Volume 3, Issue 2, 2025

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

A COMPREHENSIVE REVIEW OF TREATMENT APPROACHES FOR CONGENITAL AND HEREDITARY ANOMALIES

Sheikh Ahmed Gull[*1], Muhammad Asghar Khan[1]†, Samreen Hashmi[2]†, Tayyaba Noor[3], Maira Ali[1], Aisha Noreen[4], Anam Ul Haq Ahsan[5], Fareeza Anwar[6], Shah Zainab[6], Jamal Shah[7], Muhammad Qasam Javed[3], Muhammad Ali[7]

[1]*M.Phil, Human Genetics Program, Department of Zoology, Faculty of Biological Sciences, Quaid-i-Azam University, Islamabad, Pakistan*

[2]*Department of Wildlife and Ecology, University of Veterinary and Animal Sciences, Lahore, Pakistan*

[3]*FCPS, Department of Urology, Benazir Bhutto Hospital, Rawalpindi, Pakistan*

[4]*Department of Zoology, Kohat University of Science and Technology, Kohat, Pakistan*

[5]*Department of Bioinformatics, Hazara University, Mansehra, Pakistan*

[6]*Department of Zoology, Hazara University, Mansehra, Pakistan*

[7]*Molecular Biology Laboratory, Department of Zoology, Faculty of Biological Sciences, Quaid-i-Azam University, Islamabad, Pakistan*

†*These authors contributed equally and share second authorship.*

DOI: https://doi.org/10.5281/zenodo.15286622

Keywords
Congenital and hereditary anomalies, Therapeutics, Surgeries, Medications, Stem cell therapy, Genome editing, CRISPR-Cas9, Neurochips, Ethical challenges.

Article History
Received on 16 March 2025
Accepted on 16 April 2025
Published on 26 April 2025

Corresponding Author: *
Sheikh Ahmed Gull
ahmedgull@bs.qau.edu.pk

Abstract

Congenital and hereditary anomalies (CHA) are functional/structural deformities that may be present at birth or develop later in life, potentially leading to significant health problems globally. Prevalence is high in low- and middle-income countries and causes a large number of mortalities annually, necessitating treatment interventions for effective management. The objectives of this study were to highlight various treatment methods for CHA and to evaluate the effectiveness of advanced medicinal therapies, such as stem cell therapy, nanomedicine, and genome editing, in controlling associated diseases. Diagnosis of CHA has been significantly improved through initiatives like newborn screening programs, which enable the early detection of abnormalities in affected infants. The treatment of CHA varies depending on the type of disorder and the specific needs of the affected individuals. For structural disorders, surgery is often recommended. Additionally, CHA can be addressed through stem cell therapies, medications, gene therapies, neurochips, and CRISPR/Cas9 gene editing. Medical interventions for CHA differ greatly based on the type and severity of the disorder. For example, steroids are commonly prescribed for muscular dystrophy, while physical therapy is beneficial for maintaining muscle strength and reducing weakness. Speech therapy plays a crucial role in developing communication skills in children. Hematopoietic stem cell transplantation (HSCT) is often recommended for various blood cancers and diseases. Furthermore, advancements in technologies such as CRISPR-Cas9 and improvements in prenatal and neonatal care have significantly enhanced

Volume 3, Issue 2, 2025

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

survival rates among children with CHA. Despite advancements in treatments, further research is still needed to overcome certain difficulties and treatments.

INTRODUCTION

Congenital and hereditary anomalies (CHA) are functional or structural abnormalities that can be imparted before birth such as microtia, congenital distortions of the limbs or hands, cleft lip and palate, etc. surgical modifications are required to remove these CHA after birth or there are CHA that can emerge after birth like Alzheimer's disease, hearing loss etc. wherein affected persons stay symptomless for years till they acquire impediments like arrhythmias or congestive heart failure because of the slow weakening of cardiac performance, and may steer to analytical, physical, developmental incapacities, and other health issues (1,2). Alzheimer's disease, thalassemia, cancers like colon, ovarian, and breast cancers, diabetes mellitus, Turner syndrome, sickle-cell anemia, hemophilia, hypertension, cardiovascular disorders, Down syndrome etc. are the generic categories of CHA (3,4).

Conferring to an irregular evaluation the frequency of CHA is about 6% of a live births and its occurrence is greater in low and average earning states as the Worldwide dominance of CHA fluctuates from locality to locality (5). Owed to CHA, an assessed 240,000 infants expire globally in 28 days of delivery each year, and about 170,000 mortalities of kids among the ages of one month to five years are additionally caused by CHA. CHA can add to long-lasting sickness, which causes an important burden on patients, their relatives, health care organizations and polities (2,6,7).

