These preliminary results have prompted a further series of experiments in the pig that has an eye more closely resembling the human in size and morphology. Introducing such implants into the suprachoroid is technically easy, involving an incision in the outer scleral coat of the eye down to but not involving the underlying vascular choroidal layer that has a higher rate of blood flow per unit mass of tissue than any other tissue in the body. By avoiding the need to traverse this vascular layer, the risk of calamitous hemorrhage is avoided and if further experimentation proves successful, the suprachoroidal route for drug delivery to the retina may become standard practice.

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In primary glaucoma, the reason for the increased resistance to aqueous outflow may be clinically undetectable (open angle glaucoma) or the angle of the anterior chamber is obstructed by the root of the iris (angle closure glaucoma). Current research in open angle glaucoma is directed at elucidating the structural and functional changes in the trabecular meshwork that causes the increased resistance and into a possible genetic basis for these abnormalities.

Glaucoma represents a wide spectrum of different ocular disorders, most of which have an abnormally raised intraocular pressure as a characteristic feature. In normal eyes the intraocular pressure (IOP) ranges between 10–21mmHg with a mean of around 14mmHg. Any intraocular pressure maintained above 21mmHg for an extended period of time will cause progressive damage to the optic nerve head and gradual loss of vision first affecting the periphery of the visual field but later encroaching on central vision until eventually blindness ensues.

REFERENCES
absence of raised IOP (so called normal tension glaucoma), it has become apparent that the retinal and optic nerve head damage occurring in glaucoma is not due to pressure alone but involves other factors. Factors implicated have included the integrity of the blood circulation to the optic nerve head and the structural peculiarities of the affected nerve head itself. Important in this regard are the nature of its collagen make up and the spacing of the collagenous septae that surround groups of axons as they traverse the nerve head. Compression of axons by distortion and narrowing of the spaces through which they pass may result from raised IOP and this may be one of the reasons for visual loss in glaucoma.

To maintain a normal IOP, aqueous fluid is continuously pumped into the eye from the ciliary body near the front of the eye by a process involving both hydrostatically and osmotically driven ultrafiltration, together with active fluid transfer across the ciliary epithelium, a process in which a variety ions plays an important role.

**Canal of Schlemm**

Aqueous fluid exits the eye through the trabecular tissue of the iridocorneal angle to an emissary channel known as the canal of Schlemm (Figure). There is a balance between the rate of inflow of aqueous fluid and its rate of outflow. A reduction in inflow causes a low IOP. A reduced inflow may accompany inflammation in the ciliary body, or may be a sign of hyperosmolarity of the circulating blood as occurs in severe dehydration or in diabetic hyperglycaemic coma. Fortunately a low IOP is not associated with permanent visual damage unless continued for a very long period.

High IOP is almost always due to an increased resistance to outflow of aqueous rather than an increased inflow. The level of IOP is almost entirely determined by the resistance to fluid outflow through the tissues of the angle of the anterior chamber. The higher the outflow resistance the higher the IOP has to be to ensure that the outflow of fluid from the eye continues to match its inflow.

Traditionally, glaucoma has been classified as secondary where there is obvious obstruction to the outflow of aqueous fluid. For example, hemorrhage into the anterior chamber, infiltration of the tissues of the angle with tumor cells or blockage of the angle with new-formed blood vessels and fibrous tissue as can occur after thrombosis of a retinal vein.

In so-called primary glaucoma, the reason for the increased resistance to aqueous outflow may be clinically undetectable (open angle glaucoma) or more obvious, where, for example, the angle of the anterior chamber is obstructed by the root of the iris (angle closure glaucoma). Current research in open angle glaucoma is directed at elucidating the structural and functional changes in the trabecular meshwork that causes increased resistance to outflow through that tissue and into a possible genetic basis for these abnormalities.

Already by the use of gene array technology, several genes that are unregulated in association with raised IOP have been identified in trabecular tissue. One such gene is under active investigation by SERI staff. Worldwide, the chromosomal locations of several relevant genes have been defined. Another areas of interest is the identification of potential therapeutic agents capable of protecting the ganglion cells of the retina from the destructive effects of raised IOP that induces apoptotic death in these cells. Possible neuro-protective molecules include brain derived and other neurotrophic factors, fibroblast and other growth factors, alpha 2 specific adrenoreceptor agonists and even lens crystallins that share homology with some species of heat shock (stress) proteins.

**Open Angle Glaucoma**

A mainstay of management of open angle glaucoma is medical therapy to reduce the level of IOP. SERI is active in the evaluation of new pharmaceutical agents for the reduction of
IOP and particularly interested in those that additionally may have a neuro-protective effect.

