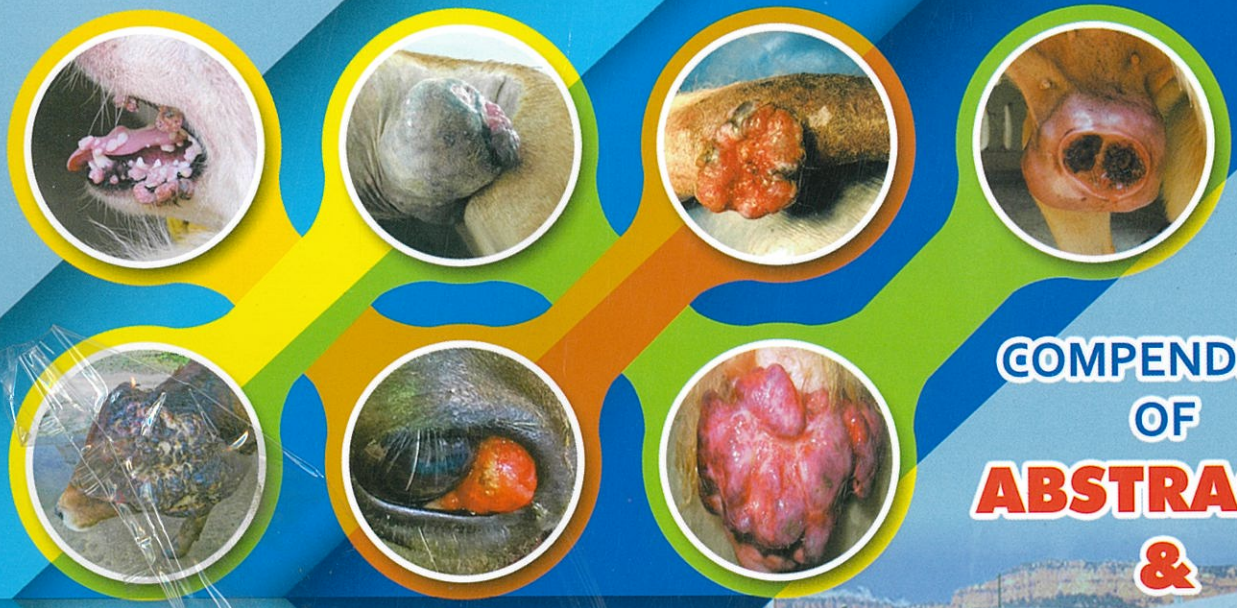
41st Annual Congress of Indian Society for Veterinary Surgery
and National Symposium
On

"NEW HORIZONS IN CANCER RESEARCH PERTAINING TO EFFECT ON HEALTH, PRODUCTION AND REPRODUCTION IN ANIMALS"

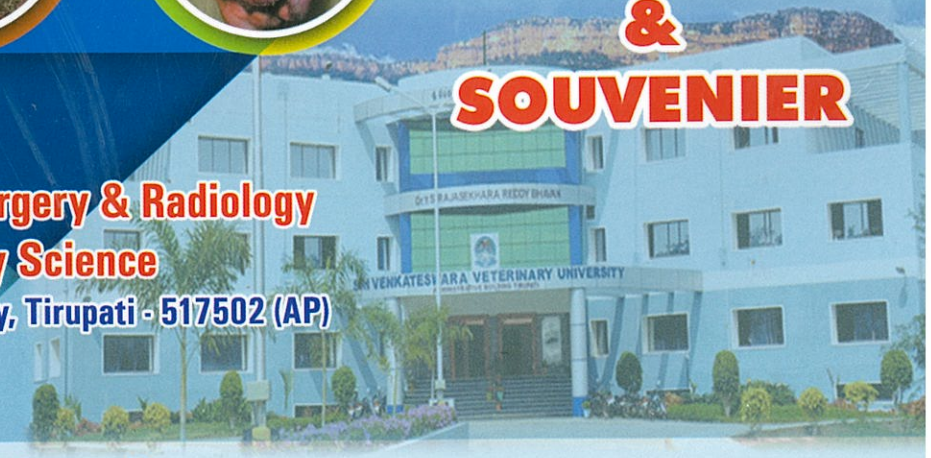
14th 15th and 16th DECEMBER 2017



COMPENDIUM OF ABSTRACTS & SOUVENIER

Organized by

Department of Veterinary Surgery & Radiology
College of Veterinary Science
Sri Venkateswara Veterinary University, Tirupati - 517502 (AP)



41st ANNUAL CONGRESS OF
INDIAN SOCIETY FOR VETERINARY SURGERY

AND

NATIONAL SYMPOSIUM
ON
"NEW HORIZONS IN CANCER RESEARCH PERTAINING TO EFFECT ON HEALTH, PRODUCTION AND REPRODUCTION IN ANIMALS"

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College of Veterinary Science
Sri Venkateswara Veterinary University
Tirupati-517502, Andhra Pradesh

WE ARE THANKFUL TO

ICAR

Canara Bank

Andhra Bank

Madala Saikumar

Virbac Animal Health India Pvt. Ltd.

Karl Storz

Anand Group & Companies, Bhimavaram

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Sri Balaji Prasad, Grameena Bank

Dr. Jayaprakash, Nellore

All Nellore & Venkatagiri Persons

Organising Committee – ISVS 2017, Tirupati

SRI VENKATESWARA VETERINARY UNIVERSITY

TIRUPATI, ANDHRA PRADESH

Dr. Y. Hari Babu,
M.V.Sc., Ph.D.,FNAVS.,M.B.A.(PE),P.G.D.E.E.,P.G.D.B.I
Vice - Chancellor

MESSAGE

It is heartening to note that the Department of Veterinary Surgery & Radiology College of Veterinary Science SVVU is organizing 41st Annual Congress of Indian Society for Veterinary Surgery and National Symposium on "New horizons in cancer research pertaining to effect on health, production and reproduction in animals" on 14th 15th and 16th December 2017.

The theme of the symposium aims at providing he unique opportunity in the light of creating awareness on increasing incidence of cancer in veterinary field. Globally many scientific organizations are working hard to reduce the incidence of caner in human subjects and animals also. It is possible with early detection and effective preventive measures. Health is the key factor responsible for production and reproduction in animals. As per the data available disease conditions like cancer is leading to mortality and losses to formers and pet owners, hence this area of specialization needs comprehensive and combined efforts by all scientists with holistic approach.

This is right time to establish VETERINARY CANCER REGISTRY in the country where by scientific groups which are working on it should take up this task on large scale in collaboration with the other institutions.

