Congenital heart diseases have been found in about 40% of cases. Ventricular septal defect appears to be the most common disorder.

GIT : Congenital disorders have been found in about 20% of cases. Cheilitis sometimes are disturbing features;

Bones : Decreased of acetabular and iliac angles, radiographs demonstrate narrowing of the cervical canal and subluxation of the atlantoaxial process. Accentuation of these abnormalities may lead to paraplegia or tetraplegia.

CNS : Mental retardation is an outstanding feature, varying from the educable retarded state to a non communicative bedridden condition. Most patients have poor articulation and an extremely limited vocabulary. Less than 5% are able to read, and even fewer can write. Although most patients have a pleasant, docile, and happy personality, some have pronounced behavioral difficulties consisting of hyper-activity and outbursts of anger with increased frequency during adolescent and adult years.

Language and communication skills : obviously delayed. The majority appear to have expressive language disabilities disproportionate to their general cognitive limitation [Miller, 1988].

Annexure 2

MODE OF ACTION OF HERBAL NUTRITIONAL SUPPLEMENT IN CASES OF DOWN'S SYNDROME

The major histological findings in brain of the cases of Down syndrome are:

1. **In general there is an overall decrease in the efficiency of cellular metabolism in neural tissues.**
2. A Decrease in the spinous processes along the apical dendrites of the pyramidal neurons
3. A lack of granular cells, specially that of aspinous stellate granular cells
4. At The age of 30-40 years there is early appearance of neurofibrillary tangles, senile plaques or both.
5. Myelination is incomplete or delayed in some cerebro cortical regions such as fronto temporal lobes, especially in U fibers and in cerebello cortex.

There is decreased in the efficiency of cellular metabolism in neural tissue. Thus even if the neurons does not reproduce or grow after 2nd year of the postnatal life, the increase in the surface area will mean that there will be an increase in the demand of energy to maintain the Resting membrane potential as well as to sustain on going neuronal activity. The increase in energy demand can be met only by increasing the regional blood flow to the effected area.

Reversal of fortune

Chemistry and Industry reports that this gene could now be the target for drugs to "downregulate" the action of the extra gene - although these drugs are some time away. Remarkably, there is some hope that a drug to reverse this gene defect could actually reverse retardation to some degree even in adults. This area of the forebrain does not require new brain cells - it already has cells, but they are simply not working properly. The theory is that a drug to restore their proper activity could have a marked effect. With the perfect drug at the right dose, the protein production by the extra copy of the gene can be reduced, which could reverse mental retardation

What is this herbal supplement by AAY achieving

How the functioning of neural cells can be determined (Chugani HT. Functional brain imaging in pediatrics. The pediatric Clinic of North America. 1992; 4: 777-799)**:**

In normal functioning tissue, cerebral blood flow and metabolism are coupled, which have been termed as local cerebral metabolic rates for glucose (LCMRglc). LCMRglc can be measured by functional brain imaging viz. Positron emission tomography (PET) and single photon emission computed tomography (SPECT) are capable of detecting functional disturbances in the brain and are referred to as functional imaging. Because of the lack of facility of PET we conducted all work on SPECT.

How the functioning of neural cells can be improved in cases of Down syndrome:

So far no therapy was available to improve the **functioning of neural cells in cases of Down syndrome.** Conventional therapies are mainly based on physiotherapy and early intervention therapy is of help with rather slow improvement and that too, not in all cases.

A recent introduction of a herbal nutritional supplement (DS care) have given a ray of hope in cases of Down syndrome by improving the cerebral perfusion, and hence the functioning of brain.

Where not to treat

- Children suffering from convulsive disorder or having tendency for convulsion
- Children suffering from congenital Heart disease
- Children suffering from pulmonary arterial hypertension

How Herbal nutritional supplement (DS care- Cerebro flo) works:

Restore the proper activity of neural cells in all areas of brain, and hence improves the working of those cells which are not working properly. **Supplementation of herbal nutritional supplement improves the cerebral perfusion, and hence the functioning of brain in toto.**

What this supplement contains:

It contains the herbal ingredients. These ingredients are FDA approved (not included in exclusion list of FDA). The toxicity studies conducted as per WHO laid down criteria's revealed it non toxic.

What needs to be understood:

- This supplement can not change the genetic code hence 100% improvement is not possible
- Best results can be achieved when the supplement starts between the age group of 2-4 years
- It is a long course of treatment. Supplement helps in overall growth as child grows with age
- 100% children do not improves
- This supplement improves the brain functioning. It can not teach or train any thing to any child, hence training and teaching is a part and partial of this treatment.

प्ररूप ओ - 2
FORM O-2

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