MEDITIME

A Medical Bulletin from TIME Pharmaceuticals (P.) Ltd.

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TIME PHARMACEUTICALS

Celebrating 20 YEARS of Excellence

MEDITIME

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Inside

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TIME Pharmaceuticals (P.) Ltd.

Editorial

TIME Pharma has made a remarkable presence in the Nepali pharmaceutical market with a glorious history of 19 years. With an overwhelming rush of emotions I feel delighted to pronounce that in upcoming Mangsir 2, 2073, we will be celebrating our 20th anniversary.

"All great achievement requires **TIME**". The vision of our Chairman and Managing Director to make our country self sufficient in medicine lead to the initiation of **TIME** Pharmaceuticals 19 years back, and a group of enthusiastic entrepreneurs set on a journey to contribute towards the health sector of the nation. Now, it feels great to stand at this point, turning over the glorious pages of our organization and look back at what we have achieved. It was a long and tough way to come but it was worth it, and I would like to thank all our well wishers and valued customers for supporting us throughout our journey without whom, it would not have been possible to make this glorious history. Moreover, I would like to congratulate all the **TIME**ians for the 20th anniversary, whose dedication and commitment towards delivering sustained and enhanced quality products and services to our customers led to the consistent growth of the organization.

I feel very delighted to share a brief prologue of our 2 decade old organization in this important issue of MEDITIME. Our 35000 Sq ft. ultra modern state of art manufacturing plant is located in Gaindakot-10, Nawalparasi, 12 KM west from Narayangarh. The plant has gone through various strategic and technological changes to adhere to various standards in quality. All the production process is with compliance of WHO-GMP standard to achieve highest quality that satisfies the need of the customers. With the zeal of highly skilled and motivated human resources, we are moving ahead as a leading pharmaceutical company in Nepal.

Our two decade journey was not a smooth one to walk through. It wouldn't have been possible to reach zenith of success without continuous support of well wishers and dedicated team work besides many ups and downs in this 20 years journey. Nepalese pharma industry is contributing about 45% in total pharma business and remaining is imported from other countries. In such a situation also, **TIME** Pharmaceuticals stand tall as one of the leading pharmaceutical company in the nation manufacturing more than 180 quality products.

We have struggled through many natural calamities, political disturbances and other challenges. Being a Nepalese company we stood together during every unpleasant situation for self-sufficiency in pharmaceutical products to make healthy nation. Besides the vision to providing quality medicine to every individual, we are also involved in conducting different CSR activities like health camp in earthquake epi-centric area, environment awareness activities etc.

Lastly, I thank my editorial team for your continuous effort in publishing different issues of MEDITIME, and now we present the 19th issue of MEDITIME at your service. Also, I would like to thank all the medical fraternities and supporters who have been providing their valuable article for the quarterly magazine from its initial issue.

Once again, HAPPY 20th ANNIVERSARY OF TIME PHARMACEUTICALS.

Sudarshan Lal Shrestha
Editor in Chief

e-bulletin can also be viewed in www.facebook.com/timepharma

Health News Line

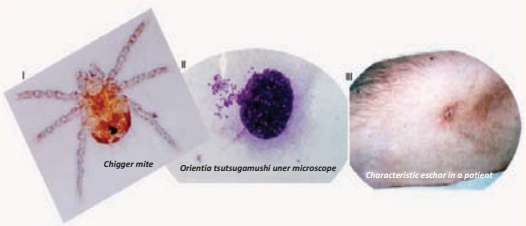
Artificial blood vessels developed in the lab can grow within the recipient

In a groundbreaking new study led by University of Minnesota biomedical engineers, artificial blood vessels bioengineered in the lab and implanted in young lambs are capable of growth within the recipient. If confirmed in humans, these new vessel grafts would prevent the need for repeated surgeries in some children with congenital heart defects. One of the greatest challenges in vessel bioengineering is designing a vessel that will grow with its new owner. In this study, University of Minnesota Department of Biomedical Engineering Professor Robert Tranquillo and his colleagues generated vessel-like tubes in the lab from a post-natal donor's skin cells and then removed the cells to minimize the chance of rejection. This also means the vessels can be stored and implanted when they are needed, without the need for customized cell growth of the recipient. When implanted in a lamb, the tube was then repopulated by the recipient's own cells allowing it to grow.

To develop the material for this study, researchers combined sheep skin cells in a gelatin-like material, called fibrin, in the form of a tube and then rhythmically pumped in nutrients necessary for cell growth using a bioreactor for up to five weeks. The pumping bioreactor provided both nutrients and "exercise" to strengthen and stiffen the tube. The bioreactor, developed with Zeeshan Syedain, a senior research associate in Tranquillo's lab, was a key component of developing the bioartificial vessel to be stronger than a native artery so it wouldn't burst in the patient. The researchers then used special detergents to wash away all the sheep cells, leaving behind a cell-free matrix that does not cause immune reaction when implanted. When the vessel graft replaced a part of the pulmonary artery in three lambs at five weeks of age, the implanted vessels were soon populated by the lambs' own cells, causing the vessel to bend its shape and grow together with the recipient until adulthood.

"What's important is that when the graft was implanted in the sheep, the cells repopulated the blood vessel tube matrix," Tranquillo said. "If the cells don't repopulate the graft, the vessel can't grow. This is the perfect marriage between tissue engineering and regenerative medicine where tissue is grown in the lab and then, after implanting the decellularized tissue, the natural processes of the recipient's body makes it a living tissue again." At 50 weeks of age, the sheep's blood vessel graft had increased 56 percent in diameter and the amount of blood that could be pumped through the vessel increased 216 percent. The collagen protein also had increased 465 percent, proving that the vessel had not merely stretched but had actually grown. No adverse effects such as clotting, vessel narrowing, or calcification were observed. Tranquillo said the next step is talking with doctors to determine the feasibility of requesting approval from the Food and Drug Administration (FDA) for human clinical trials within the next few years.

Scrub typhus infection taking toll in Chitwan



More than 200 people have been found suffering from scrub typhus, a bacterial disease that spreads from mice bite, in Chitwan district alone. District Public Health Office Chitwan's insect control inspector, Ram KC, said the exact number of patients suffering from scrub typhus was known after the result that came out of blood tests conducted from April/May till mid-September at three different hospitals in the district.

"A total of 613 patients in question got their blood tested and among them, 205 have so far been found to have contracted the disease," he said. As per the records at the office, as many as 188, nine and eight persons were diagnosed with the disease over the period of four to five months at Chitwan Medical College, Narayani Community Hospital and Bharatpur Hospital respectively.

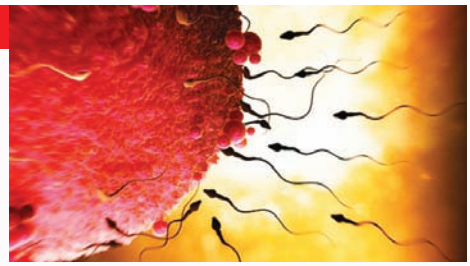
These are the only health facilities that conduct screening for the disease. The disease has so far killed two persons. Meanwhile, Bharatpur Hospital lately has made the blood test for the disease free of cost. The free of cost lab test has become possible after the District Public Health Office provided the hospital with 200 kits.