On this propitious occasion I wish to appeal all the faculty, scientists, researchers and students join hands to reduce cancer incidence in humans as well as in animals. I urge all the members of the august body to extrapolate the information from medical side towards Veterinary Oncological Research. I hope this conference will be fruitful in fulfilling the quest for scientific temperament.

On this occasion I congratulate Organizing Committee of ISVS 2017 and team, and wish them a great success.

(Y. HARI BABU)

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TAMIL NADU VETERINARY AND ANIMAL SCIENCES UNIVERSITY

Dr. S. THILAGAR
Vice - Chancellor
and
President ISVS

MESSAGE

It is gratifying to learn that the Department of Veterinary Surgery and Radiology is organizing 41st ISVS National Symposium on **"New Horizons in Cancer Research Pertaining to Health, Production and Reproduction in Animals"** from 14th to 16th December 2017 at College of Veterinary Science, Sri Venkateswara Veterinary University (SVVU), Tirupati.

Cancer research is common area of interest for both in human and veterinary medicine since the incidence of cancer is increasing day by day Animal husbandry plays pivotal role in agriculture in turn farmers economy, where in animal production and reproduction mainly depends on animal health. Highest death rates in canines are reported to be due to cancer. Domestic animals and wild animals do suffer from varieties of cancer however may go unnoticed. It is the time for veterinary clinician to concentrate on different aspects of cancer in collaboration with medical and allied scientific fields.

Keeping in view the contributions made by the faculty and need of the hour the theme was rightly selected by the organizing committee of SVVU. I strongly urge the authorities to initiate the steps to establish VETERINARY CANCER REGISTRY IN INDIA like in cancer registries from human side. I wish the deliberations by subject experts, presentations by researchers, faculty be useful to the budding veterinary surgeons for planning their career and research.

I congratulate the organizers for starting a separate VETERINARY OPHTHALMOLOGY session in this symposium. I also appreciate the continuous attempts made by organizers in this area of research and wish them all the best.

Date : 23-11-2017
Place : Chennai-51

(S. THILAGAR)

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From the Executive Secretary's Pen

Dr. D.B. Patil
Executive Secretary
Indian Society for Veterinary Surgery (ISVS)
Director of Research & Dean PG Studies
Kamdhenu University, Gandhinagar, Gujarat

MESSAGE

I am glad that the ISVA is organizing the 41st Annual Congress and National Symposium on an important topic **"New Horizons in Cancer Research Pertaining to Effect on Health, Production and Reproduction in Animals".** Cancer research demands multi-institutional and transdisciplinary approaches to arrive at meaningful solutions for clinicians. The theme will underpin the need for Veterinary Clinicians at pan India level to adopt uniform case reporting policy policy and digitise in order to start 'Veterinary Cancer Registry'.

Veterinary Surgery demands team work. Here I wish to quote from Chemistry Noble Laureate (2017) Jacques Dubochet.

- "In our group it was a necessary requirement that one has to able to collaborate".
- "I hate personal competition and so each time in my career I came in a field where it was highly competitive I gave up".
- "Reading science seriously.... there are so many possibilities".

This is dream environs for all of us....!

I am confident of meaningful deliberations different scientific sessions. The technical interactions will go a long way in updating academicians, postgraduates and field vets and this Meet will facilitate possible further collaborations. During this Symposium a separate Session on 'Veterinary Ophthalmology' is planned.

I am sure 41st ISVS Symposium in this Temple City, Tirupati will be cherished by one and all for a long time.

I wish this event a grand success and trust you will enjoy amidst divine environs and also get spiritually updated.

(D.B. Patil)

SRI VENKATESWARA VETERINARY UNIVERSITY

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Dr. T.S. Chandrasekhara Rao
M.V.Sc., Ph.D., FNAVS, FIAVA
Dean Faculty of Veterinary Science

MESSAGE

I am delighted to note that 41st annual congress of Indian society for Veterinary Surgery and National Symposium on "New horizons in cancer research pertaining to effect on Health, Production and Reproduction in animals" will be held from 14th to 16th December 2017 by the department of Veterinary Surgery and Rediology College of Veterinary Science SVVU Tirupati.

SVVU the premier university recently ranked 4th by NIRF among state veterinary universitities is committed to provide quality education to students, and professional services for substantital economic growth for farmers with innovative technologies. It is crucial that animal health is very important for Production and Reproduction. The wellness of animals, humans, and ecosystem forms the basis for the one health concept wherein cancer is one of the condition common to humans and animals leading to mortality and production lossess. Cancer is one of the dreadful disease - causing deaths in dogs, productoin and reproductive losses in large animals.

21st century is the era of multidisciplinary research where in holistic direction is required. Though advancements in Oncology area is taking place throughout the world at a greater pace still the number of cases reported are increasing in human as well as in animals which require global and comprehensive aproach. This occasion forms a platform for clinicians and budding Veterinary Surgeons to interact with other fellow Surgeons not only in cancer research but also in different speciality areas. This symposium includes keynote address, oration lectures, lead papers from eminent professionals in different sessions oral / poster presentations from delegates and practical demonstration by experts. I hope this symposium will be very much useful to all that all the participants.

I wish organizing committee and symposium all the best.

(T.S. CHANDRASEKHA RAO)

SRI VENKATESWARA VETERINARY UNIVERSITY

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Prof. D. Srinivasa Rao
M.V.Sc., Ph.D. (U.K.), FANA
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MESSAGE

I am happy to learn that the Department of Veterinary Surgery and Radiology College of Veterinary Science SVVU Tirupati is organizing 41st Annual congress of Indian Society for Veterinary Surgery and National symposium on "New horizons in Cancer Research pertaining to effect on Health production and reproduction in animals" which will be held from 14th to 16th December 2017.

Animal husbandry practices are mainly dependant on animal health wherein early diagnosis of diseases is important. Among various disease conditions veterinarians encounter, cancer is one of the important disease leading to mortality and also production losses. Since there is substantial increase in cancer cases in different species of animals at different places of the country necessitating us to proceed further in this area of research.

This area of research requires multidisciplinary involvement and support. Though cases are reported at different places of the country availability of expertise, facilities, cost economics play role in treating cases. At this juncture there is a need to admit and treat cases on scientific lines. In this connection I personally feel that the present theme is opt for symposium. I request the participants to make use of this opportunity for future development.

I whole heartedly congratulate the ISVS 2017 Team and wish the symposium a grand success.

D Srinivasa Rao 24/11/2017

(Prof. D. Srinivasa Rao)

SRI VENKATESWARA VETERINARY UNIVERSITY

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Dr. E. Raghava Rao
M.V.Sc., Ph.D.
Director of Research

MESSAGE

It's my pleasure to note that the Department of Veterinary Surgery & Radiology College of Veterinary Science SVVU is organizing 41st Annual congress of Indian Society for Veterinary surgery and national symposium on "New horizons in Cancer Research pertaining to effect on health, production and reproduction in animals" on 14th 15th and 16th December 2017.

