This report describes a new, non-surgical treatment that may facilitate management of a serious, sight-threatening complication of diabetes in many patients.

Bleeding in the Eye (Vitreous Haemorrhage)

Vitreous haemorrhage (VH) may be the result of trauma, macular degeneration and a variety of other retinal diseases. The most common causes of spontaneous vitreous haemorrhage according to Spraul and Grossniklaus are proliferative diabetic retinopathy (32%), retinal tear (30%), proliferative retinopathy after retinal vein occlusion (11%) and posterior vitreous detachment without retinal tear (8%). In Singapore, 22% of 13,296 patients screened were found to have diabetic retinopathy, half of whom had sight threatening retinopathy. The rate reported in Taipei was similar to that in Singapore where 27% of 471 diabetics screened had diabetic retinopathy. The prevalence rate reported by Peking Union Medical College Hospital from screening 662 diabetics was 51.3%, about twice that of Singapore and Taipei.

Incidence of Vitreous Haemorrhage in Singapore

Although reports on the rate of diabetic retinopathy in Singapore are available, published data on the prevalence rate of vitreous haemorrhage is not. Information obtained from the Singapore National Eye Centre (SNEC), indicated that the number of new cases of vitreous haemorrhage seen by ophthalmologists at the SNEC is about 10 – 15 per month, half of whom are likely to have severe persistent haemorrhage lasting for months. Not only is the underlying retinal condition remaining undiagnosed and untreated, the visual loss especially in one-eyed patients is a serious cause of concern to both the patient and the ophthalmologist. Moreover there is a risk of secondary complications of persistent non-clearing vitreous haemorrhage such as glaucoma or hemosiderosis bulbi.

Current Treatment for Vitreous Haemorrhage

Vitreous haemorrhage is managed based on the severity and duration of the haemorrhage. The first line management of patients at the SNEC is to determine the likely cause of the bleeding and attempt to assess the state of the retina through clinical and ultrasound examination. Some cases need immediate surgery, but the majority will be observed for a period of weeks to see if there is spontaneous clearing of the VH. Although published data are not available, it is observed in our clinical practice that vitreous haemorrhage can spontaneously clear and the range is between 4 – 6 weeks for mild VH to 8 – 12 months for severe VH.

If the haemorrhage does not clear within 3 – 6 months, a vitrectomy is usually recommended. Vitrectomy is the established treatment option for non-clearing vitreous haemorrhage and is a surgical procedure that removes the blood filled vitreous gel. The vitreous is replaced with a gas bubble or a clear fluid. As with any surgical procedure, there is a risk of complications. The number of vitrectomies performed in Singapore are on the increase and are reported to have increased from 266 in 1991 to 564 in 1995. This trend is likely to persist as the number of people suffering from dia-betes and other age related retinal diseases are projected to increase with the increasing aging population.

Research into VH Treatment

Vitrectomy is the acceptable procedure for clearing vitreous haemorrhage at the present moment. However, research into non-surgical approaches for the management of this condition is underway. Vitrase™, a specially purified enzyme, has been developed for clearance of vitreous haemorrhage. This investigational drug (see Figs. 1 and 2), administered as an intravitreal injection, has undergone Phase I and Phase II trials in the United States and in Mexico. Data from prospective, randomized, double-masked studies evaluating three different doses in subjects with chronic, non-clearing haemorrhage persisting for a minimum of one month have been presented by Quiroz, et al., by Boyer et al., by Harper and Thomas, and by Thomas. More than half of the treated subjects experienced haemorrhage clearance sufficient to enable diagnosis and treatment for the underlying cause of the haemorrhage within the 8-week study period. Patients in the high dose group experienced the highest rate of clearance of severe haemorrhage. Sterile hypopyon was observed in some eyes within 1 – 2 days after injection and resolved within one week after onset. Patients in the...
high dose group experienced the highest incidence of sterile hypopyon. Retinal detachments were reported in three patients (one in each dose group). These latter sequelae and other serious adverse experiences (for example, hospitalization for diabetes-related complications) were not considered to be drug-related.

The results appear encouraging and indicate that this treatment may offer advantages of a non-surgical approach to the management of vitreous haemorrhage. Patients may benefit by having reduced risk of complications associated with surgery and the ophthalmologists may benefit by being able to perform the procedure in a clinic setting rather than the operating theatre. The potential for non-surgical treatment will significantly reduce the morbidity and ultimately translate into lower health care costs for the patient as well as for the country. The SNEC is involved in a Phase III trial of Vitrase™ and is the first site to recruit Asian subjects.

**Conclusion**

Non-surgical pharmacologic treatment to facilitate clearance of vitreous haemorrhage may produce a useful adjunct to current techniques to treat vitreoretinal disorders. The area of research investigating a non-invasive approach to vitreoretinal disorders according to Sebag is “beginning to be met by new methods of altering the state of the corpus vitreous, intended to eliminate untoward effects on the retina and vision. Pharmacologic vitreolysis can be a useful adjunct to current vitreous surgery techniques and can also be performed to replace vitrectomy…” Although the day when vitreous surgery is replaced by non-invasive therapy remains far in the future, these developments hold great promise…”

The future may be just a few years away, and the Singapore site will be actively contributing safety and efficacy data towards the development of Vitrase™ as a simpler and less invasive agent in the management of vitreoretinal disease.