Memory Loss: Not an Inevitable Part of Aging

US Scientists say memory loss is not an inevitable part of ageing. The study was conducted on a unique group of adults in their 60s and 70s with minds as sharp as people in their 20s. Researchers at Massachusetts General Hospital found that these individuals, called "super agers", performed just as well on memory tests as people a third of their age.

Regions involved with learning and retaining new information showed no sign of typical age-related shrinkage. Also, memory test scores correlated with brain size. Those who performed best in the tests also had greater thickness in the key brain regions the researchers measured on MRI scans. The study authors say their work, outlined in the Journal of Neuroscience, could ultimately help with understanding the processes that lead to dementia and if there are ways to avoid them.

Making babies without eggs may be possible, say scientists



Scientists say early experiments suggest it may one day be possible to make babies without using eggs. They have succeeded in creating healthy baby mice by tricking sperm into believing they were fertilizing normal eggs. The findings could, in the distant future, mean women can be removed from the baby-making process, say the researchers.

The University of Bath scientists started with an unfertilized egg in their experiments. They used chemicals to trick it into becoming a pseudo-embryo. These "fake" embryos share much in common with ordinary cells, such as skin cells, in the way they divide and control their DNA. The researchers reasoned that if injecting sperm into mouse pseudo-embryos could produce healthy babies, then it might one day be possible to achieve a similar result in humans using cells that are not from eggs.

In the mouse experiments, the odds of achieving a successful pregnancy were one in four. Dr Tony Perry, one of the researchers, told the BBC News website: "This is the first time that anyone has been able to show that anything other than an egg can combine with a sperm in this way to give rise to offspring. It overturns nearly 200 years of thinking. Those baby mice were healthy, had a normal life expectancy and had healthy pups of their own.

In-Vitro Fertilization-Short History to IVF Protocols

Dr. Sanu Maiya Shrestha
MD, DGO, M.Sc, FICS
Sr. Con. Gynecologist & Obstetrician

In-vitro Fertilization (IVF) stands for "Fertilization in glass", i.e. fertilization of male and female gametes in glass. In 1878, the first attempts at IVF of mammalian eggs were made by the Viennese embryologist Schenk (Trounson, 1999). In 1891, Heape Walter demonstrated for the first time that fertilized eggs from a rabbit could be retrieved and subsequently transferred to a recipient, who then gave birth to live off-spring (Heape, 1891). The first successful in-vitro fertilization of mammalian egg with subsequent birth was reported by Chang in 1959 (Chang, 1959). The first reports of implantation and pregnancy in human using IVF were published during 1970s by Steptoe and Edwards (Edwards and Steptoe, 1974; Steptoe and Edwards, 1976). Since then, IVF has become the most rapidly evolving approach to overcoming human infertility problem.

IVF involves fertilization of the human ovum with spermatozoa outside the woman's womb and transfer of the resulting embryo to her uterus. There are many treatment modalities in IVF. The first IVF baby was born as a result of an oocyte picked up in a natural menstrual cycle (Steptoe and Edwards, 1978). However, the success rate of this type of protocol is very low compared to the other IVF protocols involving ovarian stimulation where more than one mature follicle is obtained. The Monash group was then first to introduce ovarian stimulation in IVF using clomiphene citrate and human menopausal gonadotrophin (hMG) combined, yielding a large number of eggs and improving the pregnancy rate (Trounson et al., 1981). From then onwards, several other regimens using these two drugs were reported.

A common problem with these products is that about 20% of women who undergo this treatment, have a premature LH surge leading to the cancellation of treatment (Loenen et al., 2003). Likewise, ovulation can also occur at inconvenient times of day (Elder-Geva et al., 1999). These problems have been overcome by the introduction of GnRH agonist and antagonist treatments that desensitized the pituitary, thus preventing the premature LH surge and allowing scheduling of the oocyte pick-up (OPU). GnRH was first isolated and characterized by Schally and colleagues in 1971 (Schally et al., 1971). Knobil was the first to demonstrate that GnRH when given continuously caused a decrease in LH and FSH secretion (Knobil, 1980). Continuous administration of exogenous GnRH analogue initially up-regulates the GnRH receptors in the pituitary for the first 2-3 days, increasing the secretion of LH and FSH. After this time, the GnRH receptors in the pituitary are down regulated and the secretion of LH and FSH is reduced as long as the analogue is given. Unlike GnRH agonists, the antagonists cause an immediate and reversible suppression of gonadotrophin secretion.

Use of GnRH agonist enables recovery of a larger number of oocytes, resulting in a larger number of embryos, which in turn, allows better selection of embryos leading to an increase in the pregnancy rate (Leonen et al., 2002).

The most commonly used stimulation protocols in IVF are:

1. IVF Long Protocol (IVFLP)
2. IVF Short Protocol (IVFSP)
3. IVF Antagonist Protocol (IVFANT)

IVF Long Protocol (IVFLP)

In most centers, this has become the standard protocol. GnRH agonists are given for 10 to 14 days or longer ("long protocol") for pituitary desensitization before administering an exogeneous gonadotropin. GnRH agonist treatment is usually commenced in the mid-luteal phase of the menstrual cycle. In some centers, the long protocol is combined with pre-treatment with Oral-Contraceptive Pills (OCPs). In OCP treatment, the GnRH agonist is usually commenced on the twentieth day of a 25 day OCP regime (Leonen, 2002). It is believed that pretreatment with OCP reduces the risk of ovarian cysts induced by the initial flare effect of GnRH agonists (Bijan et al., 1998).

After 10 to 14 days of agonist treatment, pituitary down-regulation is verified by determining the serum E2 (E2<120pmol/L) or transvaginal ultrasound (no follicles > 5 or 10mm). Following pituitary down-regulation, FSH injections are commenced for ovarian stimulation. FSH injections and GnRH agonists are discontinued on the day of the hCG trigger. The trigger injection is given when the leading follicle(s) is 3^{1}2E18mm and there are at least two follicles with a mean diameter of 16mm or greater. Transvaginal sonography guided ovum pick-up (TVSOPU) is performed 35 to 38 hours after the hCG injection.

IVF Short Protocol (IVFSP)

This protocol is sometimes named the "flare" protocol. In this protocol, the GnRH agonist is commenced from menstrual cycle Day 2 and the gonadotrophin injections for ovarian stimulation are commenced on Day 3 of the menstrual cycle. Both FSH injections and GnRH agonists are discontinued on the day of hCG trigger. The trigger injection is given when the leading follicle(s) is 3^{1}2E18mm and there are at least two follicles with a mean diameter of 16mm or greater. TVSOPU is performed 35 to 38 hours after the hCG injection.