Veterinary surgery is witnessing marked changes with the addition of scientific innovations useful to the clinicians. Developements parallel to medical field are being taken up in veterinary science also for well being of animals. In this context, research on cancer and its effects on health, production and reproduction was rightly selected as theme for symposium.

In day to day clinical practice veterinarians come across varieties of cancer cases in different species of animals *however* no comprehensive information is available at national level. Many a times these conditions go unnoticed leaving *heavy* production losses to the farmers. Hence it's the time for all the veterinary clinicians to report, recrod the cancer cases to the authorities to *evolve* a policy based on epidemiological data gathered from different areas.

This symposium is providing a common platform for such professional activity in collaboration with fellow veterinarians attending here. I request all the delegates to involve themselves in different sessions to know newer thing to plan further research.

I wish symposium a grand success.

24/11/17

(Prof. E. Raghava Rao)

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Date : 25-11-2017

Dr. P. Eswara Prasad
M.V.Sc., Ph.D.
Associate Dean

MESSAGE

I with to congratulate the Dept. of Veterinary Surgery & Radiology on organizing 41st Annual Congress of Indian Society for Veterinary Surgery and National Symposium on "New horizons in Cancer Research pertaining to effect on Health production and reproduction in animals" from 14th to 16th December, 2017 at College of Veterianry Science, Tirupati.

It is a mater of pride that the faculty of the department have made significant contributions in the field of veterinary surgery in particular Large animal and Small animal surgery, Anaesthesia, Biomaterials and Surgical oncology. Cancer being the dereadful clinical condition, affects animal health thereby decreases production and reproduction.

In this scenario of globalization we need to concentrate on this type conditions in depth to safeguard our livestock, pets etc. The theme of the symposium so selected is rightly based on the need of the hour. Scientists, faculty and researchers shall give at most priority for reporting the cases with valid information to pool up data for developing vaccine or, for conducting drug trials.

I request all the delegates to make use of this symposium as platform to discuss various issues. The deliberations and experiences of speakers would be of great use to carryout research in a more meaningful way.

All the best.

(Dr. P. Eswara Prasad)

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VETERINARY SURGERY AND RADIOLOGY

The Department of Surgery and Gynecology was started on 09.07.1958 and Gynecology department was separated from Surgery in the year 1960. During 1980 the Department was re-designed as Dept. of Surgery and Radiology. The PG programme was started during 1968-69 and 120 candidates were awarded with M.V.Sc. degree so far. The Ph.D programme was started during 1982-83 and 16 candidates were awarded with Ph.D so far. The department is a referral centre for critical and special surgical cases from all corners of the state

The Department staff has published around 520 National and 60 International articles and they also participated in several National conferences, workshops etc. This Department is known for its noteworthy contributions like Patellar desmotomy set in Bovines (Prof. S.V. Rao), Electroanaesthesia in Buffalo (Prof. N.V. Rao), Acupunture Anaesthesia, Acupuncture treatment (Prof. G.V. Lakshmipathi) and Embryo Transfer Technique (Prof. O. Ramakrishna and Prof. K.V. Rao). New methods of clinical investigations like non-invasive method of pregnancy diagnosis in canines, endoscopic investigations of canine upper gastrointestinal tract, preemptive analgesia and canine dental problems were adopted in the department. The senior faculty of department handled research schemes of ICAR, Indo-US projects on Embryo transfer, Electroanaesthesia. Acupunture anaesthesia. . The department is extending technical help to many traditional and medical universities in their scientific works.

The department has organized national symposia in 1977, 1981 and 1994 with Dr. O. Ramakrishna as organizing secretary, in 2016 and 2017 Dr. R.V. Suresh Kumar as organizing secretary.

The department has facilities like fully air-conditioned small animal operation theatre ultrasound scan, endoscopy, Bio monitor, laparoscopy, surgical and medical diathermy, Therapeutic ultrasound, muscle stimulator, large animal hydraulic operation table, 500mA X-ray unit, Computerized Radiography Unit, ECG, Pulse oximeter and cardiac defibrillator. Surgical camps are being conducted at different places of the state as and when the requests are made. Refresher training courses are being conducted for veterinarians of State Animal Husbandry department to update their surgical skills. Also 10 days ICAR short training programs and 14 days DBT training programs were conducted to the faculty. The department is now working in upstream areas like Oncology, Biomaterials and Small animal Surgery.

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ORGANIZING COMMITTEE – ISVS 2017

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Hon'ble Vice Chancellor
SVVU, Tirupati-517502 (AP)

Patron

Dr. T.S. Chandrasekhara Rao
Dean
Faculty of Veterinary Science
SVVU, Tirupati-517502 (AP)

Chairman

Dr. P. Eswara Prasad
Associate Dean
College of Veterinary Science
TIRUPATI-517502 (AP)

Organizing Secretary

Dr. R.V. Suresh Kumar
Professor & University Head
Department of Veterinary Surgery & Radiology
College of Veterinary Science
TIRUPATI – 517 502 (AP)

Conference Secretariat

Dr. P. Veena
Professor
Department of Veterinary Surgery & Radiology
College of Veterinary Science
TIRUPATI – 517 502 (AP)

Technical Assistance

Sri. M. Viswanatha Reddy
Radiographer
Department of Veterinary Surgery & Radiology
College of Veterinary Science
TIRUPATI – 517 502 (AP)

PROGRAMME SHEET

14-12-2017

Sl.No.	Time	Event	Venue
1.	07:30 to 09:00 am	**Breakfast**	Examination Hall
2.	08:00 to 09:30 am	Registration	Model Class Room
3.	09:30 to 11:00 am	Inaugural Function	Auditorium
4.	11:00 to 11:15 am	**Tea Break**	HUT adjacent to Auditorium
5.	11:15 to 12:00 noon	Keynote Address by Dr. T.S. Ravi Kumar	Auditorium
6.	12:00 to 12:30 pm	RPS Tyagi Oration Lecture by Dr. Amarpal	Auditorium
7.	12:30 to 01:00 pm	Guest Lecture by Dr. T.N. Ganesh	Auditorium
8.	01:00 to 02:00 pm	**Lunch**	Examination Hall
9.	02:00 to 06:00 pm	Small Animal Surgery Session I	Auditorium
		Avian Surgery Session	Committee Hall
		Ophthalmology Session	Model Class Room
10.	07:00 to 8:00 pm	Cultural Programme	Auditorium
11.	08:00 pm onwards	**Dinner**	Examination Hall