To detect hearing loss syndromes and other genetic disorders soon after birth, campaigns like newborns screening have been founded. These campaigns are necessary for well-timed medication, which can considerably increase results for affected newborns (8). Holdup in the detection of CHA can occur in poor regions as approach to latest diagnostic machines remains reduced till birth, after which mediations may be less applicable (9). A multi penalizing method is used for treating CHA, marked therapies like antiangiogenic agents and inhibitors have turned out to be typical treatments that enhance results by affecting particular molecular pathways (10). In this review we will discuss about the different treatment approaches used for the handling of congenital and hereditary anomalies.

1. Outline of treatment Approaches

Nature and acuteness of the anomaly in addition to the personal requirements of the patient are the bases on which treatment methodology for CHA depends considerably. Here's an outline of available treatment possibilities (Figure, 1).

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

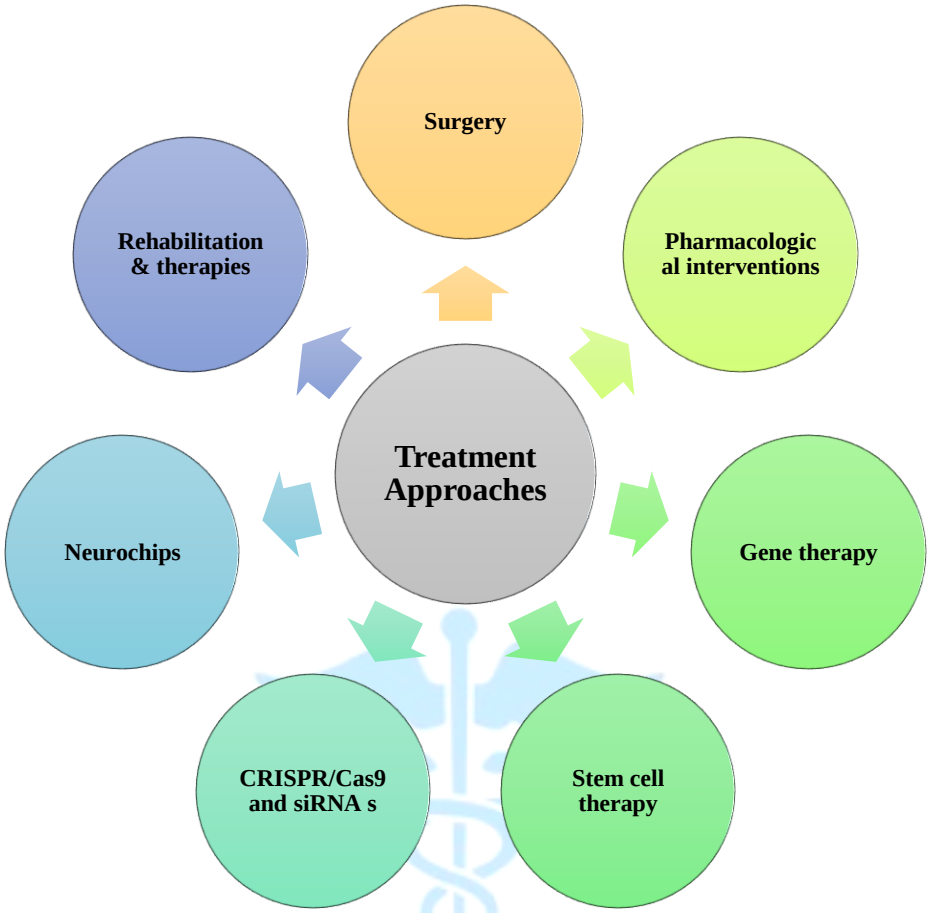

Figure 1 Flow chart of Treatment strategies for Congenital and hereditary anomalies (Source; MS word)

Surgical interventions

Sometimes surgical interventions are compulsory for treating CHA. (11,12). Anomalies that affect the internal organs or air passage are lethal and urgent surgery shortly after delivery may be required (13). Other situations like cleft palate and lip can tolerate for postponed intervention as the kid matures (11). Inequalities in healthcare systems and approaches cause the difference in the necessity of surgeries across the world. For instance, in countries like England, above 50% of the babies need surgeries during the first year of their lifespan, whereas in countries like Finland, the frequency was considerably lesser at 28% (16). Long-term consequences can be caused by these surgical interventions in newborns as these interventions impart integral hazards. In teenagers it has been proved by investigations that anesthesia utilized in such surgeries to handle CHA, creates alarms about potential influences on long-lasting cerebral performance (14,15). Moreover, the psychological pressure linked with pediatric surgical treatments can be considerable for the baby and parents equally, possibly causing shocking traumatic responses that can last prolonged after the process (16, 17).

