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Neonatal Eye Defects and its Stem Cell Therapeutics

Review Article

Table 1. Showing various neonatal eye defects and therapeutic measures.

Eye defect	Reason	Physiological Effect	Therapeutic solution	References
Limbal stem cell deficiency	direct destruction of limbal stem cells or indirectly from altered limbal stromal niche	Decrease in peripheral cornea and limbus cells, poor vision due to corneal neovascularization	Keratoplasty and autologous cell transplantation	[251][243][256] [57]257]
Infant glaucoma	Numerous genes have been implicated	Infantile glaucoma can result in blindness without early intervention. Lifelong vision loss	Surgery followed by medication and optical aids is the treatment of choice.	[180] [21]
Eye pain	Inflamed or infected cornea sometimes caused by bacterial or viral infections;	Headache, light sensitivity, heavy tearing, Discomfort or pain due problem in the eye or structures around it, including	Use of antihistamines, antibiotic, steroids	[56], [48], [194].
Nearsightedness	Common cause of blurred vision.	Objects in the distance appear blurry, Myopia	Treatment including use of eyeglasses, contact lenses and LASIK.	[1]
Bilateral congenital anophthalmia	Retinal degeneration	impose severe retinal edema with subretinal fluid	Genetic counselling	[25]
Farsightedness	Common type of refractive error where distant objects may be seen more clearly than objects that are near	Hyperopia the light rays meet at a point behind the retina. This causes nearby objects to be blurred, headaches, and eyestrain	correctable eye disorder LASIK and operation	[1]
Astigmatism	Blurred or distorted vision as its main symptom	due to the irregular shape of the cornea or the lens inside the eye	Corrected by eyeglasses	[1]
Conjunctivitis	A viral or bacterial eye infection	One or both eyes become red or pink, they may be sticky	standard treatment options and means of care and support	[74]
Allergic conjunctivitis	Inflamed due to a reaction with environmental allergins such as dender, pollen and mold spores	Redness, Intense itching or burning eyes	Take over-the-counter oral antihistamines, Apply cool compresses to the eyes, Use lubricating eye drops..	[74]
Congenital microphthalmia	Defects in primary optic vesicle.			[11]
Congenital cataract	Lens gradually becomes opaque and vision mists over, a buildup of protein in the lens that makes it cloudy	Cataracts are a degenerative form of eye disease that causes vision loss	Cataract surgery and removal of the natural lens	[135] [18]
Corneal abrasion	Common eye injuries	Sever pain	Use an ice pack to reduce swelling	[8]
Eye inflammation, and redness	Puffy eyes, swollen eyes. swollen or dilated blood vessels on the sclera, eye pain, itching, Inflammation or infection of the eyelid that causes irritation or pain	Allergies too can cause swelling and pain in the eyelids, bacteria, viruses, allergies, or other microbiologica,	Chilled cucumbers make a good remedy for treating puffy eyes. The enzymes and the astringent properties in cucumbers help reduce inflammation. eye drops or rest	[55], [48], [194].
Dry eyes	Keratoconjunctivitis	soft contact lenses, common disorder of the tear film,	There is no cure for dry eye syndrome, Artificial tear drops and ointments. Temporary punctal occlusion.	[74]
Visual disturbances	Halos or blurred vision	ocular migraines usually require no treatment	Use of steroids or corticoids, as well as optical correction.	[45]
External eyelid stye	Irritated, external hordeolum	Localized infection or inflammation of the eyelid margin involving hair follicles of the eyelashes (ie, external hordeolum) or meibomian .	The primary mode of treatment for a stye is application of warm of the eyelid, depending if the stye is pointing externally	
Watery eyes	eyes produce too many tears, A blocked tear duct is the most common cause.	Pink eye (conjunctivitis, particularly in older people	DCR surgery, eye drops	
Entropion	Eyelid turns inward, rubbing against the eye, making it red, irritated, and sensitive to light and wind.	Surgical treatment involves tightening of the eyelid	botulinum toxin (BOTOX®) (approximately 5 U) are quite effective for the treatment of spastic entropion.	
Eye burning	Caused by allergy, dryness, tiredness, vision stress, heat or chemical exposure.	Eye fatigue or eye strain is a common and annoying condition	oral antibiotics to help fight the eye infection	
Eyelid twitch	Repetitive, uncontrollable blinking or spasm of the eyelid.	involuntary spasm of the eyelid muscles	treatment options include Botox injections	