15-12-2017

Sl.No.	Time	Event	Venue
1.	07:30 to 08:30 am	**Breakfast**	Examination Hall
2.	08:00 to 09:00 am	Large Animal Anaesthesia demonstration	New TVCC
3.	09:00 to 01:00 pm	Small Animal Surgery Session II	Auditorium
		Orthopedic Surgery Session	Model Class Room
		Anesthesiology Session	Committee Hall
4.	01:00 to 02:00 pm	**Lunch**	Examination Hall
5.	02:00 to 05:00 pm	Ruminant Surgery Session	Auditorium
		Equine Surgery Session	
		Radiology and Imaging Session	Model Class Room
		Wild and Zoo Animal Surgery Session	Committee Hall
		Large animal poster session	
6.	08:00 pm onwards	**Dinner**	Examination Hall

16-12-2017

Sl.No.	Time	Event	Venue
1.	07:30 to 08:30 am	**Breakfast**	Examination Hall
2.	08:00 to 09:00 am	Large Animal Anesthesia demonstration	New TVCC
3.	09:30 to 10:30 am	Award (Dr. M.R. Patel Award for Best Field Veterinarian) Session	Auditorium
4.	10:00 to 12:00 noon	Small animal poster session	
5.	10:30 to 01:00 am	Plenary Session and General Body Meeting	Auditorium
6.	01:00 to 02:00 pm	**Lunch**	Examination Hall
7.	02:00 to 04:00 pm	Valedictory Function	Auditorium

CONTENTS

Dr. R.P.S. Tyagi Oration Award

STEM CELL THERAPY: PRESENT STATUS AND FUTURE PERSPECTIVES IN VETERINARY SCIENCES

Amarpal
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Abstract

Stem cells are defined as unspecialized cells having capacity of self-renewal by cell division, to proliferate extensively, and to differentiate into one or more cell/tissue types. Broadly stem cells can be categorized as embryonic stem cells and, adult or tissue-specific stem cells or induced pluripotent stem cells. Recent advances in stem cell biology have explained different mechanisms of their ability to repair damaged tissue, possibility of their allogenic and xenogenic application. Adult stem cells are now becoming popular choice for treating joint and bone diseases; haematological and bone marrow disorders, cardiac defects, non-healing wounds, spinal cord injuries, brain stroke and several other degenerative disorders. The application of embryonic stem cells (ESC) and induced pluripotent stem cells (iPS) are still in infancy.

Introduction

The stem cell (SC) application concept is one of the most exciting research topics of 21st century. The cells are currently considered to carry an all-in-one therapeutic potential for diverse clinical ailments owing to their characteristic properties of self-renewal, multiplication, immuno-modulation, and multi-lineage differentiation potential. They are like a blank microchip that can ultimately be programmed, under certain physiologic or experimental conditions, to become tissue or organ-specific cells with special functions. Stem cells may be totipotent, pluripotent, multipotent that corresponds to the cellular potential in zygote/morula. Depending upon their isolation they can categorised as embryonic stem cells and, various types of adult or tissue-specific stem cells that exist in a number of different fetal and adult tissues, and reprogrammed induced pluripotent stem cells (iPSCs). Among various stem cells, currently multipotent mesenchymal stem cells (MSCs) mainly contribute the stem cell therapy

Potency of stem cells

Stem cells can be classified according to their origin as embryonic, fetal, cord blood, amniotic fluid and adult stem cell. They are also classified according to their potency, which is described in terms of the ability of these cells to differentiate into various kinds of cells. Potency may be classified as uni-, multi-, pluri-, and totipotency, depending on the number of different tissue types the stem cell can produce.

Non-immunogenic characteristics of stem cells

Conventionally, use of autologous culture-derived cells seems to be logical as allogeneic cells could be associated with risk of rejection. However, use of autogenic mesenchymal stem

cells for therapeutic application may be hampered by the time lag required for expansion of allogenic stem cells before application. Interestingly, marrow-derived stem cells appear to enjoy a degree of immune privilege and their use may require minimal need for immunosuppressive drugs. It has been demonstrated that MSCs may be immune-privileged cells that avoid allogeneic rejection because they are hypoimmunogenic, often lacking major histocompatibility complex (MHC)-II and costimulatory molecule expression, which prevents T-cell responses through modulation of dendritic cells and disrupting natural killer (NK), as well as CD8+, CD4+ T cell function. Mesenchymal stromal cells (MSC) thus show great promise as a biological therapeutic for a diverse range of unmet medical needs.

MSC sources, culture and characterization

MSCs may be derived from variable body tissues like bone marrow, adipose tissue, embryonic tissue, synovial fluid and membrane, umbilical cord and peripheral blood, periosteum, muscle, gingival, periodontal ligament and nucleus pulposus, annulus fibrosus and cartilage end plate. However, the most commonly utilized sources include bone marrow, adipose tissue and fetal tissues like umbilical cord. MSCs are commonly isolated by 3 different protocols like ficoll hypaque, percoll and classic protocol. MSCs are generally cultured in a medium containing fetal bovine serum (FBS) of variable concentrations. Stem are characterized based on the recommendation of International Society for Cell Therapy (ISCT) like plastic adherence, expression of surface receptors (CD105, CD90, CD73, CD90) and inability to express CD45, CD34, CD14 or CD11b, CD79a or CD19 and HLA-DR. In addition, the cells should differentiate at least into osteogenic, chondrogenic and adipogenic lineages in respective media.

Applications of stem cells

Tissue regeneration using the stem cells is the only therapeutic option in certain degenerative diseases in animals. Stem cells possess significant potential for tissue generation to replace diseased or damaged areas in the body that also with risk of rejection and side effects at minimum level. Stem cell therapy involves the transplantation of autologous or allogeneic stem cells into patients, either through local delivery or systemic infusion. Three basic mechanisms have been proposed to explain how MSCs could repair tissue injury: a) creation of a milieu that enhances regeneration of endogenous cells, b) transdifferentiation, or c) cell fusion

Wound healing

Adult bone marrow cells can give rise to epidermal keratinocytes, follicular epithelial cells, sebaceous gland cells, dendritic cells after their transplantation in mice. Autologous bone marrow derived nucleated cells have been transplanted in experimental rabbits and clinical cases to evaluate their tissue regeneration potential in full thickness wounds, burn wounds and corneal alkali burn wounds. Several studies indicated that mesenchymal stem cells derived from the BM could significantly impact wound healing in diabetic and nondiabetic animals, through cell differentiation and the release of paracrine factors. Culture expanded bone marrow-derived mesenchymal stem cells (BM-MSCs) have been shown to promote the healing of diabetic wounds. Allogeneic BM-MSCs exhibited similar survival, engraftment, and effect as syngeneic BM-MSCs in promoting wound healing. Mesenchymal stem cells cooperate with bone marrow cells in therapy of diabetes. Bone marrow derived mesenchymal stem cells were injected around

wound and their application to the wound bed in an excisional wound model enhanced healing significantly in normal and diabetic mice. BMMSC- treated wounds exhibited significantly faster wound closure, with increased re-epithelialization, cellularity, and angiogenesis. In addition to differentiating into keratinocytes and forming appendage-like structures, BM-MSCs in the wound enhance the proliferation of endogenous keratinocytes and increase the number of regenerating appendage-like structures.

