

# Chromosomal Imbalance and Therapeutic Considerations in Down Syndrome

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## DESCRIPTION

Down syndrome is one of the most widely recognized chromosomal disorders and arises due to the presence of an extra copy of chromosome 21. This condition, also known as trisomy 21, results in a gene dosage imbalance that affects multiple biological systems. Unlike monogenic disorders caused by alterations in a single gene, Down syndrome involves the overexpression of numerous genes located on chromosome 21, leading to a complex and variable phenotype.

The genetic basis of Down syndrome can occur through three primary mechanisms: full trisomy 21, translocation, and mosaicism. Full trisomy is the most common form and results from nondisjunction during meiosis, leading to three complete copies of chromosome 21 in all cells. Translocation involves the attachment of an extra copy of chromosome 21 material to another chromosome, often chromosome 14. Mosaicism occurs when only a subset of cells carries the additional chromosome, resulting in a milder or variable clinical presentation. These different mechanisms influence both diagnosis and genetic counseling. At the molecular level, the presence of an additional chromosome leads to increased expression of genes such as *APP*, *DYRK1A*, and *SOD1*. Overexpression of *APP* is associated with early-onset Alzheimer-like neuropathology, which is commonly observed in adults with Down syndrome. The *DYRK1A* gene contributes to altered neuronal development and cognitive impairment, while *SOD1* influences oxidative stress pathways. The combined effects of these and other genes create a complex network of dysregulated biological processes.

Clinically, individuals with Down syndrome present with a characteristic set of physical and developmental features. Common findings include hypotonia, a flat facial profile, upward slanting palpebral fissures, and a single transverse palmar crease. Cognitive impairment is a consistent feature, although its severity varies widely. Developmental delays are typically evident in early childhood, affecting speech, motor skills, and learning abilities. Congenital heart defects are among the most significant medical concerns associated with Down syndrome. Atrioventricular septal defects are particularly common and require early diagnosis and management.

Advances in pediatric cardiology and surgical techniques have greatly improved survival rates. In addition to cardiac anomalies, individuals may experience gastrointestinal abnormalities, thyroid dysfunction, and an increased susceptibility to infections.

The neurological aspects of Down syndrome are closely linked to altered brain development. Reduced brain volume, particularly in the hippocampus and cerebellum, has been observed through imaging studies. These structural differences correlate with deficits in memory, coordination, and learning. Over time, many individuals develop neuropathological features similar to Alzheimer's disease, including amyloid plaques and neurofibrillary tangles, largely because of overexpression of *APP*. Diagnosis of Down syndrome is typically established through cytogenetic analysis, such as karyotyping, which identifies the additional chromosome. Prenatal screening methods, including non-invasive prenatal testing and ultrasound markers, allow for early detection during pregnancy. Confirmatory diagnostic procedures such as amniocentesis or chorionic villus sampling provide definitive results.

Therapeutic approaches for Down syndrome focus on managing associated medical conditions and supporting development. Early intervention programs play a crucial role in improving cognitive and motor outcomes. These programs often include speech therapy, physical therapy, and specialized educational support. Individualized care plans are essential due to the variability in clinical presentation. Pharmacological research in Down syndrome is increasingly targeting specific molecular pathways. One area of interest involves modulation of *DYRK1A* activity, as its overexpression is linked to impaired neurogenesis and cognitive deficits. Experimental compounds that inhibit this kinase are being studied for their potential to improve cognitive function. Although these treatments are still under investigation, they represent a shift toward mechanism-based therapy. Another therapeutic avenue involves addressing oxidative stress the result from increased expression of genes like *SOD1*. Antioxidant therapies have been explored to counteract cellular damage, although results have been mixed. Continued research is needed to determine the effectiveness and appropriate application of such treatments.

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Gene dosage correction is an emerging concept in the field. While still far from clinical application, these approaches highlight innovative directions in genetic therapy that aim to address the root cause of the disorder. Behavioral and social support systems are critical components of care. Inclusion in educational and community settings enhances social development and quality of life. Families benefit from access to counseling services, support groups, and resources that assist in long-term planning and care coordination.

## CONCLUSION

Down syndrome is a complex chromosomal condition resulting from an additional copy of chromosome 21, leading to

widespread gene overexpression and multisystem involvement. Advances in medical care, education, and social support have greatly improved outcomes for affected individuals. Ongoing research into molecular mechanisms and targeted therapies continues to expand understanding and offers potential for future interventions aimed at improving cognitive and health outcomes.