Glaucoma	Build-up of fluid in the eye creates pressure, damaging the optic nerve	causes damage to your eye's optic nerve and gets worse over time, cause of irreversible blindness	Glaucoma surgery improves the flow of fluid out of the eye, resulting in lower eye pressure. Laser trabeculoplasty	[180] [21]
Black eye	Caused when blood and other fluids collect in the space around the eye, bruising to the tissue under the skin surrounding eye	Head injuries, allergic relations, cosmetics, Double vision, Loss of sight, Loss of consciousness	Pain medication	
Subconjctival hemorrhage	A subconjunctival hemorrhage appears as a bright red or dark red patch on the white of the eye.	When blood collects under this transparent tissue, it's known as bleeding under the conjunctiva, or subconjunctival hemorrhage.	Avoid the use of aspirin, ibuprofen, naproxyn, or other nonsteroidal anti-inflammatory medications as these can increased bleeding, no treatment is required.	
Retinal detachment	mall bits of debris in your field of vision that look like spots, hairs or strings	Darkening of your peripheral (side) vision.	Surgery	
Lazy eye	Due to esotropia	Strabismus	The surgery is designed to increase or decrease the tension of the small muscles outside the eye.	
Pterygium	Wing-like triangular membrane.	Winglet of the conjunctiva, caused by prolonged exposure of the eyes to wind and weather	Surgical procedures including laser treatment.	[9].
Diabetic retinopathy	complication of diabetes, affects the blood vessels in the retina	damage done may be permanent. Diabetic retinopathy can often be prevented by lifestyle modification, including weight loss, dietary changes, and exercise. ew abnormal fragile vessels develop on the surface of the retina and may grow toward the center of the eye.	Treatment is by laser surgery or surgery on the vitreous	
Nightblindness	an acquired condition usually resolves after the underlying condition is treated	nyctalopia, means a person cannot see well at night or in poor light	Night blindness caused by nearsightedness, cataracts, or vitamin A deficiency is treatable	
Visual impairment	Astigmatism is a common form of visual impairment in which an image is blurred due to an irregularity in the curvature of the	Cognitive impairment	Natural healing	[2][8]
Hypertensive retinopathy	Glaucoma is a common cause of true tunnel vision, drugs/Toxins Hypertensive Retinopathy Trauma	Cause a generalized loss of vision, serious active bleeding, artificial heart valves, bleeding or blood disorders	keep your blood pressure in control by changing your diet, exercising more, and taking your high blood pressure medications. In addition, see your doctor on a regular basis for follow-up care.	[36]
Age related macular degeneration	Physical disturbance of the center of the retina called the macula.	gradually destroys the central vision., its onset usually after age 60 that can progressively destroy the macula	Treatment includes laser surgery, photodynamic therapy, and injections into the eye.	[106]
Bulging eyes	bulging of the large vessel	Irritability, This process may lead to eyelid retraction (stare), proptosis (bulging eyes), diplopia (double vision) and dry eyes		
Uveitis	Uveitis is the inflammation of the inside the eye, specifically affecting one or more of the three parts of the eye that make up the uvea.	involves all inflammatory processes of the middle layers of the eye, also called the uveal	eye drops containing steroids to reduce swelling and drugs to relieve pain. Antibiotics are used in patients with infectious uveitis. Dark glasses will help with light sensitivity.	[219]
Retinoblastoma	Intraocular malignancy in early childhood..	It usually presents after infancy as leukocoria, esotropia, or masquerades as uveitis.	A prosthesis needs to be implanted in the child's eye to prevent the contracture of the socket.	
Hazy vision	vision will probably be hazy or blurry	tearing, pain, redness, swollen eyelids, headache, a gritty feeling in the eyes, halos around lights, hazy vision, and temporary loss of vision	LASIK: Refractive Surgery for Vision Correction	
Scleritis	Inflammation of the white part of the eye	Systemic treatment with NSAIDs.	Systemic treatment with NSAIDs, corticosteroids, methotrexate, butazathioprine, mycophenolate mofetil,cyclophosphamide, or cyclosporine, Anti-TNF agents biologicsinflixi-mab (Remicade) or adalimumab	
Corneal ulcer	due to a bacteria or virus causing a painful, red eye.	People who wear contact lenses are at an increased risk of corneal ulcers.	Surgery	[57]