IVF Antagonist Protocol (IVFANT)

GnRH antagonists have recently been introduced in clinical practice for pituitary down regulation in IVF cycles. In this protocol, FSH injections for ovarian stimulation are administered from Day 1 or 2 of the menstrual cycle. The antagonist is usually administered from Day-6 of the gonadotrophin injections, or from the day when at least one of the follicles has reached the size of 14mm. Antagonist and gonadotrophin are continued until the day of hCG trigger. The trigger injection is given when the leading follicle(s) is 3^{1}2E18mm and there are at least two follicles with mean diameter of 16mm or greater. TVSOPU is performed 35 to 38 hours after the hCG injection.

Why "Creator's IVF Nepal Pvt. Ltd."?

The negative consequences of childlessness are much stronger in developing nations than in developed nations due to the lack of expertise and technology. Unfortunately, the infertility problem in developing nations has been ignored as an international health problem. The world has focused more on the high birth rate and family planning strategies in the developing countries than on the problems of infertility. Nevertheless, the high birth rate and the infertility rates are the two sides of the same coin in the developing countries. The prevalence of infertility in developing countries can vary from low to high. Sub-Saharan Africa, for example, combines the highest level of fertility in the world with the highest prevalence of infertility (Puttemens et al., 1995). However, there is a lack of epidemiological studies to confirm the incidence of infertility in developing countries.

Myself being the experienced person of feeling sub-fertility pain, determined to gain expertise and academic knowledge in Assisted Reproduction Technology (ART), so that I could provide service to such couple with empathy.

Fortunately, I was given the opportunity to gain wide theoretical and practical knowledge in ART from University of New South Wales (UNSW), Australia during my Masters studies. After completion, I was further able to sharpen my skills in this area during my three years job at Om IVF center, Om Hospital, Nepal.

However, more than eight years of my independent work at IVF Nepal Pvt. Ltd., Global Hospital gave me a vision and confidence that such ART center requires much privacy and good consideration of emotional factors of couples along with competent staffs, as well as precise equipments. Thus, the concept of "Creator's IVF Nepal Pvt. Ltd." finally emerged.

Creator's IVF Nepal Pvt. Ltd. was established in Mangsir, 2072 and located at Satdobato-15, Lalitpur with an exclusive provision to manage infertility couples. This center provides all facilities from simple Timed-Intercourse (TI) treatment to complex Intra-Cytoplasmic Sperm Injection (ICSI) services with vision to increase other facilities related to ART.

Until now, we have conducted 54 batches of IVF successfully under my leadership and outcomes of 50 IVF batches are analyzed and presented in the table below.

Batch No.	Total Cycles Completed	Total Pregnancy	Total Clinical Pregnancy	Total Biochemical Pregnancy	Single Pregnancy	Twin Pregnancy	Triplet Pregnancy	Quadriplet pregnancy	Blighted ovum	Missed Abortion	Induced Abortion	Total single delivery	Total twin delivery	Total triplet delivery	Total male babies	Total female babies	Total OHSS*	Ectopic Pregnancy
1 to 50	573	259	214	45	144	52	13	1	21	27	7	109	37	8	106	11	9	4
		45%	37%	8%	25%	9%	2%	0.2%	4%	5%	1%	19%	7%	1.4%	49%	51%	2%	0.7%

Total Delivery = Total Single Delivery + Total Twin Delivery + Total Triplet Delivery = 109 + 37 + 8 = 154

Take Home Baby Rate = 27% **Total Clinical Pregnancy Rate = 37%** **Total Pregnancy Rate = 45%**

**OHSS: Ovarian Hyperstimulation Syndrome*

Apologizes for the mistake in data printed in 18th issue. Reprinted with correction.

SiTA-M

Product Profile

Therapeutic Category : Anti-Diabetic Drug
Route of Administration : Oral (Taken after meal)
Pregnancy Category : B
Dose : 2 daily with meal

Composition

- SITA-M 500 : Sitagliptin 50 mg + Metformin 500 mg Tablet
- SITA- M 850 : Sitagliptin 50 mg + Metformin 850 mg Tablet
- SITA-M 1000 : Sitagliptin 50 mg + Metformin 1000 mg Tablet

Description : SITA-M

Sitagliptin, an oral & highly selective dipeptidyl peptidase-4 inhibitor (DPP-4) , represents a novel therapeutic approach for the treatment of patients with T2DM. Dipeptidyl peptidase-4 inhibitor prevent the enzymatic degradation and inactivation of glucagon- like peptide (GLP)-1 and glucose-dependent insulinotropic peptide, the major incretin involved in glucose homeostasis.

Metformin a biguanidethat reduces elevated blood glucose levels by reducing hepatic glucose output and also by improving insulin resistance. Metformin increases active GLP-1 concentration by 1.5-2 folds following oral administration.

SITA-M in,

- Type 2 diabetes mellitus to improve glycemic control when uncontrolled on metformin monotherapy alone
- T2DM who are unable to reach HbA1c Goal

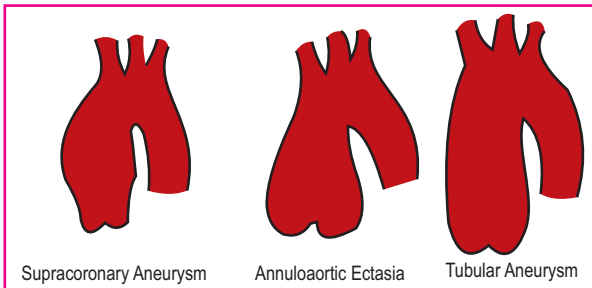
ABOUT- SITA-M

- SITA-M lower glucose concentrations through different, but potentially complementary, mechanisms. The combination of Sitagliptin with Metformin provides effective, potentially additive Glycemic control".
- SITA-M is effective in improving HOMA-IR, Glucagon level, HOMA- β and all β- cell measurement than with Metformin alone.
- "Sitagliptin shows osteogenic & anti-osteoporotic property which could positively regulate bone metabolism in postmenopausal diabetic women".

Ascending Aortic Aneurysm:
An active bomb in the thorax

Dr Kaushal K Tiwari
Asso. Professor & In-Charge
Department of Cardiothoracic and Vascular Surgery
CMSTH, Bharatpur

Aortic aneurysm can be defined as a localized undue dilation with 50% increase in size over the normal diameter. The "normal diameter" strictly depends on age, sex and body size, as well as the anatomical localization of the affected aorta. For the physiologically smaller abdominal aorta, the term aneurysm is usually limited to diameters exceeding 30mm, while, on the contrary, a thoracic aortic aneurysm should be conventionally larger than 40mm. According to Elefteriades J, ascending aortic aneurysms are divided into three categories, according to the pattern of the involvement of the aortic root. These are supracoronay aneurysm, annuloaortic ectasia (Marfanoid) and tubular diffuse enlargement of the aorta.