Even xenogenic human MSCs were used for incisional wound healing and tissue regeneration in rabbit and fetal sheep. In caprine Wharton's jelly mesenchymal stem cells (WJMSCs) of umbilical cord were used to treat cutaneous wounds in goat. Culture expanded bone marrow-derived mesenchymal stem cells (BM-MSCs) have been shown to promote the healing of diabetic wounds, implying a profound therapeutic potential for skin defects such as chronic wounds and burns. BMMSC- treated wounds exhibited significantly faster wound closure, with increased re-epithelialization, cellularity, and angiogenesis. In addition to differentiating into keratinocytes and forming appendage-like structures, BM-MSCs in the wound enhance the proliferation of endogenous keratinocytes and increase the number of regenerating appendage-like structures.

Bone repair

MSCs stimulates of new bone formation in areas of implant site, indicating that either these cells were infiltrating the adjacent host bone or stimulating the host bone to regenerate new bone. MSCs are the most commonly used seed cells for bone repair, having the potential for in vitro expansion and osteogenic differentiation. Clinical trials indicated that bone constructed using autologous MSCs has strong osteogenic ability but allogenic BM-MSCs are also attractive alternative to autogenic marrow-derived cells (MDCs) for reconstructive surgery. Recent studies suggested that there is minimal chances of rejection or immunogenic reaction when allogenic mesenchymal stem cells are used and they as effective as autogenic stem cells in the repair of experimewntal bone defects. Canine segmental bone defects were treated with bone marrow derived MSCs loaded onto porous ceramic cylinders. Goat bone marrow derived MSCs cultured with scaffolds could repair the segmental bone defect in tibia by 8 weeks after surgery Autologous adipose derived stem cells (ADSCs) (3.2 × 107 cells) seeded on a composition scaffold made from hydroxyapatite (HA) and chitosan (CH) fibers has been successfully used for the treatment of nonunion of radius/ulna in a cross bred dog. In one of our studies, $2X10^6$ bone marrow derived stem cells were injected at the site of nonunion in a non-healing fracture of humerus in a Doberman dog. One month later, the animals showed good bony union without the signs of lameness.

Cartilage repair

MSCs can differentiate into chondrogenic lineage and utilized to treat cartilage defects. MSCs have been used *in vivo* to repair full-thickness, joint cartilage defects in animal models using various carrier matrices. In rabbits, repair of full-thickness defects of joint cartilage was observed after transplantation of autologous MSCs dispersed in a type I collagen gel. Similarly, in the same animal model, encouraging results have been obtained by injecting calcium phosphate and hyaluronan sponge, previously loaded with autologous bone-marrow derived

MSCs, in knees with osteochondral defects. Single intra-articular injection of AD-MSC has been found to be efficacious in chronic osteoarthritis of the coxo-femoral joint in dogs. Mesenchymal stem cells play important role in tissue repair as well as injured joint regeneration; and following induction of osteoarthritis in the knee joints of caprine, injection of autologous preparation of stem cells is found to be effective. The articular cartilage defects were treated with MSCs with polymers, type I collagen, and polylactic acid. Infrapatellar fat pad derived mesenchymal stem cells were used in rabbits for treatment of osteoarthritis. Canine MSCs seeded in type I collagenglycosaminoglycan (CG) matrices were used in dogs for repair of cartilage defects of knee joints. In large-animal models, sheep were treated with in vitro differentiated MSCs for repair of chronic osteochondral defect. Delivery of bone marrow concentrate to acute full-thickness cartilage defects has been reported to improve cartilage healing in rabbit and canine model.

Tendon and ligament repair

Induction of MSC differentiation into connective tissues other than bone and cartilage, such as tendons and ligaments, has been investigated for a potential clinical application. Reimplantation of culture-expanded autologous bone marrow-derived MSCs into a spontaneously occurring core lesion of the superficial digital flexor tendon has been reported. This case demonstrated the feasibility of using culture-expanded MSCs therapeutically.

Ligament healing can be enhance by transplantation of mesenchymal stem cells (MSCs), which are demonstrated to differentiate into fibroblast-like cells in ligament injury sites in rats and survive up to 28 days. The mechanical properties of healing tendons and ligaments are, however, not comparable to those of normal tissue. The quality of the tendon and ligament healing can be improved with stem cell therapy. Bone marrow derived autologous MSCs along with collagen gel were used to repair surgically induced patellar tendon and Achilles tendon defect in adult New Zealand White rabbits. It was found that MSCs treated groups regained the normal tendon maximum force, stress, modulus, and strain energy density compared with controls. In equine, autologous bone marrow derived MSCs after in vitro expansion were utilized and found effective for regeneration tendon matrix in superficial flexor tendon injury

Spinal cord injuries

Acute spinal injuries are common in canines and felines that lead to loss of tissue, including myelinated fibre tracts responsible for carrying nerve impulses. The nervous tissue has limited regeneration capacity and complete restoration of locomotor activity is challenge to modern therapeutics. The mesenchymal stem cells were found to have ability to differentiate into oligodendrocytes and other cell types needed to restore neuronal function. Therefore transplantation of stem cells with the ability to differentiate into neurons and supporting cells may be a practical method for recovery. Alternatively, they may secrete growth factors that could support neuroprotection and/or axon regeneration. The potential of stem cells to support spinal cord repair has been studied extensively. In order to repair spinal cord injuries, therapies based on stem cells have been found fruitful. Bone marrow derived MSCs were first used in Rhesus monkeys for nervous tissue regeneration which appeared promising. Intrathecal implantation of autologus bone marrow derived MSCs improved locomotor activity significantly

in dogs within one week. Similarly allogenic UCB derived MSC transplantation resulted in nerve regeneration in canine fetuses.

Ischeamic brain injury

Neural stem cell therapy has raised the hopes in order to treat neurodegenerative diseases. In order to properly integrate in the brain cells that are injured, isolation as well as enrichment and propagation of neural stem cells is necessary. Use of compliant conditions of culture and differentiation of both embryonic as well as somatic stem cells in a directional manner the clinical application of such therapies is possible nowadays.