Photophobia	Bright lights hurt eyes, and a reaction occurs due to drugs	Irritation and pain	Intermittent photophobia associated with migraine usually respond to acute medications such as triptans, non-steroidals	
Hyphema	A pooling or collection of blood inside the anterior chamber of the eye (the space between the cornea and the iris). The blood may cover most or all of the iris and the pupil, blocking vision partially or completely.	Increase in eye pressure, no reading	The best way to prevent hyphema is to wear eye protection when playing sports	
Ophthalmolplegia	paralysis or weakness of one or more of the muscles that control eye movement	Problem in perfect vision	Vitamin E, Coenzyme Q, Ubiquinone, Surgery	
Ocular migraines	Frontal bossing and ocular hypertelorism	Cause temporary vision loss, sudden tightening (or constriction) of blood vessels, Flashing lights, Blind spots in field of vision	Tricyclic antidepressants or anti-seizuremedications -- can help prevent permanent vision loss	
Sarcoidosis		Avoiding exposure to dust, chemicals, fumes, gases, toxic inhalants,	There is no cure for sarcoidosis, corticosteroids	
Retinal vascular occlusion	Central retinal vein occlusion	Swelling of the macula	Anti-vascular endothelial growth factor (anti-VEGF) drugs into the eye. Laser treatment to prevent the growth of new, abnormal blood vessels that leads to glaucoma, Treatment with injections of Avastin or Lucentis.	
Optic neuritis	an inflammation of the eye's optic nerve	Optic neuritis causes can include diseases such as multiple sclerosis, diabetes, mumps, measles, influenza and bacterial or viral infections.	There is no proven effective treatment for nonarteritic anterior ischemic optic neuropathy (NAION), corticosteroids	[1].
Myasthenia gravis	Myasthenia gravis is a chronic autoimmune disorder that causes muscles to weaken and tire easily	damages the muscles' receptors	Pyridostigmine, an acetylcholinesterase inhibitor	
Bulging eyes	When one or both eyes protrude from the eye sockets due to space taking lesions such as swelling of the muscles, fat, and tissue behind the eye.	Proptosis occurs when one or both eyes protrude from the eye sockets due to space taking lesions such as swelling of the muscles, fat, and tissue behind the eye	Bulging eyes are exposed to more air making it difficult to keep them lubricated. To combat excessive dryness, artificial tears and eye drops can be used for moisture and lubrication	
CMV Retinitis	serious infection of the retina	affect people with other immune disorders.	Antiretroviral therapy	[1][30]
Colour blindness	colour vision deficiency	Problem of colour matching.	No known treatment	
Crossed eyes	when a person's eyes are not able to align on the same point at the same time	Vision appear to be misaligned or pointed in different directions	There is no known treatment for color blindness.	
Diabetic Macular Oedema	fluid accumulation in the macula	Patients typically experience blurred vision which can be severe.	Laser photocoagulation	
Eye floaters and eye flashes	small specks or clouds that move across field of vision	Occurs when looking at a bright, plain background, like a blank wall or a cloudless blue sky.	Floaters and flashes treatment may not be needed if they are not related to a retina tear.	
Keratoconus	When the cornea in the front of the eye, which normally is round, becomes thin and cone shaped	Impairment of vision	Correction of distorted vision	
Amblyopia	eye that does not receive adequate use during early childhood.	poor vision in an eye, amblyopia is caused by severe refractive errors and/or anisometropia	Glasses are prescribed	
Ocular hypertension	Increased pressure in the eye	Pain during sight seeing	Laser and surgical therapy	[252]
Blepharitis	Inflammation of eyelids	Responds very well to natural cures such as castor oil, coconut and tea tree oil	self-care for this eyelid	[48]
Conjuctivitis	Inflammation of the conjuctival	Usually clears up by itself.	Use of antihistamines	[48][193]
Keratitis	Inflammation of the cornea	Bacterial, viral, fungal keratitis	Antiviral or antibiotic eye drops	[12]
Episcleritis	Inflammation of the sub-conjuctival connective tissue and the blood vessels that course between the sclera and conjuctiva	Irritation and inflammation of the episclera, a thin layer of tissue covering the white par	Episcleritis most often improves without treatment	[1]
Scleritis	Inflammation of the sclera	Red eyeball, pain, watering eyes	Corticosteroid eye drops to help reduce the inflammation.	[1]
Leber's congenital amaurosis	Autosomal recessive condition that manifests in infancy.	The fundus may be normal or show peripheral chorioretinal atrophy and granularity with nystagmus	Anti-oncological treatment	
Oculodigital syndrome	Infant constantly rubs or presses on the eyes which leads to enophthalmos	Other common features include learning disability, deafness, and epilepsy	Genetic counselling	

