The object of gene therapy is to treat diseases by introducing functional genes into the body to alter the cells involved in the disease process by either replacing missing genes or providing copies of functioning genes to replace non-functioning ones. The inserted genes may be genetically altered or in their own natural state for the desired effect.

2. Gene therapy may be nucleic acid based (in vivo) treatment or cell-based (ex vivo) treatment. Nucleic acid based gene therapy uses vectors, like viruses, to deliver modified genes to target cells. Cell-based gene
therapy techniques remove cells from the patient in order to genetically modify them and then reintroduce these to the patient’s body. For each disease, it must be determined if ex vivo or in vitro technology is the best approach. Ex vivo therapy is considered to be more expensive and time consuming but allows greater control. Both processes require the use of a vector to get the desired gene across the cell membrane and into a cell.

3. There are different methods to replace or repair the genes targeted in gene therapy -

(i) A normal gene may be inserted in to a non-specific location with the genome to replace a non-functional gene, which is the most common approach.

(ii) An abnormal gene could be swapped for a normal gene through homologous recombination.

(iii) The abnormal gene could be repaired through selective reverse mutation, which returns the gene to its normal function.
(iv) The regulation (degree to which a gene is turned on or off) of a particular gene could be altered.

4. In gene therapy, the drug (DNA) must be delivered to the nucleus of a cell in order to function, and a huge number of individual cells must each receive the DNA, for the treatment to be effective. A successful gene therapy often requires highly efficient delivery of DNA to a very restricted population of cells within the body. To achieve these goals, a carrier called vector must be used to deliver the therapeutic gene to the patient’s target cells. The most common type of vectors are viruses, which have been genetically altered to carry normal human DNA. Scientists have tried to harness the ability of viruses of encapsulating and delivering their genes to human cells in pathogenic manner, by manipulating the viral genome to remove disease causing genes and insert therapeutic ones. The genes in the virus that cause disease are removed and they are replaced with genes
and coding aimed at the desired effect. The procedure must ensure that the genes which allow virus to insert its genome into its host’s genome are left intact. By re-engineering the virus, the therapeutic gene will be introduced in the host’s cells genome without causing any disease which the unaltered virus would be capable of. However, numerous problems can arise unless the method is perfected because therapy using viral vectors may produce undesired effects and infect the cells which are not targets. Therefore, before resorting to gene therapy using viral vector, it should be ensured that the inserted gene does not disrupt any vital genes already in the genome. The doctors and scientists are working hard to fix any potential problems that could exist. Legal problems are bound to arise in this field as they do in the context of other medical therapies and the evidence of medical experts.
5. The current knowledge of stem-cells applications in neuro-ophthalmology would lead to novel therapies that may be applied in the neuro-ophthalmology, including optic nerve re-generation strategies and gene therapy. A truly effective neuroprotective strategy would ideally preserve the structure and function of all retinal ganglion cell components. Retinal ganglion cells, like other central nervous system neurons, fail to regenerate their axons after axonal injury. Once the neuron has died and axon has disappeared, visual function cannot be restored unless a new neuron is delivered and connected to the appropriate afferent and efferent targets. The scientists are researching the applications of stem cells to neuro-ophthalmic disorders, and particularly optic nerve and retinal disorders. Stem cells, whether embryonic stem cells, adult stems cells, or more differentiated neural progenitor cells have been considered to re-populate and repair damaged neural tissue. In order to restore vision lost from optic
neuropathies, it is necessary to find ways of efficiently differentiating a neural progenitor cell into an identified retinal ganglion cell, and both reconnecting the dendritic and bipolar and amacrine cells while extending its axon to the lateral geniculate nucleus. It is thought, that even if, replacement and regeneration could be achieved, without appropriate mapping to retinotopic targets, vision would be of low resolution (See the “Novel Approaches to Treatment”, symposium organized and moderated by Lenoard A. Levin M.D., Ph.D., University of Montreal, Canada – 33rd Annual North American Neuro-Ophthalmology Society Meeting, Disclosures by Naney J. Newmen, MD).