Types of ascending aortic aneurysms

Aortic aneurysms probably represent the most lethal and indolent enemy of the medical community. Usually, they silently and asymptomatically grow up until an acute and often catastrophic complication occurs. The threats of a non-operated aortic aneurysm include dissection or rupture of the aorta, subsequently leading to death. In contrast, despite the armamentarium of modern perioperative and post-operative cardiac surgical care, the risk of surgery includes paraplegia, stroke, bleeding, and mortality ranging from 3 to 9% after elective surgery. Conversely, in cases of acute events mortality can be as high as 90%. In the United States, aortic aneurysms (thoracic and abdominal) constitute the 17th leading cause of death in the general population and the 15th for individuals older than 65 years. Approximately 15,000 individuals die every year from this pathology in the United States of America, which is more than death caused by HIV infection.

Etiology

Risk factors for the development of thoracic aortic aneurysms include hypertension, smoking, and chronic obstructive pulmonary diseases. Ascending aortic aneurysms are also related with bicuspid aortic valve. Additionally, several genetic syndromes with a predisposition for ascending aortic aneurysms have been identified. Most common genetic diseases effecting thoracic aorta are: Marfan Syndrome, Loeys-Dietz Syndrome, Ehler-Danlos Syndrome, Turner Syndrome, familial thoracic aortic aneurysm Syndrome, and still others are idiopathic.

Symptoms of Aortic Aneurysm

Patients with a TAA are usually asymptomatic and diagnosed by chest X-rays or CT-scan requested for other reason. Thoracic aortic aneurysm can cause symptoms by compressing nearby structure. Hoarseness of voice could be a presenting symptom if it compresses recurrent laryngeal nerve; stridor, dyspnea from tracheal, bronchial or lung compression; dysphagia from esophageal compression; and plethora and edema, from superior vena cava compression. A dull and vague pain in neck and jaw may be an indication of aortic arch aneurysms, while back, interscapular, and/or left shoulder pain may occur with descending aortic aneurysms. Frequently, patients present with sign and symptoms of aortic insufficiency, which ought to be the main reason behind patient coming to clinical attention. Ultimately, acute syndroms like aortic dissection or aortic rupture, if could make to the hospital, might present with potentially lethal outcomes.

Diagnosis

Instrumental Evaluation of The Ascending Aorta

For the diagnosis of aortic aneurysm several diagnostic tools are available ranging from non-invasive examination like Chest X-ray, Echocardiography, Computed tomography and MRI to invasive examination like Angiography. Noninvasive imaging is essential for assessment of aortic size and in some cases functional parameters. It is important to know the accurate size of the aorta because key decisions regarding management of the aortic aneurysm depend on size.

Chest X-Ray

Chest X-ray often performed as a part of general examination in patients with potential cardio-pulmonary disease. It sporadically detects abnormalities of aortic contour or size that require definitive aortic imaging.

Echocardiography

Echocardiography is one of the most used imaging modality in the cardiology, which has a high sensibility and specificity in diagnosing variety of cardiac pathology including ascending aortic aneurysm. Transthoracic echocardiography (TTE) is more readily available, easy to use, transportable and cost effective. No need of contrast and sedation make it as a first line diagnostic tool in clinical set up. However, transesophageal echocardiography (TEE) is superior to TTE and more accurate for assessment of the thoracic aorta, but sometime requires sedation and has a small risk of complications like esophageal perforation (less than 0.03%). In addition, with diagnosis of aortic dilatation, echocardiography may reveal other associated pathology that suggests the underlying etiology of the aortic disease (eg, bicuspid aortic valve). Nevertheless, for accurate evaluation of ascending aortic aneurysm and to confirm the indication for surgery, there are some restrictions. TTE and TEE are user dependent. TTE can only visualize the proximal part of the ascending aorta, thus it can miss an aneurysm of the mid-portion of the ascending aorta. Even TEE is limited by the interposed tracheal air column and can be "blinded" to the upper portion of the ascending aorta. Furthermore, there is no universal agreement for exact place of aortic diameter measurement and whether the aortic wall should be included or excluded in the aortic diameter measurement.

CT Scan

New generation helical CT scan has sensitivity up to 100% and specificities of 98% to 99% for diagnosing abnormalities of the thoracic aorta. IRAD data shows that in some centers, CT has been used more frequently than Echo in case of aortic dissection. Major advantages of CT scan are: very wide availability, ability to image entire aorta, including lumen, wall and periaortic region. Additionally, CT scan is more or less exact in the size measurement, and it has a shorter examination time. Three dimensional reconstructions of CT images have an important role in the planning of surgery. However, a CT scan with axial images cannot properly evaluate the very proximal portion of the ascending aorta. In addition, motion artifact can adversely affect the resolution of CT images of the aorta, although technology is improving, especially with ECG gated tomographic angiography. Furthermore, risk of renal damage from the contrast media used during CT scan is a real obstacle in some patients.

Angiography

The shape of the aorta is ideally seen angiographically. Images of the aortic contour are exceptional and morphology of the aortic can be seen beautifully. This can facilitate accurate surgical planning. Additionally, it allow for evaluation and treatment of coronary artery disease, aortic branch disease, as well as assessment of aortic valve and left ventricular function. However, diameter of the ascending aorta from the angiographic images is not always accurate and simple to calculate. It is not available universally because it requires the presence of experienced physician to perform. It has disadvantage of being invasive procedure that is time consuming and require contrast medium with exposure to radiation.

Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) has been recommended as the technique of first choice for the detection and follow-up of both aortic complications and premorbid conditions, such as intramural hematoma, and aortic aneurysm. Its other advantages are ability to assess branch artery involvement, diagnosing aortic valve pathology, and left ventricular dysfunction. MRI is inherently a multiplane modality that can provide high quality images of the aorta in transverse, axial, sagittal, and coronal plane, as well as in left anterior oblique view. MRI has shown high sensibility and specificity both for initial diagnosis and progression of aneurismal disease. MRI offers a non-invasive and accurate evaluation of TAA and it doesn't require nephro-toxic contrast agent or ionizing radiation, although it takes longer time to acquire images and might need sedation in some patients and is not widely available in an emergency basis. It is also contraindicated in claustrophobic patients, and patients with metallic prosthesis and pacemakers. Use of cine-MRI techniques, combined to non-invasive haemodynamic data, offers both a morphological and functional examination of the entire aorta, which can provide with information about diameter, geometry, blood flow and aortic wall mechanical properties.

Functional MRI Examination

Most of the study to evaluate ascending aorta using functional MRI has been done in Marfan patients or patients with bicuspid aortic valve. However, its role in evaluating biomechanical property of the ascending aorta in other patients could be valuable as well. Information supplied by functional MRI may have utility in thoracic aortic disease management.

Treatment

Gold standard for treatment of the ascending aortic aneurysm is the surgical treatment. However, conservative treatment could be advised at the initial stage with smaller aortic diameter and in patients with morbidity, high risk factors for negative surgical outcome and who are not suitable for surgical treatment due to other coexisting disease.

In adult patients, conservative managements consist of smoking cessation, life style modification, a stringent control of hypertension, lipid profile optimization, and other measure to reduce risk of atherosclerotic process.