**References**


**Fig 1:** The drug is injected into the vitreous of the eye, where the blood clot is present.

**Fig 2:** The blood clot has fallen to the bottom of the eye where it is absorbed by natural mechanisms. The visual path is no longer obstructed.
Efforts to Clone Disease Causing Genes

On 4 December 1998, China’s key National Laboratory on Medical Genetics (Hunan Medical University) declared that it has successfully, and for the first time in the world, cloned human genes which cause nerve deafness. An international patent right protection has been issued to the cloning of such genes. This latest research development was published in the January issue of *Nature Genetics* — an internationally renowned academic journal.

Deafness is one of the most commonly occurring diseases in human society. It has been reported that up to 50% of the aged population (aged 75 and above) suffers from hearing handicap, and the majority of serious dementia hearing handicapped cases are mainly attributed to their genetic defects. Only 5 out of 40 or more deafness-controlling genes have been cloned. Information from these cloned genes will be applied in clinic diagnosis.

Genes are the vehicles of genetic information. So far, the medical community has cloned 890 disease triggering genes. Such genes have been carefully sequenced, its code combination interpreted and possible gene mutations (with direct relationships to certain diseases) analyzed.

The intensive research efforts of Prof. Xia Jiahui of Hunan Medical University have led to the formulation of mature techniques for cloning disease triggering genes. In 1997, by combining data from the international genome research project, Prof. Xia’s team created computer-based disease-triggering gene cloning technology, the first of its kind in China. They have so far cloned seven disease-related full-length genes. These genes are registered and coded in the International Gene Bank.

Gene Therapy May Help Patients with Low Blood Counts

Researchers at the Institute for Human Gene Therapy (IHGH) at the University of Pennsylvania have succeeded in using genetic information implanted in a virus to alter the function of blood-making cells in rhesus monkeys. Specific genes of an adeno-associated virus were removed and replaced by an erythropoietin (EPO) gene which stimulates the production of red blood cells. The adeno-associated virus is a small virus with only two genes which can be easily removed, and therapeutic genes can be inserted in their place. Another advantage of using the adeno-associated virus is that the human immune system does not overly react to the virus.

The EPO gene is activated by a two-part switch. Genes that make two halves of the switch are inserted into a second adeno-associated virus. Both viruses are injected into the muscle cells of rhesus monkeys. The fibrous muscle cells have many nuclei, thus providing more targets for the viruses. Upon penetrating the cell’s nuclei, the viruses insert their altered genes into the cell’s DNA. Inside the nucleus, the two halves of the on-off switch are released into the cell. The two-halves assemble into a working switch only in the presence of the drug rapamycin, which is administered as a pill. This means that the activation of the gene will depend on whether the subject has taken the rapamycin pill. This in turn activates the EPO gene, causing increased production of EPO. In the treated monkeys, the gene remained active for several days.

Such treatment will benefit people with low blood counts. At present the treatment of such patients include regular injections of EPO. If this method works in humans as well, the EPO gene can be inserted into the patients muscle cells and activated whenever necessary with the rapamycin pill.
New Method to Test Blood and Other Biological Samples

A new way to test blood and other biological samples have been founded by a group of researchers from Showa University in Tokyo, Japan.

Using immufluorescence, this new method can test three different substances in blood and other biological samples at the same time. It is based on standard antigen-antibody reactions, but the use of the special fluorescent markets allows the same sample to provide up to three times more information on disease-related proteins and gene mutations. This would therefore bring about greater cost savings when carrying out laboratory tests on diseases and genetic diagnostics.

The new immufluorescence technique works in the following way: An antibody will bind with a target antigen in the body, usually a protein or gene marker associated with a particular disease. The antibody is conjugated with a fluorescent molecule, so that when it is mixed with the sample, its binding with the antigen can be easily detected under a fluorescent lamp, thereby revealing the presence of the target substance.

Rare earth elements, europium and samarium, are used as fluorescent tags. As these elements detect light of different wavelengths, they can be used simultaneously in a test. Each element also attached to a different antibody, so one test can actually detect the presence of two different antigens in a single sample. Moreover, three antigens can be detected at once by attaching europium to different antibodies and then separating them after the antibody-antigen reaction, but prior to shining the fluorescent on the sample.

Unlike the usual radioimmunoassays which makes use of radioactive substances, this new method is more sensitive, easier to work, and cost effective.

CHINESE MEDICINE

China to Upgrade Rural TCM Medical Services

China is actively improving medical services in rural areas using Traditional Chinese Medicine (TCM). The State Administration of Traditional Chinese Medicine has plans to establish a sound TCM service network by the year 2005. The aim of the project is to improve TCM health facilities in remote areas that are facing a shortage of medicine and qualified doctors. The 1800 county-level TCM hospitals are also expected to upgrade their services and to cut down treatment costs. Meanwhile village and township clinics should already have access to professionals with the capability to treat patients using TCM methods. Currently, almost one-third of rural folks rely on TCM to treat ailments because of the poor access to modern medicine.

This is an important step for protecting China's 900 million rural residents and is the key to fulfilling the country's "health for all" national strategy. Apart from TCM development in rural areas, the State Administration in TCM will also be expanding the TCM services in urban communities this year.