Ophthalmia neonatorum	This is an eminently preventable condition in which the eyes of the infant become infected in the birth passage during delivery	Obstruction in vision	Credé's prophylaxis entails cleaning the infants' eyes immediately after birth with instillation of a topical antibiotic (eg, tetracycline eye ointment) or antiseptic (eg, 2.5% povidone iodine). Traditionally, a 2% solution of silver nitrate was used for Credé's prophylaxis	
Preseptal or Orbital Cellulitis	It is an infection related to trauma, an upper respiratory infection or an eyelid infection.	decreased vision	Ophthalmic treatment	
Nystagmus	Eyes involuntarily move back and forth.	Nystagmus causes the eyes to drift slowly in one direction and then 'jump' back in the other direction	Ophthalmic treatment	
Ptosis	involves a drooping upper eyelid that covers the eye either somewhat or entirely	Blocks vision	Ophthalmic treatment	

Table 2. Various genes and factors which play important role in cell programming and regeneration.

Gene/factors family	Action	Regulatory function	References
Figures (Figure1, Figure2, Figure3)	Figure1 plays an independent role in lens development	Differentiation	(Zhao et al, 2006)[103]
LEDGF/p75	lens epithelial to fibre cell terminal differentiation	Differentiation	Chylack et al, 2004)[101]
Eya and dac genes	plays a central role in fly eye development and controls a subordinate regulatory network	Controls a subordinate regulatory network	(Purcell et al, 2005)[99]
Pax6/eyeless	Create differences in morphology, photoreceptor-type usage and lens	Activation of photoreceptor cells	(Erclik et al, 2009)[69]
HLA-typed allogeneic LECs	Reconstruct ocular surface	Allogenicity	[Meller D et al, 2009][166]
FLG	Risk factor for atopic dermatitis	Apoptosis	
COL4A3/COL4A4	Corneal collagen structure, function and	Restore corneal function, Regulate development during embryology	
MIR184	Expressed in the cornea and lens 3'UTR of two target genes	Corneal healing after injury	Differentiation
TGBFI	A cytokine interacting with extra-cellular matrix protein	plays a role in tissue injury and repair	Injury and repair
ZEB1	Modulating epithelial –to-mesenchymal transition	Cellular induction	Cellular induction
SOD1	Major cytoplasmic antioxidant enzymes	Provides defense against oxygen toxicity	Immune defense
VSX1	Craniofacial and ocular development	Vision correction	Vision perfection
IFN-γ and TNF-α	pro-inflammatory cytokines	Modulation	Wen et al, 2014[200]
TGF-β, IL-10, IDO, PGE-2, sHLA-G5, HO, and Galectin-3	Secreted by MSCs	induce cell to cell interaction and generate immunomodulatory effects on innate and adaptive cells of the immune system	Rahimzadeh et al, 2015[196]
p38 and c-Jun N-terminal kinase	Stimulatory	endothelial wound-healing	Miyamoto et al, 2010)[211]
Sox2, Oct-4 and Nanog	differentiate into neuronal-like cells, and provide a promising source for stem cells and may be used	extensively in the field of regenerative medicine	Chang et al, 2010).[213]
poly(ethyl acrylate) (PEA)-based copolymers	copolymers, extracellular matrix-protein coating and colonization with adipose-derived MSCs	Increased cell survival rate.	Alió del Barrio et al, 2014).[215]
PEUU fibers		Cell adhesion	
poly(ε-caprolactone, fibroin, human anterior lens capsule, keratin, poly(lactide-co-glycolide), polymethacrylate, hydroxyethylmethacrylate and poly(ethylene glycol	Polymers, extracellular matrix-protein coating	Biomaterials used in tissue regeneration	Feng Y et al, 2014[251]
Electrospin a biodegradable membrane of poly(lactic-co-glycolic acid	microfabricated structures.	Scaffold material for regeneration	Ortega et al, 2013).[54]
collagen vitrigel	Supports corneal epithelial differentiation and prevents epithelial hypertrophy.	It is also as used as a scaffold material for for hLEC transplantation without having complications	Chae et al, 2014[242]
Human keratoplasty lenticules (HKLs	Induces proliferation, express differentiation markers, and bind to the underlying stroma with no alterations in clonogenic potential.	HKLs allow cell growth with no feeder layers	(Barbaro ET AL, 2009).[247]
CRYBB2	Express in lens, retina and brain	Cataract	Visual problems

NYX	Code nyctalopin	Photoreceptor cells, ganglion cells and bipolar neurons	Vision
CACNA1F	L-voltage gates calcium channel	Retina specific expression at the photoreceptor to bipolar cell synapsis	
GNAT1	Alpha subunit of rod transducin	Rod outer segment	Enzymes of phototransduction cascade
RHO	Retinal degeneration	Retinitis pigmentosa	

Table 3. Scaffold biomaterials, their composition, properties and uses in tissue engineering.