Pharmacological interventions

Pharmacological interventions play a crucial role in the management of CHA, aiming to improve survival rates and quality of life for affected individuals. For congenital heart disease (CHD), angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, beta-blockers, and potassium-sparing diuretics are frequently used and have shown benefits in reducing mortality. Additionally, endothelin receptor antagonists, phosphodiesterase-5 inhibitors, prostaglandins, and soluble guanylyl cyclase stimulators are beneficial for patients with pulmonary artery hypertension (18). Levodopa remains the most effective treatment for Parkinson

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

disease (PD), often combined with peripheral decarboxylase inhibitors to enhance its efficacy and other symptomatic treatments including dopamine agonists (amantadine, apomorphine, bromocriptine, cabergoline, lisuride, pergolide, pramipexole, ropinirole, rotigotine), monoamine oxidase (MAO) inhibitors (selegiline, rasagiline), and catechol-O-methyltransferase (COMT) inhibitors (entacapone, tolcapone). However, chronic use can lead to complications such as the "wearing-off phenomenon" and other motor fluctuations (19). Similarly, for Epilepsy and seizures specific antiepileptic drugs (AEDs) is recommended as first-line treatment. For partial onset seizures, carbamazepine and lamotrigine are commonly prescribed, while sodium valproate is preferred for generalized onset seizures. Levetiracetam is also considered a suitable alternative for both seizure types, particularly for individuals of childbearing potential due to the teratogenic risks associated with sodium valproate (20). Pharmacological interventions for CHD are tailored based on the specific condition, severity, and individual patient needs. These treatments often require careful monitoring and may be part of a broader multidisciplinary approach that includes surgery, physical therapy, and genetic counseling.

CHA can be treated through medical interventions, comprising of a wide range of technologies, depending upon the type and severity of each disorder. For example, in case of muscular dystrophy steroids are prescribed to the patients, moreover strengthening of muscles and reduction of weakness is sustained by physical therapies (21). Latest advancements in neurological disorder therapies have opened new horizons of treatments for individuals suffering with disorders like migraines, multiple sclerosis, etc. (22). At the same time an exclusive role in treating various neurological diseases is performed by traditional medicines, utilizing many plant-extracted chemicals. (23). A major transformation in the dominion of medical interventions has been brought about by the innovation of nanomedicines, that have improved the distribution of medicines across the blood-brain barrier, thus increasing bio accessibility, and decreasing harmful results (24).

Gene therapy

Scientists are analyzing gene therapy in experimental tests to rectify the disorder at a cellular stage for example in case of treating Fanconi anemia, in which bone marrow washout is the main issue (25,26,27). In case of Leber Congenital Amaurosis, that are heritable retinal defects, the FDA-approved Luxturna is a revolution through which vision can be repaired by switching off malfunctioning genes (28). Researchers have revealed that enzyme action can be reconditioned by gene therapy, as in the case of Congenital Adrenal Hyperplasia, thus contributing to a new therapy pathway (29). Gene therapy has brought renovated aspiration for kids having Diamond-Blackfan Anemia who don't show any response to conventional medications (30).

Stem cell therapy

Stem cells like mesenchymal stem cells (MSCs) originated from amniotic fluid have been found by the scientists to be useful in many animal mockups (31,32). Trans amniotic stem cell therapy (TRASCET) is a procedure that controls these MSCs to heal or diminish the effect of CHA such as gastroschisis and spina bifida (33). Intravenous, intracoronary, and intramyocardial methods are certain procedures of providing stem cells that have been verified for CHA (34). Hematopoietic stem cell transplantation (HSCT) which is also known as Bone marrow transplantation (BMT) has turn out to be a critical therapy for different blood cancers and diseases. (35).

Stem cells from peripheral blood, umbilical cord blood or bone marrow can be used for HSCT and there are different ways to get stem cells like autologous (the patient's own cells), syngeneic (from an identical twin), and allogeneic (from an HLA-matched donor), every type having its specific array of advances and trials (36).

CRISPR/Cas9 and siRNA-based approach

In order to tackle disorders like CHD CRISPR-Cas9 possesses capacity by effectively generating or modifying genetic alterations (37). Gene expression modulation, high-throughput screening, and cellular tracking are certain techniques in which CRISPR-Cas9 is also utilized in addition to gene editing (38). In order to investigate initial developing

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

imperfections lately after a few hours of fertilization it has become exclusively significant as it is capable to transform both alleles in the F0 generation (39).