Damage caused by stroke injury to the central nervous system (CNS) is a major cause of death and disability in humans. Transplantation of MSC directly into adult rodent brain was found safe and it reduced functional deficits associated with stroke. This supported the notion that MSCs can adopt neural cell fates and are feasible candidates for the treatment of stroke injury. Exogenous stem cells offer the complementary advantages of being available in unlimited numbers with additional control over fate, cell number, timing, and site of delivery. The fact that substantial functional gains have been observed in animal models after delivery of cells of both neural and non-neural origin in preclinical models of ischemic brain injury is encouraging. MSCs were also found useful for treating cerebral infarction and ischemia in experimental models.

Myocardial infarcts

In dogs, cardiac disease causes significant morbidity and mortality, contributing to over 50% of mortalities in some breeds such as the Cavalier King Charles spaniel. Adipose as well as bone marrow derived stem cells have successfully been used to heal the heart followed by myocardial infarction in dog; resulting in improved contractility and decrease in damaged area. Use of autologous bone marrow stem cells (a specific type) for treatment of myocardial infarction is a novel application of stem cell therapy that is gaining popularity nowadays. Clinical experiences based on animal studies at the early stages have shown that mesenchymal stem cells (MSCs) when therapeutically delivered improve function of heart after an acute myocardial infarction. This is due to the fact that MSCs can generate various signalling molecules that are cardio-protective and can differentiate into myocyte as well as lineage of the vascular system.

In a canine acute myocardial ischemia model, 100×10^6 MSCs were delivered 7 days after acute myocardial infarction (AMI) via intracoronary (IC) and transendocardial (TE) routes. This study suggested that MSC treatment is probably safe and effective after AMI. TE group showed higher cell retention (clusters even in the injury center of the infarct) with an increased vascularity and greater functional improvement than did the IC group (no clusters; cells at the border of the infarct). The higher local cell density in the TE group may be important for therapeutic effectiveness. Treatment of infarction in heart of rat with embryonic stem cells helps in generating new cardiomyocytes (embryonic origin) that gets integrated within the infracted part of the myocardium of the host. Such therapy normalizes the architecture of the ventricles and reduces the signs of myocardial necrosis.

Future perspectives

Hepatic applications

The existence of liver stem cells within the adult bone marrow was first reported in 1999 and since then it has been confirmed in multiple further studies. MSC can be induced to a hepatic lineage by incubation with specific growth factors such as hepatocyte growth factor (HGF) and have not only been isolated from bone marrow, but can also be obtained from a number of other tissues such as umbilical cord blood and adipose tissue. The effectiveness of systemically administered MSC in the repair and regeneration of liver tissue has been most extensively studied in the carbon tetrachloride (CCl4) model of progressive liver fibrosis in mice. The studies documented only limited engraftment of donor MSC in the damaged liver.

Organ transplantation

The use of MSC for preventing acute rejection following solid organ transplantation may have significant advantages, as immunosuppression is coupled with the ability to repair ischaemic damage and therefore MSC transplantation has the potential to target both inflammatory and alloimmune pathways. MSCs exert immunomodulatory effect towards a large number of immune effector cells, including CD4 + and CD8 + T cells, NK cells, B cells, monocytes and dendritic cells. However, results on prolongation of graft survival have been conflicting.

Control of infection

Mesenchymal stem cells may be able to help treat sepsis, a deadly condition that can occur when an infection spreads throughout the body. In a study bacteria from the gut were released into the abdomen, resulting in severe infection, inflammation and organ damage throughout the body. Six hours after inducing the infection, approximately half the mice were given an intravenous injection of mouse mesenchymal stem cells, while the other half received a control injection of a saline solution. Both groups of animals also received antibiotics, which is the standard treatment for sepsis in the clinic. After five days, 50 per cent of the animals that received the cells were alive, compared to just 15 per cent of the control animals that did not receive the cells.

Recent in vivo study in human also indicated that mesenchymal stem cells (MSCs) may have beneficial effects in the treatment of sepsis induced by bacterial infection. In another *in vivo* mouse model of *E.coli* pneumonia, intratracheal administration of MSCs reduced bacterial growth (in colony-forming unit) in the lung homogenates and in the bronchoalveolar lavage (BAL) fluid, and administration of MSCs simultaneously with a neutralizing antibody to LL-37 resulted in a decrease in bacterial clearance.

Reproductive disorders

Stem cells may play an important role in normal uterine and ovarian physiology. They are likely to be involved in the response of these tissues to injury and disease. Among the various reproductive disorders, adult stem cells have been studied in endometriosis. The cells were found to home glandular as well as non-glandular endometrial tissue, immune-modulate

endometriosis and replenish endometrial cells in pregnancy failure. All such findings have raised hope among researchers in utilizing the stem cells to address issues associated with reproductive problems.

Cancer therapy

Cancer stem cells (CSC) have been identified in both humans and dogs. Various cancer types such as follicular lymphoma, head and neck carcinoma, oseosarcoma, glioma, breast, gastric, colon and prostate have been reported to contain stem cells. Analysis from human prostatectomies showed that MSCs represented 0.01–1.1% of total cells present in the prostate tumour. However, despite the evidence suggesting that cancer is initiated and propagated by cells with stem-like characteristics, it remains unclear whether the CSC is a normal tissue stem cell which has undergone malignant transformation, or a tissue somatic cell which has acquired more primitive, stem-like characteristics as a result of mutation or dedifferentiation.

In recent studies, it has been shown that MSCs contribute to tumour growth and progression. They have been found to increase the metastatic potential of tumour cells by promoting their motility and invasiveness as well as having a role in the creation of a metastatic niche at the secondary site. Contrary to the tumour promoting role, there is evidence to suggest that MSCs can also have an inhibitory effect on tumour growth. Suppression of tumour growth has been noted in breast cancer, Kaposi's sarcoma, hepatoma and melanoma models. Human MSCs derived from the umbilical cord and adipose tissue were implanted into a breast cancer metastasis mouse model and found to inhibit metastasis to the lung and reduce tumour growth. It is not clear however, whether the effect is predominantly tumour promoting or suppressive. It is therefore imperative to understand how they communicate with tumour cells, whether there are phenotypic differences in MSCs that are isolated from different tumour types and whether the MSC responds to the tumour according to its stage of progression. Better understanding of the role of stem cells in cancer biology may provide clues for therapeutic possibilities in cancer patients.