Name	Composition	Properties	Therapeutic use	Applications
Poly(methyl acrylate) (PMA)	Hydrophobic synthetic acrylate polymer	softer than polymethyl methacrylate(PMMA	Used as macroinitiator to initiate the copolymerisation of HEMA and DMAEMA	PMA is water-sensitive and unlike PMMA, is not stable against alkalies, tough, leathery, and flexible
Collagen vitrigel	Soft and turbid collagen gel	An excellent scaffold for three-dimensional cell culture models, as cells can be cultured on both sides.	ocular repair and regeneration applications Soft and turbid collagen gel disks, vitrification of heat-denatured of protein	HGF-containingcollagen vitrigel sheet' is used as an effective drug delivery system in mouse liver, high fibril density
Copolymer PA6/12	Synthesized via successive in-situ polymerization of styrene (free radical polymerization), equimolar Laurolactam (LL) and Caprolactam (CL) (anionic ring-opening polymerization)	diameter ranging from 9.2 to 138.0 microns and narrow size distribution "nylon 6,12" or "PA 612" is acopolymer of a 6C diamine and a 12C diacid, Glass transition temperature: 46oC.	Preparation of thermoplastics based on PA6, PA6.6, copolymers, PA6.10	Matrix for cell culture and drug delivery
Dual-layer fibroin scaffolds	Silkfibroin (SF) scaffold tissue engineering biomaterial tissue repair	pore sizes in the range of 100–160 μm , good interconnectivity and high porosity, biocompatible and cytocompatible	silk fibroin/chitosan scaffolds might be a promising biohybrid material for tissue engineering	Repairing of corneal stromal defects, silk fibroin nanoparticles improved the water contact angle and enhanced cell interaction
human keratoplasty lenticules	suitable scaffold for corneal epithelial stem cells	Reconstruction of a human hemicornea through natural scaffolds compatible with the growth of corneal epithelial stem cells and stromal keratocytes	native conformation with collagen fibrils interconnected to the network and parallel to the corneal surface, microkeratome resection	Treatment of LSCD
Hevin	an antiadhesive extracellular matrix protein	metalloproteinase-3 produces a SPARC-like fragment (SLF) associated with neovasculature	Matricellular protein, hevin, is homologous to SPARC	Suppresses Inflammation
poly(ester urethane)urea	polymerization of epsilon-caprolactone with polyethylene glycol (PEG)	PEEUUs exhibited low glass transition temperatures and possessed tensile strengths ranging from 8 to 20MPa and breaking strains from 325% to 560%	transparent connective tissue of the corneal stroma by differentiated keratocytes	Elastomeric mechanical properties, tunable biodegradation properties and cytocompatibility