Furthermore, several other medical treatment options have been studied. In a randomized control study showed that Marfan patients treated daily with Propranolol has slowed aortic root dilation (0.023 vs 0.084 per year). In another recent randomized trial, angiotensin receptor blocker, losartan, added to beta blocker in a group of pediatric population with Marfan syndrome shows more effective protection to slow the progression of aortic root dilatation. Additionally, a matrix metalloproteinase inhibitor, antibiotic doxycycline has shown promising effect in the slowing down of the growth rate of the abdominal aortic aneurysm, but no study has reported effect of doxycycline on ascending aortic aneurysm. To summarize it, none of the studies has shown proven clinical benefit of these medical therapies in the treatment of ascending aortic aneurysm.

Indications For Surgery

If medical therapy can have a palliative role only in high-risk cases, thoracic aortic aneurysm surgery significantly improves 2-year survival from 24% in un-operated patients to 70% in patients undergoing aortic replacement surgery.

Surgical treatment is indicated in symptomatic and asymptomatic patients with aortic diameter more than 5.5 cm in otherwise normal patient, while 4.0-5.0 cm in Marfan patients and patients with genetically mediated process. Postoperative morbidity and mortality has significantly decreased due to better anesthetic management, improved surgical techniques and progress in preoperative and postoperative care.

Surgical treatment of the ascending aortic aneurysm compromises endovascular grafting and open surgical procedure. The decision to treat an aneurysm must be made with same rigor for endovascular therapy as for open surgical therapy. The presence of a small thoracic aneurysm is not a valid indication for endovascular therapy just because stent therapy is available. Furthermore, stent deployment for the ascending aortic aneurysm is not approved in most of the countries.

Company Profile

With the vision to provide sustainable solution to the health care challenges and support nation's self sufficiency in medicine, TIME Pharmaceuticals has made a remarkable presence in the Nepali pharmaceutical market with a glorious history of 19 years.

"Inspired by excellence" and adhering high ethical standards, TIME Pharma is committed to deliver best of health care services to every individual for a healthier life catering more than 180 products of major therapeutic segments.

Being consistent with our responsibility as nation's premier innovation based technology driven company we intend to collaborate with health care providers, governing bodies and local communities to provide access to quality and affordable medicines.

We believe in continual evolution with technological advancement which has been accomplished with the newly built state of art cephalosporin block and technical collaboration with MNC.

About Us

Commercial Operation Started : November 1997
Current Human Resources : 210
Production Area : 35,000 sq ft
Production : Separate Manufacturing Facilities for
Penicillin,
Non Penicillin,
Sterile Products &
Cephalosporin Products

We Manufacture

Tablets:
82 million Units
Capsules:
50 million Units

Liquid:
3 million Units
Dry Syrup:
1 million Units

Ointments:
2.3 million Units

Eye/Ear/Nasal drops:
0.5 million Units

Cephalosporin
Block
Tablets: 128.3 million Units
Capsules: 29.7 million Units
Dry Syrup:36.6 million Units

Manufacturing Unit





Sinex
Pseudoephedrine 30 mg + Paracetamol 500 mg + Chlorpheniramine Maleate 2 mg Tablets/Suspension

COMPANY HISTORY

20th Years

Celebrating 20 YEARS 2054-2073 of service

Technical Collaboration with Multi-National Company

2072

Established separate Cephalosporin block with ultra modern manufacturing facility

2072

Introduction of COSMO Division with focus on Dermatology, ENT, Gynaecology & Urology therapeutic segments

2070

Expansion of separate manufacturing facility of Sterile Products esp. E/E Drops

2067

Introduction of NEXUS Division with focus on Orthopedic, Neurology, Gastroenterology & Dental therapeutic segments

2066

Certified with WHO:GMP, ISO 9001 & ISO 14001

2065

Expansion of facility- Oral Liquid Production

2064

Modernization of Infrastructures with separate Penicillin Block

2063

Launching of speciality division GENESIS with focus on Cardiology, Diabetology & Endocrionology & Psychiatric therapeutic segments

2063

Expansion of product range- Cephalosporin Products

2059

Expansion of facility- Ointment Production

2056

Expansion of product range- Penicillin Products

2054

Commercial Operation Started

2054

Management of Acute Ischemic Stroke: Time is Brain

Dr. Gopal Sedain
Assistant Professor
Department of Neurosurgery
IOM, TUTH

Acute Ischemic Stroke (AIS) is a leading cause of morbidity and mortality in adult population. AIS care has undergone a revolution since the approval of intravenous (IV) recombinant tissue plasminogen activator (rt-PA) for acute ischemic stroke by the US Food and Drug Administration (FDA) in 1995. As rt-PA has a time window of 4.5 hours, numerous clinical trials are ongoing to expand treatment windows, increase the number of patients eligible for therapy, and evaluate new and innovative therapies, particularly for neuroprotection.

Pathophysiology

In ischemic stroke, decreased or absent circulating blood flow deprives neurons of necessary metabolic substrates. Because the brain does not store glucose, ischemia is tolerated poorly. Cerebral blood flow usually is compromised because of occlusion of a cerebral artery by a clot. The amount of collateral flow can influence the size of the infarct and ischemic penumbra. Temperature and glucose metabolism also have effects on cell death and tissue injury. An important concept in AIS is the penumbra. When an artery occludes, neurons are affected differently, depending upon the amount of residual blood flow. Normal cerebral blood flow is greater than 50 mL/100 mg/min. Once blood flow decreases to less than 20 mL/100 mg/min, infarction occurs. If blood flow decreases to less than 10 mL/100 mg/min, irreversible neuronal death occurs rapidly. Blood flow between 11 and 20 mL/100 mg/min is thought to represent the ischemic penumbra, an area where the cells are functionally silent because of ischemia, but are still able to recover if blood flow is restored. Many acute stroke therapies are targeted toward restoring flow or function to the ischemic penumbra.

Thrombolysis

The first method to restore cerebral perfusion is clot lysis, with the goal of re-establishing blood flow to the affected tissue. Endogenous tissue-plasminogen activator converts circulation plasminogen to plasmin, an enzyme responsible for fibrin dissolution and maintaining coagulation homeostasis. Fibrinolysis is enhanced powerfully by rt-PA. Patient who received rt-PA were 30% more likely to have minimal or no disability at 3 months.

Who should receive I/V thrombolysis?