An inventive mode to transport siRNA or CRISPR/Cas9 to target cell is by using nanoparticles. Polymer-based and lipid-based nanoparticles can compact these gene-editing gears, thus boosting their distribution proficiency. Transmission of siRNA or CRISPR/Cas9 can also be carried out through manufactured dendritic cells, exosomes obtained from stem cells or macrophages (40).

Neurochips: Innovative therapies for Congenital neurological disorders

A true transformation is carried out by latest progresses in neurochip techniques in order to treat neurological diseases. For instance, the device analyzing with a comprehensive 256-channel sensor arrangement unites with **NeuralTree** system from the École Polytechnique Fédérale de Lausanne to identify and supervise indications of Parkinson's disease and epilepsy at right time (41). Similarly, **Neuralink** which is Elon musk 's company has come into headings through its initial human experiment of a brain transplant that allows individuals having quadriplegia to regulate machines only by imagining, although owed to continuing study and security alarms it is yet initial time for its extensive usage (42,43). In addition to all these works, scientists of Harvard University have shaped neuron-like grafts which boost tissue restoration and reduce immune reactions, thus possibly modernizing the methods of treating neurodegenerative disorders like Alzheimer's (44).

Rehabilitation and Therapies

In order to improve practical consequences in kids with CAs rehabilitation therapies are necessary. The necessity for therapy is predominantly amplified in situations including genetic disorders, analgesic reparation, and prematureness (45). Trials in neurodevelopmental results, for example perception, motor and sensory tasks, interaction, and behavior can be addressed through rehabilitation (46). Speech therapy plays an important role in developing the communication abilities in kids suffering with interaction trials alike individuals having cleft palate or lip, as they are required to correspond efficiently (47). Orthotics and prosthetics are performing crucial roles in rehabilitation for persons having CAs and amputations (48). An extensive variety of mediations and methodologies is being embraced by this field of rehabilitation (49). Psychotherapy is essential, providing assistance to families as they try to cope up with the economic and emotive challenges of nurturing a kid having congenital disorder. In this situation, much- desired assistance and assets can be provided by supportive parties and communities, thus enabling it to be comfortable for families to handle these trials (50).

2. Ethical Challenges and Limitations in Treatment

CHA present significant challenges and ethical considerations in treatment in Low midle income countries like Africa, superstitious beliefs about these anomalies create psychosocial challenges for affected families. These conditions often lead to chronic illness, disabilities, and poor quality of life (51). Techniques like CRISPR-Cas9 holds promise for cancer therapy; however, challenges such as the fitness of edited cells, editing efficiency, delivery methods, and potential off-target effects must be addressed before its implications in clinical settings (52).

Advancements in technologies for prenatal and neonatal care have improved survival rates for conditions like CHD and severe kidney anomalies, but raise ethical questions about patient-hood, distributive justice, and the balance between research and standard care. Multidisciplinary counseling is a crucial for decision-making, especially given the complex, lifelong medical care required (53,54). In case of neonatal surgery ethical concerns also arise regarding the use of life-sustaining therapies, prenatal diagnosis counseling, and the responsibility to provide high-quality care through participation in clinical trials.

3. Conclusion

The fruitful results of advancements in medical, genetical and surgical therapies, are the significant developments in CHA treatment. In spite of this advancement, there are hazards linked with these treatments, especially causing damages to permanent

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

intellectual growth and psychological consequences on individuals suffering from CHA and their relatives. New horizons to cope up with hereditary and neurological disorders have been opened by affiliation of advanced techniques like nanomedicine and gene therapy with medical techniques. CRISPR/Cas9 gene editing, stem cell therapy and Neurochips have shown possibilities of treating CHA such as bone marrow and retinal disorders. Despite of all these advancements in the fields of medicines, treatments, and research, still there exist certain difficulties such as restrictions in approaching the places containing resources, the emotional and psychological pressure of these treatments, and the need of making all this advancement and proceeding research to be consequential.

Acknowledgements

We would like to acknowledge Professor Dr. Sajid Malik for his support and guidance in publication process.