Key Note Address

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ANAESTHESIOLOGY

No of abstracts		**:**	**46**
Lead paper	**1**	**:**	**Dr. N. S. Jadon**
	2	**:**	**Dr. S. Senthil Kumar**
Chairman		**:**	**Dr. P.T. Jadhao**
Co-chairman		**:**	**Dr. J.K. Das**
Rapporteur		**:**	**Dr. K. Srinivasa Murthy**

PAIN MANAGEMENT IN ANIMALS

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Pain in domestic animals is also defined as an aversive sensory and emotional experience representing an awareness by the animal of damage or threat to the integrity of its tissues; it changes the animal's physiologic responses and behavior to reduce or avoid damage to decrease the likelihood of recurrence and to promote recovery

- **JCAHO (joint commission on accreditation of healthcare organizations)** mandated, in 2000, human hospitals to elevate pain to fifth vital sign (along with temperature, pulse, respiration, and blood pressure). **AAHA - In 2003, the American Animal Hospital Association (AAHA)** elevated pain to the fourth vital sign in animals (in addition to temperature, pulse and respiration.)

NEUROANATOMY OF NOCICEPTIVE PATHWAYS

Nociception is the reception of signals from activation of nociceptors, which are receptors that detect tissue-damaging (noxious) stimuli. Pain implies that noxious stimuli have been perceived at the cortical level. Activating stimuli for nociceptors include mechanical, thermal and chemical stimuli.

Polymodal nociceptors: These types of nociceptors respond to a variety of pain perceptions which may be mechanical, thermal and chemical stimuli.

Monomodal Receptors: These nociceptors respond to a single type of stimuli. Nociceptors are naked (non-encapsulated) nerve endings, widely distributed in skin and deep tissues.

A-8 fibers are associated with sharp, pricking pain

C fibers Slow-conducting (0.5 to 2.0 m/s), unmyelinated C fibers are associated with a slower, burning type of pain. Both types of nociceptive fibers innervate the skin (superficial pain) and deep somatic or visceral structures (deep pain). Each is associated with an anatomically and functionally segregated central pain pathway; they are differentially susceptible to injury, and they are examined separately in a neurological examination.

Silent nociceptor: The high threshold of this nerve ending ensures that under normal circumstances it is relatively insensitive to any stimuli. The presence of silent nociceptors is one mechanism by which inflammation produces primary hyperalgesia.

Types of pain

Superficial pain results from stimulation of the pain receptors in the skin. Superficial pain may be subdivided into fast (first) pain, caused by stimulation of cutaneous nociceptors with small myelinated fibers and slow (or second) pain, arising from stimulation of receptors with unmyelinated fibers.

Deep pain arises from underlying structures like muscles, joints, tendons, periosteum, and ligaments.

Visceral pain arises from stretch receptors in the visceral wall, sensitive to changes in shape and tension. Depending on duration, pain can be acute or chronic.

Acute pain. It is the result of a traumatic, surgical, or infectious event that begins abruptly and is relatively brief. It is generally alleviated by analgesic drugs. Lasts for the duration of the healing process of an injury.

Chronic pain may have no obvious cause or temporal onset. There are several definitions of chronic pain, pain having duration of more than 6 months, pain that persists beyond the expected healing time of a disease or injury, or pain involving an alteration in the nervous system that is capable of maintaining a painful state without reinforcement by repetition of the initiating causal factors.

Nociceptive Pathways

- Pain pathways exhibit variable degrees of connectivity with a number of subcortical regions of the brain and through these connections elicit a variety of nonconscious responses.
- A behaviorally important aspect of nociception (and other sensory modalities) is the degree to which it affects mental alertness. This relationship between sensation and consciousness is orchestrated in the reticular formation (RF), a loose aggregate of nuclei in the central core of the brain stem, extending from diencephalon through medulla oblongata. It plays role in regulation of heart and respiratory rates, selective attention to stimuli, maintenance of consciousness and cortical alertness.

Nociceptive pathways send collateral projections to the mesencephalon (midbrain). One set of nuclear targets in the midbrain consist of motor neurons that coordinate orienting movements of the head and eyes toward the noxious stimulus. Other neurons that form the periaqueductal grey matter of the midbrain activate important descending pain modulatory systems.

Ascending Spinal Pathway of nociception

Spinocervicothalamic pathway

The spinocervicothalamic pathway is concerned with the transmission of superficial pain and tactile sensations and is regarded as the primary conscious pain pathway in carnivores.

Spinoreticular pathway

The spinoreticular tract is primarily concerned with transmission of deep-pain and visceral sensation.

Trigeminal System pathway

For the head, nociception and tactile information are transmitted by the trigeminal system

Spinocervicothalamic pathway

- The transmission of superficial pain and tactile sensations.
- This is regarded as the primary conscious pain pathway in carnivores.
- The primary afferents of this pathway synapse in the dorsal horn, from which secondary afferents then mediate local reflexes and project cranial in an ipsilateral tract in the dorsal part of the lateral funiculus.

- The axons in this tract ascend to spinal cord segments CI and C2, where they synapse in the lateral cervical nucleus.
- The fibers arising from this nucleus will then decussate and project through the brain stem to the thalamus. Some collaterals of the ascending fibers will terminate in the RF. From the thalamus, fibers project to the somatosensory cortex.
- Clinically, function of the spinocervicothalamic tract is tested by lightly pinching the skin with fingers or a mosquito hemostat. This stimulus is applied lightly and briefly so as to activate the spinocervicothalamic pathway preferentially.