The surgical treatment of open angle glaucoma involves “drainage surgery” designed to bypass the obstructed angle tissues. While generally successful, there is a significant failure rate especially among some races including the Chinese. The failure is due to excess scar tissue formation blocking the new-formed drainage pathways. Non-specific antimetabolites such as 5 fluorouracil (5FU) or mitomycin C to suppress fibroblastic activity and the laying down of scar tissue have proved to be of benefit in reducing the incidence of surgical failure but can have adverse side effects. A major research project in SNEC in collaboration with Moorfields Eye Hospital in London is studying the long-term outcome of glaucoma drainage surgery accompanied with the use of anti-metabolites. More targeted therapy such as anti-TGFβ may prove to be superior.

Closed Angle Glaucoma

In closed angle glaucoma, the commonest underlying abnormality is a lens that is disproportionately large for the size of the eye that contains it. The condition is thus commoner in hypermetropic (longsighted) eyes that have reduced ocular dimensions but a normal sized lens. In a normal eye, the pupillary margin of the iris rests lightly on the front surface of the lens and aqueous fluid is pumped into the eye from the ciliary body that lies behind the iris. The fluid passes forward between the iris and lens, enters the anterior chamber of the eye through the pupil from behind and exits the eye through the angle of the anterior chamber.

Where the lens is disproportionately large, the pupil margin is pressed firmly against the front of the lens making it difficult for fluid to enter the anterior chamber through the pupil. As a result, pressure behind the iris becomes higher than in front of it causing forward bowing of the iris (iris bombé) and eventually closure of the angle by contact and later adhesion between the root of the iris and the posterior surface of the cornea. The result is an elevation of intraocular pressure that may become extreme.

The subject of closed angle glaucoma and its management is addressed by Prof. Arthur Lim in the following article.

Further progress in the understanding of glaucoma will come from a better classification of the various subtypes of glaucoma each probably with its own genetic predisposition, and the application of more refined molecular biological techniques to the study of open angle glaucoma that still today largely remains a mystery.

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of 60 million patients suffering from glaucoma will become blind. With our aging population, the number of patients with glaucoma will continue to increase.

There are basically two common types of glaucoma — open angle glaucoma and closed angle glaucoma. In open angle glaucoma, the pathology is in the trabecular meshwork. The pressure is raised as the outflow is decreased because of microscopic changes in the trabecular meshwork.

In closed angle glaucoma, the trabecular meshwork is normal. The condition is mechanical and is the result of anatomical occlusion of a normal but narrow angle by the iris coming into contact with the peripheral cornea — known as iridocorneal contact. This contact obstructs outflow of aqueous and leads to raised intraocular pressure. Depending on the extent and rapidity of the occlusion, the condition can present clinically as acute, sub-acute, or chronic closed angle glaucoma.

Today, acute closed angle glaucoma (acute glaucoma) is fast becoming one of the world’s most important causes of blindness with approximately 1.5 million patients suffering from it. Attacks of acute glaucoma can lead to irreversible blindness in the affected eye. Blindness can be effectively prevented in acute glaucoma if the condition is recognized early in its development. The severity of symptoms will often draw the attention of the patient to the problem, who will then seek medical care. It is essential therefore to educate the public, doctors and healthcare workers about symptoms of acute glaucoma and the danger that it poses to sight.

It is important to emphasize that with early diagnosis and treatment to the affected eye, and prophylactic laser iridotomy to the fellow eye — bilateral blindness from acute glaucoma can be prevented. Iridotomy by making a hole in the iris equalizes the pressure on either side of it and collapses the iris bombé.

Reading in dim lighting or reading can increase the pupillary block and iris bombé, causing closure of the narrow angle, which can trigger off acute glaucoma.

Laser iridoplasty is especially valuable in the management of closed angle glaucoma. It has been known for some time that YAG laser iridotomy is effective in the thin blue iris of Caucasians, but is far less effective in the thick brown iris in Chinese, for whom a combination of Argon laser with the YAG appears to be the most effective approach.

Laser iridoplasty, an important procedure creates contracting burns in the peripheral iris and pulls the iris from the angle. It is of particular value in the management of acute closed angle glaucoma. However, the effectiveness of iridoplasty is usually temporary and many eyes will require additional medical, laser or surgical treatment.

Of all the fascinating challenges we will confront in the 21st century, glaucoma promises to be the most intriguing. Young ophthalmologists eager to face the challenges of ophthalmology will find themselves drawn to the study, management, and surgery of glaucoma. As glaucoma is not only an affliction of individuals, but also a leading preventable cause of world blindness, they will find themselves embarking on an exiting and profitable odyssey of global significance.

REFERENCES