REFERENCES

1. Song J, Chen Y, Wei L, Ma Y, Tian N, Huang SY, et al. Early-life exposure to air pollutants and adverse pregnancy outcomes: protocol for a prospective cohort study in Beijing. BMJ Open. 2017 Sep 3;7(9):e015895. doi: 10.1136/bmjopen-2017-015895. PMID: 28871018; PMCID: PMC5588991.
2. World Health Organization. Congenital disorders [Internet]. Geneva: World Health Organization; 2023 Feb 27 [cited 2025 Feb 27]. Available from: https://www.who.int/news-room/fact-sheets/detail/birth-defects
3. Boloor A, Nayak R. Exam preparatory manual for undergraduates: medicine. JP Medical Ltd; 2018 Sep 30.
4. Kolanis S, Kotanidou EP, Tsinopoulou VR, Georgiou E, Hatzipantelis E, Fidani L, Galli-Tsinopoulou A. MTHFR gene polymorphisms and cancer risk in children and adolescents: a systematic review and meta-analysis. Children (Basel). 2025 Jan 17;12(1):108. doi: 10.3390/children12010108. PMID: 39857939; PMCID: PMC11764102.
5. Anane-Fenin B, Opoku DA, Chauke L. Prevalence, pattern, and outcome of congenital anomalies admitted to a neonatal unit in a low-income country-a ten-year retrospective study. Matern Child Health J. 2023 May;27(5):837-849. doi: 10.1007/s10995-023-03591-x. Epub 2023 Feb 28. PMID: 36853373; PMCID: PMC10115728.
6. Tantanokit J, Sansiriphun N, Sripichyakan K, Klunklin P. Prenatal harmful substances: Thai pregnant women's experiences. Belitung Nurs J. 2023 Aug 28;9(4):302-312. doi: 10.33546/bnj.2708. PMID: 37645574; PMCID: PMC10461167.
7. Xie Y, Wu R, Li H, Dong W, Zhou G, Zhao H. Statistical methods for assessing the effects of de novo variants on birth defects. Hum Genomics. 2024 Mar 14;18(1):25. doi: 10.1186/s40246-024-00590-z. PMID: 38486307; PMCID: PMC10938830.
8. Writing Group for Practice Guidelines for Diagnosis and Treatment of Genetic Diseases, Medical Genetics Branch of Chinese Medical Association, Yuan H, Dai P, Liu Y, Yang T. [Clinical practice guidelines for hereditary non-syndromic deafness]. Zhonghua Yi Xue Yi Chuan Xue Za Zhi. 2020 Mar;37(3):269-276. doi: 10.3760/cma.j.issn.1003-9406.2020.03.008. PMID: 32128743.
9. Goley SM, Sakula-Barry S, Adofo-Ansong N, Isaaya Ntawunga L, Tekyiwa Botchway M, Kelly AH, Wright N. Investigating the use of ultrasonography for the antenatal diagnosis of structural congenital anomalies in low-income and middle-income countries: a systematic review. BMJ Paediatr Open. 2020 Aug 20;4(1):e000684. doi: 10.1136/bmjpo-2020-000684. PMID: 32864479; PMCID: PMC7443309.