Inclusion criteria

- Clinical signs and symptoms consistent with ischemic stroke
- Patient last seen normal within 4.5 hours
- Measurable neurologic deficit

Exclusion criteria

- Any hemorrhage on neuroimaging (CT or MRI)
- Hypodensity greater than one third cerebral hemisphere on CT
- Systolic Blood Pressure (SBP) greater than 185 mm Hg or
- Diastolic Blood Pressure (DBP) greater than 110 mm Hg
- Serum glucose less than 50 mg/dL
- Platelet count less than 1 lakh/mm^3
- International normalized ratio (INR) greater than 1.7
- Elevated Partial Thromboplastin Time (PTT)
- Any history of intracranial hemorrhage
- Arterial puncture at a noncompressible site in past 7 days
- Major surgery in past 14 days
- Gastrointestinal (GI) bleed or hematuria in past 21 days
- Ischemic stroke, myocardial infarction, or serious head trauma in past 3 months

Protocol

- Total dose of rt-PA: 0.9 mg/kg (maximum dose 90 mg)
- Give 10% as initial IV bolus; Infuse remainder over 1 hour
- Admit patient to an ICU or stroke unit for monitoring Neurologic assessments: every 15 minutes during infusion, then every 30 minutes for next 6 hours, then every hour until 24 hours after treatment
- BP monitoring: every 15 minutes for 2 hours, then every 30 minutes for next 6 hours, then every hour until 24 hours after treatment
- Administer antihypertensive medication to maintain systolic BP less than or equal to 180 mm Hg and diastolic BP less than or equal to 105 mm Hg
- Delay placement of nasogastric tubes, indwelling bladder catheters, or IA pressure catheters
- Follow-up CT or MRI scan at approximately 24 hours after rt-PA, before starting anticoagulation or antiplatelet agents
- Delay antithrombotic agents for 24 hours after rt-PA

Early detection of stroke

B – Balance : A sudden loss of balance or coordination, such as not being able to walk a straight line or touch a finger to the nose.
E – Eyes : Sudden vision changes, such as or in one eye.
F – Face Drooping : Droopiness or numbness on one side of the face, such as an uneven smile.
A – Arm Weakness : in one arm, such as not being able to raise both arms.
S – Speech Difficulty : Slurred speech or speech that is difficult to understand.
T – Time to Call : If any of the above symptoms are present, it's important to call emergency or go to the ER right away, even if symptoms seem to disappear. Be sure to record the time when symptoms started.

Technical issues

Stroke patients attend the emergency hence emphasis has to be to educate the staff in emergency department regarding early detection of ischemic stroke. The availability of alteplase (rt- PA) in the hospital pharmacy is another essential part. The cost of the treatment is relatively high. Alteplase is available in 50mg vials (around 75000 NRs). A 70 kg patient would require 63mg (0.9x70) of the drug. The cost of 2 vials would be around 1.5 lakh rupees. Considering the long term cost and sequelae of ischemic stroke, it is worth considering treatment with thrombolysis whenever appropriate. rt- PA is available in Nepal and we should use it in our patients whenever indicated to decrease the morbidity due to Ischemic stroke.

Winner of MEDITIME 18th Issue:

- ***Dr. Kalyan Sapkota***
  Internal Medicine
  Bharatpur Hospital
- ***Dr. Rupak Bhandari***
  MDGP & ENT
  BPKISH Dharan
- ***Dr. Pukar Thapa***
  Internal Medicine
  Alka Hospital
- ***Dr. Bhola Shrestha***
  Orthopedic Surgeon
  Pokhara
- ***Dr. Tulika Dube***
  ENT Specialist
  Fewa City Hospital
- ***Dr. Prakriti Gyawali***
  Dermatologist
  Hetauda Hospital
- ***Dr. Sagun Panta***
  Psychiatry
  TUTH, Kathmadu
- ***Dr. Krishna Bahadur Thapa***
  MD Physician
  GMC, Pokhara

Self-Management of Peripheral Artery Diseases

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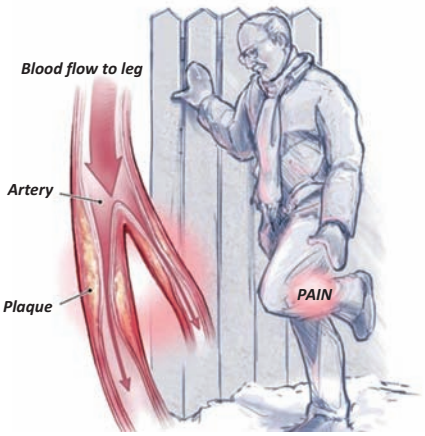
Consultant Vascular & Endovascular surgeon, Norvic hospital

1. Lifestyle and home remedies : Many people can manage the symptoms of peripheral artery disease and stop the progression of the disease through lifestyle changes, especially quitting smoking. To stabilize or improve PAD:

a. Stop smoking. Smoking contributes to constriction and damage of your arteries and is a significant risk factor for the development and worsening of PAD. If you smoke, quitting is the most important thing you can do to reduce your risk of complications. If you're having trouble quitting on your own, ask your doctor about smoking cessation options, including medications to help you quit.

b. Exercise. This is a key component. Success in treatment of PAD is often measured by how far you can walk without pain. Proper exercise helps condition your muscles to use oxygen more efficiently. Your doctor can help you develop an appropriate exercise plan. He or she may refer you to a claudication exercise rehabilitation program.

Individual with peripheral arterial diseases



c. Eat a healthy diet. A heart-healthy diet low in saturated fat can help control your blood pressure and cholesterol levels, which contribute to atherosclerosis.

d. Avoid certain cold medications. Over-the-counter cold remedies that contain pseudoephedrine (Advil Cold & Sinus, Aleve-D Sinus & Headache, Claritin-D, Sudafed, Tylenol Cold, Zyrtec-D, others) constrict your blood vessels and may increase your PAD symptoms.

2. Careful foot care : In addition to the above suggestions, take good care of your feet. People with peripheral artery disease, especially those who also have diabetes, are at risk of poor healing of sores on the lower legs and feet. Poor blood circulation can postpone or prevent proper healing and increases the risk of infection. Follow this advice to care for your feet:

a. Wash your feet daily, dry them thoroughly and moisturize often to prevent cracks that can lead to infection. Don't moisturize between the toes, however, as this can encourage fungal growth.

b. Wear well-fitting shoes and thick, dry socks.

c. Promptly treat any fungal infections of the feet, such as athlete's foot.

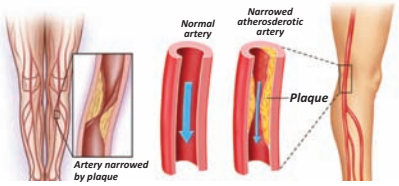
d. Take care when trimming your nails.

e. Inspect your feet daily for injuries.

f. Have a foot doctor (podiatrist) treat bunions, corns or calluses.

g. See your vascular specialist at the first sign of a sore or injury to your skin.

Peripheral Arterial Disease in the lower extremities is aslo linked to coronary artery disease.



3. Coping and support: Peripheral artery disease can be frustrating, especially when the exercise that will help you get better causes you pain. Don't get discouraged, however. As you continue exercising, you'll increase the distance you can walk without pain. You may find it helpful to raise the head of your bed by 4 to 6 inches (10 to 15 centimeters), because keeping your legs below the level of your heart usually lessens pain. Another tip for reducing your symptoms is to avoid cold temperatures as much as possible. If you can't avoid the cold, be sure to dress in warm layers.

4. Prevention:The best way to prevent claudication is to maintain a healthy lifestyle such as

a. Quit smoking if you're a smoker.

B. If you have diabetes, keep your blood sugar in good control.

c. Exercise regularly. Aim for 30 minutes several times a week after you have gotten your doctor's OK.

d. Lower your cholesterol and blood pressure levels, if applicable.

e. Eat foods that are low in saturated fat.

f. Maintain a healthy weight.