6. The most exciting work currently on the brink of human applications is gene therapy of inherited retinal disorders. Dr. William Hauswirth, University of Florida and his colleagues have used viral vectors (AAV) to deliver the gene based therapies to the retina in animal models, the principle variables being the serotype, the promoter
used to express the passenger cDNA at the site of
intraocular injection. AVV vectors that are properly
constructed are likely to be clinically viable for recessive
single gene retinal diseases affecting many retinal cell
types AVV vector-mediated gene replacement strategies.

7. Gene therapy is also being investigated for
LHON. LHON is a maternally inherited bilateral optic
neuropathy that typically results vision loss during the
second through fourth decades of life. The disease is
caused by one of several point mutations in the
mitochondrial DNA (mtDNA). Dr. Jhon Guy, University of
Florida, has done a groundbreaking work and produced a
mouse model of LHON using the techniques of “allotypic
expression”. Because currently it is not possible to deliver
gene directly in to mtDNA within the mitochondria of cells,
Dr. Guy and his colleagues created a ND-4 sub-unit with
the LHON 11778 mutation and made it compatible with
the nuclear genetic code so it could be delivered with a
viral vector in to the nuclear DNA of mouse retinal ganglion cells via intra-vitreal injections.

8. On 1st May, 2007 Moorfields Eye hospital and University college, London’s Institute of Opthalology announced the world’s first gene therapy trial for inherited retinal disease. The first operation was carried out on a 23 years old British male, Robert Jhonson in early 2007.

9. It is reported that, a group of scientists at the Scripps Research Institute has been awarded a five-year grant of US $ 17,037,185 from the National Eye Institute (NEI), part of the National Institutes of Health. The grant will support the development of the use of adult stem cells as a therapy for treating the most common types of eye vision loss. The “Adult Stem Cells for Therapy of Visual Disorders”, grant will help the project in exploring novel technologies and approaches to understanding and developing treatments for retinal vascular regenerative
diseases including diabetic retinopathy, age related macular degeneration, glaucoma and retinitis pigmentosa.

10. While the progress in Bio-ophthalmology and researches undertaken by the scientists world over will translate into applications for the treatment of blinding eye diseases, they will also bring about new legal situations arising from the applications of the novel approaches. While peer approvals, publications, trials make the new approaches acceptable in the scientific field, a large number of questions will arise in relation to the liabilities of the professionals in connection with their expertise and the proper care and caution that is required to be taken while applying the novel treatment processes for curing visual disorders.

11. For treating neo-vascular eye diseases, adult stem cells – pluripotent cells capable of differentiating into a variety of cell types – harvested from bone marrow are used. These adult stem cells are injected into the eye
that is forming abnormal blood vessels. Once in the eye, it has been found that the stem cells migrate to sites of new blood vessel formation, where they can become blood vessel (endothelial) or vessel-associated cells such as microglia. The endothelial cells can incorporate into forming blood vessels and help to stabilize the growing vasculature, making it function more normally; the vessel-associated cells, or microglia, can exert a “paracrine” (helper) effect and facilitate normalization of the leaking vessels. In addition to targeting and stabilizing blood vessels that would otherwise degenerate in the eye, adult stem cells can also rescue nerve cells in the surrounding tissue. (See News & Views Online Weekly of the Scripps Research Institute Vol.7).

12. When treatment is successful, hardly any legal issue will arise from the patient. The use and methodology of novel treatment can, however, be surrounded by intellectual propriety right issues. Apart from ethical aspects, legal issues may emerge on case to
case basis when there is want of due care and caution in administering the gene treatment. This possibility gets compounded when the non-expert forums assisted by non-expert representatives of the affected parties, govern the decision making processes. It is, therefore, essential that the standard of duty to take care be identified and laid down by the specialist expert bodies and duly publicized, so that it can be widely known by the professionals imparting treatment, and those deciding disputes may adopt and apply correct approaches on the issue of reasonable care that is required to be taken while treating the patients with gene therapy.

(Justice R. K. Abichandani)