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

10. Al-Samkari H, Eng W. A precision medicine approach to hereditary hemorrhagic telangiectasia and complex vascular anomalies. J Thromb Haemost. 2022 May;20(5):1077-1088. doi: 10.1111/jth.15715. Epub 2022 Apr 7. PMID: 35343049; PMCID: PMC10044495.
11. American Society of Plastic Surgeons [Internet]. Congenital anomalies [cited 2024 Aug 8]. Available from: https://www.plasticsurgery.org/reconstructive-procedures/congenital-anomalies
12. Farmer D, Sitkin N, Lofberg K, Donkor P, Ozgediz D. Surgical interventions for congenital anomalies. In: Debas HT, Donkor P, Gawande A, Jamison DT, Kruk ME, Mock CN, editors. *Essential Surgery: Disease Control Priorities, Third Edition (Volume 1).* Washington (DC): The International Bank for Reconstruction and Development / The World Bank; 2015 Apr 2. Chapter 8. PMID: 26741013.
13. Ferrantella A, Ford HR, Sola JE. Surgical management of critical congenital malformations in the delivery room. Semin Fetal Neonatal Med. 2019 Dec;24(6):101045. doi: 10.1016/j.siny.2019.101045. Epub 2019 Nov 11. PMID: 31727572; PMCID: PMC7802585.
14. Garne E, Loane M, Tan J, Ballardini E, Brigden J, Cavero-Carbonell C, Coi A, Damkjaer M, Garcia-Villodre L, Gissler M, Given J, Heino A, Jordan S, Limb E, Neville A, Rissmann A, Santoro M, Scanlon I, Urhøj SK, Wellesley D, Morris J. European study showed that children with congenital anomalies often underwent multiple surgical procedures at different ages across Europe. Acta Paediatr. 2023 Jun;112(6):1304-1311. doi: 10.1111/apa.16726. Epub 2023 Mar 8. PMID: 36823678.
15. Ing C, DiMaggio C, Whitehouse A, Hegarty MK, Brady J, von Ungern-Sternberg BS, Davidson A, Wood AJ, Li G, Sun LS. Long-term differences in language and cognitive function after childhood exposure to anesthesia. Pediatrics. 2012 Sep;130(3):e476-85. doi: 10.1542/peds.2011-3822. Epub 2012 Aug 20. PMID: 22908104.
16. Muscara F, McCarthy MC, Woolf C, Hearps SJ, Burke K, Anderson VA. Early psychological reactions in parents of children with a life-threatening illness within a pediatric hospital setting. Eur Psychiatry. 2015 Jul;30(5):555-61. doi: 10.1016/j.eurpsy.2014.12.008. Epub 2015 Jan 22. PMID: 25618445.
17. Hemetsberger J, Mestermann S, Nicol H, Purbojo A, Cesnjevar RA, Kratz O, Eichler A, Gerlach J. The impact of early surgical ventricular septal defect repair on parenting behavior and mother-child relationship: a prospective longitudinal study. Front Pediatr. 2024 Oct 23;12:1455310. doi: 10.3389/fped.2024.1455310. PMID: 39507499; PMCID: PMC11537904.
18. Varela-Chinchilla CD, Sánchez-Mejía DE, Trinidad-Calderón PA. Congenital heart disease: the state-of-the-art on its pharmacological therapeutics. J Cardiovasc Dev Dis. 2022 Jun 26;9(7):201. doi: 10.3390/jcdd9070201. PMID: 35877563; PMCID: PMC9316572.
19. Cacabelos R. Parkinson's disease: from pathogenesis to pharmacogenomics. Int J Mol Sci. 2017 Mar 4;18(3):551. doi: 10.3390/ijms18030551. PMID: 28273839; PMCID: PMC5372567.
20. Nevitt SJ, Sudell M, Cividini S, Marson AG, Tudur Smith C. Antiepileptic drug monotherapy for epilepsy: a network meta-analysis of individual participant data. Cochrane Database Syst Rev. 2022 Apr 1;4(4):CD011412. doi: 10.1002/14651858.CD011412.pub4. PMID: 35363878; PMCID: PMC8974892.

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

21. Chorna O, Heathcock J, Key A, Noritz G, Carey H, Hamm E, Nelin MA, Murray M, Needham A, Slaughter JC, Maitre NL. Early childhood constraint therapy for sensory/motor impairment in cerebral palsy: a randomised clinical trial protocol. BMJ Open. 2015 Dec 7;5(12):e010212. doi: 10.1136/bmjopen-2015-010212. PMID: 26644127; PMCID: PMC4679990.
22. Litvinova O, Baral B, Wochele-Thoma T, Matin M, Tzvetkov NT, Adamska O, Kamińska A, Łapiński M, Stolarczyk A, Atanasov AG. Efficiency and safety of cannabinoid medical use: an analysis of discussions and observed trends on Instagram. Front Public Health. 2024 Dec 4;12:1494018. doi: 10.3389/fpubh.2024.1494018. PMID: 39697283; PMCID: PMC11652663.
23. Karim N, Abdelhalim H, Gavande N, Khan I, Khan H. Natural Products as an Emerging Therapeutic Alternative in the Treatment of Neurological Disorders. Evid Based Complement Alternat Med. 2018 Apr 3;2018:3056847. doi: 10.1155/2018/3056847. PMID: 29849700; PMCID: PMC5903314.
24. Tang L, Feng Y, Gao S, Mu Q, Liu C. Nanotherapeutics Overcoming the Blood-Brain Barrier for Glioblastoma Treatment. Front Pharmacol. 2021 Nov 25;12:786700. doi: 10.3389/fphar.2021.786700. PMID: 34899350; PMCID: PMC8655904.
25. Haworth KG, Ironside C, Ramirez MA, Weitz S, Beard BC, Schwartz JD, Adair JE, Kiem HP. Minimal conditioning in Fanconi anemia promotes multi-lineage marrow engraftment at 10-fold lower cell doses. J Gene Med. 2018 Oct;20(10-11):e3050. doi: 10.1002/jgm.3050. Epub 2018 Oct 1. PMID: 30129972.
26. Holdreith N, Lee G, Chandra V, Salinas CS, Nicholas P, Olson TS, Tong W. LNK (SH2B3) inhibition expands healthy and Fanconi anemia human hematopoietic stem and progenitor cells. Blood Adv. 2022 Feb 8;6(3):731-745. doi: 10.1182/bloodadvances.2021004205. PMID: 34844262; PMCID: PMC8945310.
27. Shafqat S, Tariq E, Parnes AD, Dasouki MJ, Ahmed SO, Hashmi SK. Role of gene therapy in Fanconi anemia: A systematic and literature review with future directions. Hematol Oncol Stem Cell Ther. 2021 Dec;14(4):290-301. doi: 10.1016/j.hemonc.2021.02.001. Epub 2021 Mar 7. PMID: 33736979.
28. Chiu W, Lin TY, Chang YC, Isahwan-Ahmad Mulyadi, Lai H, Lin SC, Ma C, Yarmishyn AA, Lin SC, Chang KJ, Chou YB, Hsu CC, Lin TC, Chen SJ, Chien Y, Yang YP, Hwang DK. An Update on Gene Therapy for Inherited Retinal Dystrophy: Experience in Leber Congenital Amaurosis Clinical Trials. Int J Mol Sci. 2021 Apr 26;22(9):4534. doi: 10.3390/ijms22094534. PMID: 33926102; PMCID: PMC8123696.
29. Naiki Y, Miyado M, Shindo M, Horikawa R, Hasegawa Y, Katsumata N, Takada S, Akutsu H, Onodera M, Fukami M. Adeno-Associated Virus-Mediated Gene Therapy for Patients' Fibroblasts, Induced Pluripotent Stem Cells, and a Mouse Model of Congenital Adrenal Hyperplasia. Hum Gene Ther. 2022 Aug;33(15-16):801-809. doi: 10.1089/hum.2022.005. PMID: 35838129.
30. Bhoopalan SV, Suryaprakash S, Sharma A, Wlodarski MW. Hematopoietic cell transplantation and gene therapy for Diamond-Blackfan anemia: state of the art and science. Front Oncol. 2023 Sep 11;13:1236038. doi: 10.3389/fonc.2023.1236038. PMID: 37752993; PMCID: PMC10518466.