Scrub Typhus

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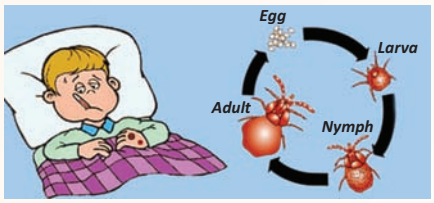
Green City Hospital

Scrub typhus is caused by bacterial organism called Rickettsia *(Rickettsia tsutsugamushi)* via the mite *Leptotrombidium akamushi* and possibly *Leptotrombidium deliense*. Once the mite is infected, it acts as a reservoir for Rickettsia.The infection is maintained in mites from generation to generation by transovarial transmission. Humans are accidental hosts in scrub typhus; rats, mice, and larger mammals are the usual hosts.



It occurs in the Western Pacific Region, Northern Australia, and the Indian subcontinent. This infection is in rise in Nepal this year. The incidence of scrub typhus is largely unknown. Many cases are undiagnosed because of its nonspecific manifestations and the lack of laboratory diagnostic testing in endemic areas. However, one study found that the incidence of scrub typhus in Malaysia was approximately 3% per month, and multiple infections in the same individual are possible because of lack of cross-immunity among the various strains of its causative organism, *Orientia tsutsugamushi.*

History

Causes

- Overcrowding leads to close personal contact and spread of arthropod vector.
- *Lack of personal hygiene:* Infrequent bathing and changing of clothes provides a hospitable environment for body lice.
- *Appropriate season:* Cold weather may lead to overcrowding indoors and infrequent bathing and changing of clothes are advantageous for lice. Flea vectors are more abundant in warmer weather, when their hosts are more plentiful.
- Patients may have a history of mite bite.
- History may include exposure to natural disaster or war.

Symptoms

Abrupt onset of fever, headache, and rash are common symptoms in rickettsial infections.

Other less common symptoms of typhus include nonproductive cough and deafness/tinnitus.

The duration of most clinical symptoms and signs in untreated typhus is approximately 2 weeks. Several months may pass before complete recovery from fatigue and malaise.

Scrub typhus sometimes may be difficult to recognize and diagnose because the symptoms and signs of the illness are often nonspecific.

A painless papule develops at the site of the chigger bite and subsequently undergoes central necrosis with formation of an Eschar.

Regional lymphadenopathy, with development of large and tender lymph nodes, occurs at the site of the bite and may lead to generalized lymphadenopathy.

The nonspecific presentation and lack of the characteristic Eschar in 40% of patients leads to many undiagnosed cases of scrub typhus

Physical examination

Generalized lymphadenopathy may occur.

Eschar -This is found in the scrub form of typhus and is essential in confirming a clinical diagnosis. It occurs in up to 60% of cases. Eschar occurs at the site of the arthropod bite. It starts as a painless papule and the lesion becomes indurated and enlarged. The center of the lesion becomes necrotic and develops into a black scab.

Mild splenomegaly may occur.

Mild hepatomegaly may occur.

Conjunctival suffusion may occur in scrub typhus.

Investigation

Besides obtaining some abnormalities in baseline blood investigation, following laboratory work up is done:

- Indirect immunofluorescence assay (IFA) or enzyme immunoassay (EIA) testing can be used to evaluate for a rise in the immunoglobulin M (IgM) antibody titer, which indicates an acute primary disease.
- Brill-Zinsser disease can be confirmed in a patient with a history of primary epidemic typhus who has recurrent symptoms and signs of typhus and a rise in the immunoglobulin G (IgG) antibody titer, which indicates a secondary immune response.
- IFA and EIA tests can be used to confirm a diagnosis of typhus, but they do not identify the various rickettsial species.
- Polymerase chain reaction (CR) amplification of rickettsial DNA of serum or skin biopsy specimens can be used for diagnosing typhus.
- The complement fixation (CF) test is a serological test that can be used to demonstrate which specific rickettsial organism is causing disease by detection of specific antibodies. Rapid diagnostic assays for scrub typhus, such as latex agglutination tests, are currently under development.

Treatment

Besides treating acute infection with early use of antibiotics like doxycycline and chloramphenicol, supportive fluid therapy for managing complication is very important.

Signs, symptoms and potential complications of typhus are due to hematogenous spread of organisms with resultant endothelial proliferation and vasculitis.

The central nervous, musculoskeletal & cardiovascular systems may be involved, as well as the skin, lungs, and kidneys. Multiorgan system involvement is possible.

Vasculitis may result in hypovolemia, electrolyte disturbances, and digital gangrene.

Hemodynamic status and fluid/electrolyte replacement should be diligently monitored.

Secondary infections, such as bacterial pneumonia, should be treated appropriately.

सर्पदंश - एक अध्ययन

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नेपालमा पहिलो पटक स्नेक बाइट ट्रेनिङ्गको सुरुवात गरेका डा. छबिलाल थापा सर्पदंशको निजी तवरमा नै व्यवस्थापन र सेवा शुरु गर्ने पहिलो व्यक्ति हुन सर्पदंश व्यवस्थापन निर्देशिका लेखनमा महत्वपुर्ण भुमिका निर्वाह गरेका डा. थापा नेपाल सरकारको बरिष्ठ मेडिकल सुपेरीटेनडेन्ट (अनिवार्य अवकास प्राप्त) तथा टेक्नोलोजी विषेशज्ञ हुन ।

राष्ट्रिय स्तरमा नै सर्पदंश सम्वन्धि विभिन्न तालिम सुरुवात गर्ने र त्यसको निरन्तर संचालन गर्दै आएका डा. थापाले नेपाली परिवेश अनुसार उपचार विधी अर्थात गाईडलाईन बिकास गर्ने मुख्य भूमिका निर्वाह गरेका हुन । सो गाईड लाईनको मुख्य ध्यय भनेको औषधिको कम भन्दा कम प्रयोग गरि कसरी बिरामीको ज्यान बचाउन हो ।

उनैको पहलमा भएको विभिन्न कार्यक्रम र कार्ययोजना को प्रतिफाल नै सरकारले पनि सर्पदंश को निम्ति निःशुल्क औषधी बितरण गर्दै आएको छ ।

निजि क्षेत्रमा समेत सर्पदंशको उपचार विस्तार गरेका डा. थापाले सर्पदंश र त्यसको उपचार मा बिशेष अध्ययन गरेका थिए । बिदेशी बिषेशज्ञको संलग्नतामा गरिएको अध्ययनमा अन्तराष्ट्रिय गाईडलाईन र नेपाली गाईडलाईनको उपचारको पद्धतीमा अध्ययन गरिएको थियो । अन्तराष्ट्रिय गाईडलाईन अनुसार सर्पदंशमा हाईडोज प्रयोग गर्ने गर्दछ भने नेपालको गाईडलाईन अनुसार लो डोज अर्थात् कम भन्दा कम औषधि प्रयोग गरेर ज्यान बचाउने गरिन्छ । रिसर्चको मुल उद्देश्य हाई र लो डोजमा कुन चाही प्रभावकारी भन्ने थियो ।