Poly(ε-caprolactone)	Polycaprolactone (PCL) is a biodegradable polyester with a low melting point of around 60°	prepared by ring opening polymerization of ε-caprolactone using a catalyst such as stannous octoate	As drug carriers for a controlled delivery system biodegradable, biocompatible and semicrystalline polymer having a very low glass transition temperature	Used in the fabrication of scaffolds for tissue engineering applications
Siloxane hydrogel	Siloxane-hydrogel loaded with hyaluronic acid	High permeability	Polydimethylsiloxane (PDMS) is used silicon-based organic polymer	Used in preparation of contact lenses
Polymethacrylate	Acrylic or acrylic glass	Good viscosity index	Glass transition temperature (Tg) of atactic PMMA is 105 °C (221 °F)	Transparent thermoplastic often used in sheet form as a lightweight or shatter-resistant alternative to glass. The same material can be utilised as a casting resin, in inks and coatings, and has many other uses.
Hydroxyethylmethacrylate	HEMA is the monomer	Hydrophobic polymer	swell water due to the molecule's hydrophilic pendant group	Manufacture of flexible contact lenses

Polylactic-co-glycolic acid	Ring-opening co-polymerization of two different monomers, the cyclic dimers (1,4-dioxane-2,5-diones) of glycolic acid and lactic acid.	Glass transition temperature in the range of 40-60 °C. biodegradable polymer because it undergoes hydrolysis in the body to produce the original monomers, lactic acid and glycolic acid	Soluble in chlorinated or fluorinated solvents	For repairing corneal stromal defects
Polylactide-co-glycolide	co-polymerization of two different monomers	Used in preparation of synthetic degradable polymers in medicine, used in preparation of therapeutic devices	PLGAs typically show a glass transition temperature in the range of 40-60 °C.	For repairing corneal stromal defects
Poly(ethylene glycol)	Nontoxic	PEG is soluble in water, methanol, ethanol, acetonitrile, benzene, and dichloromethane, and is insoluble in diethyl ether and hexane	PEG is being used in the repair of motor neurons damaged, polymer is used as a lubricating coating for various surfaces in aqueous and non-aqueous environments	Carrier in different pharmaceutical formulations
Gelatin-chitosan	chitosan and gelatin-chitosan complex are Schiff base reaction and acetalization reaction	chitosan and gelatin-chitosan complex are Schiff base reaction and acetalization reaction	cross-linked gelatin-chitosan nanofibers produced by means of electrospinning	nanofibrous mats could be a promising candidate for tissue-engineering scaffolds
Collagen	calfskin type I collagen produced a matrix composed of 100 nm fibers that exhibited the 67 nm banding pattern that is characteristic of native collagen	Electrospinning of type I collagen in 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) to fabricate a biomimetic nanofibrous extracellular matrix for tissue engineering	Ideal tissue engineering scaffol	Collagen promotes cell growth and the penetration of cells into the engineered matrix

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