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

31. Kunisaki SM. Congenital anomalies: treatment options based on amniotic fluid-derived stem cells. Organogenesis. 2012 Jul-Sep;8(3):89-95. doi: 10.4161/org.22238. Epub 2012 Jul 1. PMID: 22986340; PMCID: PMC3527321.
32. Chi D, Chen Y, Xiang C, Yao W, Wang H, Zheng X, Xu D, Li N, Xie M, Wang S, Liu G, Li S, Yang L. Human Amnion Epithelial Cells and Their Derived Exosomes Alleviate Sepsis-Associated Acute Kidney Injury via Mitigating Endothelial Dysfunction. Front Med (Lausanne). 2022 Mar 24;9:829606. doi: 10.3389/fmed.2022.829606. PMID: 35402422; PMCID: PMC8989462.
33. Fauza DO. Transamniotic stem cell therapy: a novel strategy for the prenatal management of congenital anomalies. Pediatr Res. 2018 Jan;83(1-2):241-248. doi: 10.1038/pr.2017.228. Epub 2017 Oct 11. PMID: 28915235.
34. Tsilimigras DI, Oikonomou EK, Moris D, Schizas D, Economopoulos KP, Mylonas KS. Stem Cell Therapy for Congenital Heart Disease: A Systematic Review. Circulation. 2017 Dec 12;136(24):2373-2385. doi: 10.1161/CIRCULATIONAHA.117.029607. PMID: 29229621.
35. Dessie G, Derbew Molla M, Shibabaw T, Ayelign B. Role of Stem-Cell Transplantation in Leukemia Treatment. Stem Cells Cloning. 2020 Aug 10;13:67-77. doi: 10.2147/SCCAA.S262880. PMID: 32982314; PMCID: PMC7493021.
36. Khaddour K, Hana CK, Mewawalla P. Hematopoietic Stem Cell Transplantation. 2023 May 6. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan–. PMID: 30725636.
37. Seok H, Deng R, Cowan DB, Wang DZ. Application of CRISPR-Cas9 gene editing for congenital heart disease. Clin Exp Pediatr. 2021 Jun;64(6):269-279. doi: 10.3345/cep.2020.02096. Epub 2021 Mar 2. PMID: 33677855; PMCID: PMC8181018.
38. Doetschman T, Georgieva T. Gene Editing With CRISPR/Cas9 RNA-Directed Nuclease. Circ Res. 2017 Mar 3;120(5):876-894. doi: 10.1161/CIRCRESAHA.116.309727. PMID: 28254804.
39. Bhattacharya D, Marfo CA, Li D, Lane M, Khokha MK. CRISPR/Cas9: An inexpensive, efficient loss of function tool to screen human disease genes in Xenopus. Dev Biol. 2015 Dec 15;408(2):196-204. doi: 10.1016/j.ydbio.2015.11.003. Epub 2015 Nov 4. PMID: 26546975; PMCID: PMC4684459.
40. Vashist A, Manickam P, Raymond AD, Arias AY, Kolishetti N, Vashist A, Arias E, Nair M. Recent Advances in Nanotherapeutics for Neurological Disorders. ACS Appl Bio Mater. 2023 Jul 17;6(7):2614-2621. doi: 10.1021/acsabm.3c00254. Epub 2023 Jun 27. PMID: 37368486; PMCID: PMC10354745.
41. ScienceDaily [Internet]. A neuro-chip to manage brain disorders. 2023 Jan 30 [cited 2024 Aug 9]. Available from: https://www.sciencedaily.com/releases/2023/01/230130103022.htm.
42. Rabadán AT. Neurochips: Considerations from a neurosurgeon's standpoint. *Surg Neurol Int.* 2021;12:173. doi: 10.25259/SNI_591_2020. PMID: 34084601; PMCID: PMC8168797.
43. Shah S. How implanted brain chips like Neuralink could change our lives. *TIME.* 2024 [cited 2024 Aug 9]. Available from: https://time.com/6590258/nueralink-brain-implant-chip-first-human/.
44. Parsons L. Harvard: Neuronlike brain implants may help treat disease, mental illness. Harvard Gazette. 2019 [cited 2024 Aug 9]. Available from: https://news.harvard.edu/gazette/story/2019/03/harvard-neuronlike-brain-implants-may-help-treat-disease-mental-illness/.