सो अध्ययन अनुसार पूर्व तिर बढि गोमन सर्प पाईएको थियो भने मध्यमाञ्चल तथा पश्चिमाञ्चलमा चाहीं करेत सर्प पाईएको थियो । सामान्यत गोमन सर्पले टोक्यो भने बढि खतरा हुने तर समयमा नै उपचार पाएमा निको पनि हुन्छ भने करेतले टोक्यो भने उपचार पाएता पनि बढि जोखिम हुन्छ ।

रिसर्चबाट के पाइयो भने गोमनको लागि हाई डोज प्रभावकारी र करेतको लागि चाहिँ लो डोज र हाई डोजमा केही अन्तर पाईएन । सो रिसर्चमा बढिमा ३० भायल दिनु भन्ने थियो । यसमा एकजनालाई मात्र २९ भायल दिइएको थियो भने अरुलाई चाहि लगभग २० भाएलमा नै प्रभावकारी देखिएको थियो ।

साथै एन्टि स्नेक भेनम डिटेक्सन किट समेत रिसर्चको क्रममा बिकाश भैरहेको छ जुन अन्तिम अवस्थामा छ । सो किटको माध्यम बाट कुन सर्पले टोकेको भन्ने पत्ता लाग्छ र सर्पको जात प्रजाति अनुसार एन्टि स्नेक भेनम दिन सकिन्छ । नेपालमा प्रयोग गर्ने भारतमा बनेको औषधी हो जुन उनिहरुको देशमा पाईने सर्पको आधारमा ४ किसिमको मात्र छ । यदि भोलि त्यो प्रजातिको सर्प छुटयाउन सक्ने भएर जुन जातको सर्प छ त्यहि अनुसारको एन्टि स्नेक भेनम बनाउन सकियो भने नेपाललाई धेरै प्रभावकारी साबित हुन्छ ।

नेपालको २६ वटा जिल्लामा सर्पदंशको प्रभाव बढि छ । २६ वटा जिल्लाहरुमध्ये धेरै जस्तो तराई क्षेत्र नै पर्छ । कतिपय चाहि भित्री मधेसका जिल्ला जस्तो सिन्धुली पनि पर्दछ । नेपालमा मुख्यतः पाइने विषालु सर्पहरु भनेको गोमन र करेत जाती हो ।

संसारमै मानिस सर्पसँग डराउछन्, त्यसको बारेमा कुरा गर्न चाहदैनन् । पाल्ने कुरा त परै जाओस् । सर्प मन पराउने मान्छे विरलै छन् होला । यो अज्ञानताको कमिले गर्दा हो । सर्पले टोकेको सबैलाई विष लाग्दैन । सयमा दश जना मात्र विषलु सर्पले टोकेको हुन्छ । सर्पले टोक्दा विष भित्र दिएको छैन भने विष लाग्दैन । सर्पले टोक्ने बित्तिकै मरिहालिन्छ भन्ने धारणा गलत हो ।

बिरामीका प्रत्यक्ष लक्षणहरु नदेखिएसम्म एन्टि स्नेक भेनम चलाउन मिल्दैन । बिरामीलाई हेरेर उसले देखाउने लक्षणका आधारमा मात्र औषधी चलाउनुपर्दछ । यदि बिरामीलाई रेसपिरेटरी प्यारालाईसिस भइसकेको रैछ भने बिना भेन्टिलेसनमा नराखी उपचार गर्न गाह्रो हुन्छ । त्यसैले १ प्रतिशत जति बिरामीलाई मात्र आई सियुमा राख्नुपर्ने हुन्छ । कुनै बिरामी भेन्टिलेसनमा राख्दा पनि मृत्यु हुने कारण चाहिँ उपचार गर्न ढिला भई बिरामीको दिमागमा अक्सिजनको कमि भयो भने मात्र हो । अर्को कारण चाहि हामी कहा भएको एन्टि स्नेक भेनम अनुसारको बिरामीलाई टोकेको सर्पको प्रजाति थाहा भएन भने उपचार गर्न गाह्रो हुन्छ । गोमन सर्पको १०/१५ मिनेटमा नै विष शरिरमा फैलन्छ । करेतले टोकेको हो भने त्यसको विष ५-६ घण्टामा मात्र सुरु हुन्छ । करेतको विष लागेको लक्ष्ण ढिलो मात्र देखा पर्दछ ।

करेत घर वरपर बस्ने हुदाँ आफ्नो घर वरपर सफा राख्नुपर्छ । यो घरको छानो, ओछ्यानमा आउने हुनाले सकेसम्म भुईमा नसुत्ने तथा सुत्दा झुलको प्रयोग गर्नु पर्छ । गोमनले प्राय दिनमा टोक्ने हुदाँ सर्तक भएर हिड्नु, सर्प देखेर भाग्ने सर्पलाई चलाउने गर्नु हुदैन । रातिमा बाहिर निस्कदा टर्च लिएर निस्कने गर्नुपर्छ । सधैँ चप्पल लगाएर हिड्नुपर्छ ।

सर्प मानिसलाई टोक्न भनेर आउने होइन, मुसा उनीहरुको आहारा हो । मुसा मर्ने क्रममा मानिससँग छोइयो भने वा खतरा महसु गरेर सुरक्षाका लागि टोक्ने मात्र हो ।

सर्पले टोकेमा जति सक्दो चाडाँ अस्पताल पुऱ्याउनु पर्दछ । टोकिहालेको खण्डमा प्राथमिक उपचारको लागि टोकेको भाग भन्दा केहि तल नरम कपडाले बाँध्नुपर्दछ, आत्तिएर कुदुन चाहिँ हुदैन ।

Mushroom, Fire, Matchstick, Breath, Cold

BRAIN TEASER

1. What kind of room has no doors or windows?
2. Feed me and I live, yet give me a drink and I die.
3. Tear one off and scratch my head what was red is black instead.
4. What is as light as a feather, but even the world's strongest man couldn't hold it for more than a minute?
5. What can you catch but not throw?

Lucky winner will Get Surprise Gift From

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Winnner & Article Contribution Pictures

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Psychiatrist

Dr. Kamal Kumal
Cardiologist

Dr. Bikash Pandey
MS ENT, CMS

Last date of "Brain Teaser" answers Submission : ***Dec. 1st, 2016***

RESPONSE FORM

Name : _____

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Birthday : _____ Anniversary Day : _____

Comments : _____

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Moments in TIME

SSM Ujjwal Dev Pradhan Receiving Team Leader of the Year 72/73 Award

Achievers of FY 72/73

Marketing Team at Sun Temple, Bhuwaneshwor, Puri

Marketing Team Enjoying at Puri Beach

Team Genesis Celebrating World Heart Day at Basantapur

Participating in DEAN Conference 2016

Participating in NESON Conference 2016

Participating in SODVELONCON 2016

Celebrating 20 YEARS of service

1997-2016

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On this celebration of 20th anniversary,
we thank all our well wishers and valued customers
for supporting us throughout our journey without whom,
it would not have been possible to make this glorious history.

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Treasuring our present & Shaping our future"

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