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

45. Ubeda Tikkanen A, Nathan M, Sleeper LA, Flavin M, Lewis A, Nimec D, Mayer JE, Del Nido P. Predictors of postoperative rehabilitation therapy following congenital heart surgery. *J Am Heart Assoc.* 2018 May 12;7(10):e008094. doi: 10.1161/JAHA.117.008094. PMID: 29754124; PMCID: PMC6015299.
46. Maitre NL. Neurorehabilitation after neonatal intensive care: evidence and challenges. *Arch Dis Child Fetal Neonatal Ed.* 2015 Nov;100(6):F534-40. doi: 10.1136/archdischild-2013-305920. PMID: 25710178; PMCID: PMC4784692.
47. Williams C, Harding S, Wren Y. An exploratory study of speech and language therapy intervention for children born with cleft palate ± lip. *Cleft Palate Craniofac J.* 2021 Apr;58(4):455-469. doi: 10.1177/1055665620954734. PMID: 32945191.
48. Jochan MC, Ravikumar K. A review on prosthetics and orthotics for amputees and disabled. Journal of Critical Reviews. 2020;7(15):2175-89.
49. Sakaguchi D. Orthotics and prosthetics in rehabilitation. *Physiother Can.* 2013 Fall;65(4):399. doi: 10.3138/ptc.65.4.rev01. PMCID: PMC3817876.
50. Feto-Admin. Congenital anomalies: diagnosis and management [Internet]. 2023 Jan 16 [cited 2024 Aug 9]. Available from: https://fetoscan.in/2023/01/16/congenital-anomalies-diagnosis-and-management/
51. Emordi VC, Osifo DO. Challenges of congenital malformations: an African perspective. Ann Pediatr Surg. 2018 Feb 20;14(1). doi: 10.1097/01.XPS.0000522257.34234.7d.
52. Chen M, Mao A, Xu M, Weng Q, Mao J, Ji J. CRISPR-Cas9 for cancer therapy: Opportunities and challenges. Cancer Lett. 2019 Apr 10;447:48-55. doi: 10.1016/j.canlet.2019.01.017. PMID: 30684591.
53. Claes D, Markham KB, Cortezzo DE. An Ethical Analysis of Therapy for Severe Congenital Kidney and Urinary Tract Anomalies. Pediatrics. 2024 Jun 1;153(6):e2023064720. doi: 10.1542/peds.2023-064720. PMID: 38784992.
54. Chowdhury D, Johnson JN, Baker-Smith CM, Jaquiss RDB, Mahendran AK, Curren V, Bhat A, Patel A, Marshall AC, Fuller S, Marino BS, Fink CM, Lopez KN, Frank LH, Ather M, Torentinos N, Kranz O, Thorne V, Davies RR, Berger S, Snyder C, Saidi A, Shaffer K. Health Care Policy and Congenital Heart Disease: 2020 Focus on Our 2030 Future. J Am Heart Assoc. 2021 Oct 19;10(20):e020605. doi: 10.1161/JAHA.120.020605. PMID: 34622676; PMCID: PMC8751886.