Spinoreticular pathway

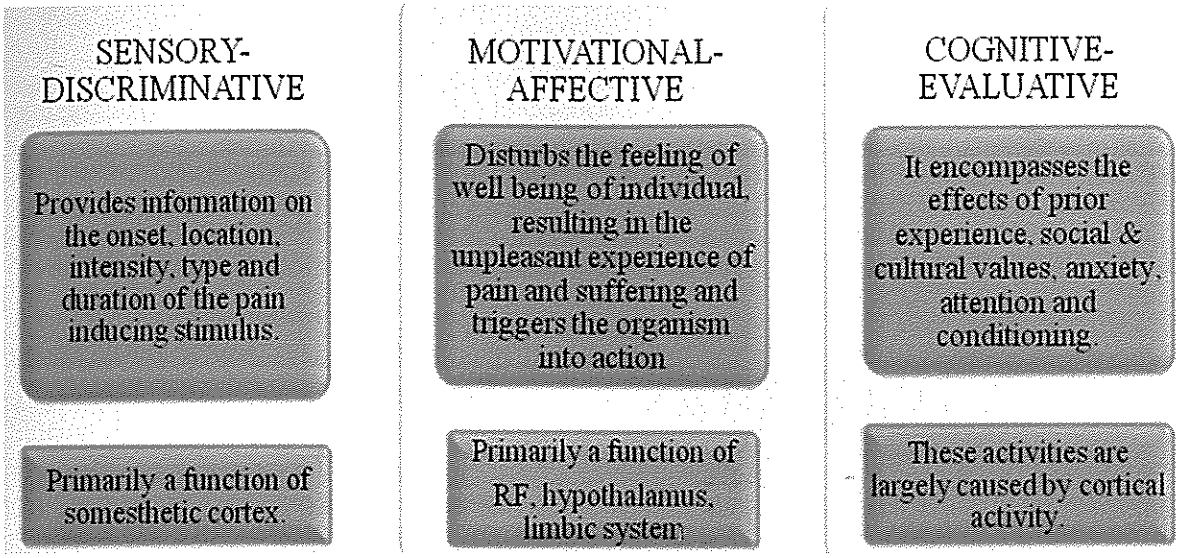
- Transmission of deep-pain and visceral sensation.
- The primary afferents of this pathway enter the cord and immediately diverge to send collaterals several segments rostral and caudal to the segment of entry.
- This spreading of information across several spinal cord segments enables these afferents to participate in intersegmental reflexes (various manifestations of withdrawal and postural reflexes in response to painful stimuli).
- Second-order neurons are found in the dorsal horn. Axons of projection neurons in this system are present diffusely in the lateral and ventral funiculi. These projections are bilateral; decussation of axons in this
- System occurs diffusely throughout the long axis of the spinal cord.
- Most ascending projections of the spinoreticular tract that reach the brain stem do not project directly to the thalamus; rather, they terminate in the RF.
- Visceral afferent fibers travel in sympathetic nerves, have large overlapping receptor fields, and respond primarily to stretch, ischemia, dilation, or spasm.
- In somatic structures the ratio of A-8 to C fibers is about 1:2, that ratio in viscera is about 1:10.
- Primary afferents from viscera follow autonomic nerves (e.g., the vagus and sympathetic nerves) to the central nervous system (CNS).
- The deep-pain pathway is tested in the neurological examination by application of a hemostats across the base of a toenail (taking care to exclude skin), a manipulation that stimulates nociceptors in the periosteum of the third phalanx.

Trigeminal System pathway

- Cell bodies of primary afferent fibers reside within the trigeminal (semilunar) ganglion. Their central processes enter the pons with the trigeminal nerve and course caudal along the lateral surface of the medulla.
- At its rostral extent in the pons, this group of cell bodies comprises the pontine sensory nucleus. More caudally, the column is known as the spinal nucleus of V. The pontine and spinal nuclei of V contain somata of the second-order neurons in this system.
- The rostral part of the spinal nucleus of V sends somatosensory information to the cerebellum. The majority of neurons in the spinal nucleus of V are concerned with nociception.

- Many of these will project to motor nuclei of cranial nerves to participate in reflex arcs (e.g., corneal and palpebral reflexes), and many more will project to the RF to affect autonomic responses and increase arousal.

PAIN EXPERIENCE DIMENSION



Response to Pain and Injury

Animals may respond to pain in 2 ways, excessive activity or lethargy. Another classification of animal responses to pain suggests 4 categories: those responses that modify the animal's behaviour by learning and so enable the animal to avoid recurrence of the experience, those that are often automatic and protect parts or the whole of the animal (withdrawal response), those that minimize pain and assist healing, and those that are designed to elicit help or to stop another animal from inflicting more pain.

Signs of acute and chronic pain may differ. In severe acute pain, animals may have signs of anxiety, changes in eye expression (including fixed and dilated pupils or tearing), restlessness, lameness, changes in appetite, changes in personality, increased or decreased physical activity, self-mutilation, and vocalization. Excessive salivation, mydriasis, tachypnea, tachycardia, and various biochemical changes (such as increased blood glucose, cortisol, ACTH, and catecholamine concentrations) may be considered as other indirect clinical signs of acute pain. In chronic pain, responses include guarding behavior in movement and posture, avoidance of pain-aggravating influences, seeking of pain-relieving factors and environments, self-care of a painful region, and signs of stress. Some of the signs in chronic distress states may include hirsutism, weight loss, in appetence, and an indefinable "unhappy eye expression."

PHYSIOLOGICAL RESPONSE

Increased neural sympathetic tone and catecholamine secretion add to that induced segmentally to further increase cardiac output, peripheral resistance, blood pressure, cardiac work and myocardial oxygen consumption. In addition, there is increased secretion of Cortisol, adrenocorticotropic hormone, glucagon, cyclic adenosine monophosphate, antidiuretic hormone, growth hormone, renin, and other catabolic hormones, and a

concomitant decrease in the anabolic hormones insulin and testosterone. The response to pain cause increased blood glucose, free fatty acids, blood lactate and ketones.

Any result in increased rate of metabolism and oxygen consumption. These responses cause substrate mobilization to central organs and injured tissues, and lead to a catabolic state and negative nitrogen balance. Increased levels of Norepinephrine, epinephrineadrenocorticotropic hormone, and Cortisol intraoperatively corresponding to surgical manipulation in dogs can be brought to normal by the preoperative administration of the a2 - agonist medetomidine.

Metabolic responses includes hyperglycemia, glycogenolysis and gluconeogenesis, increased muscle protein metabolism and increased lipolysis.

Water and electrolytes responses includes retention of water and sodium ions, increased potassium-ion excretion and decreased extracellular fluid.

Diencephalic and cortical responses includes anxiety and fear increase sympathetic responses, blood viscosity and clotting time, fibrinolysis and platelet aggregation, psychological effects, overall effects of pain, prolonged recovery and slower return to normal behaviors.

Pain assessment tools in Veterinary Medicine

Correlation between physiological variables (heart rate, respiration rate, blood pressure and pupil diameter) and pain scores have been evaluated (No study found a consistently reliable objective measures, which is not surprising as these parameters can be affected by many factors other than pain). Changes in plasma cortisol and β endorphins are correlate with pain in laboratory & clinical trials. Plasma cortisol was not a useful pain marker in dogs and is extremely unreliable in cats.

SCORING SYSTEMS

- Because animal cannot self-report, all scoring systems depend on a human observer.
- Any system used must be valid, reliable and sensitive.

1. Simple Descriptive Scales

- Most basic pain scale.
- Usually have four or five descriptors from which observers choose. No pain, mild pain, moderate pain, severe pain or very serve pain.

Advantage -Simple to use.

Disadvantage -Extremely subjective as not detect small changes in pain behaviour.

2. Numerical Rating Scales

- Same as SDS ,but assign numbers for ease of tabulation and analyses
- Further behaviour where chosen and assigned a value.
- For ex-vocalization can be divided into none (score=0), crying but responsive (score=2) & crying but non-responsive (score =3); other categories may include movement, agitation & posture.

3. Visual Analog Scale

- Tool consists of a continuous line (100mm long) anchored at either end with a description of the limits.
- For example **no pain** or **no sedation** at one end and **severe pain** or **asleep** at the other (VAS) has been widely used in veterinary medicine.
- Holton compared the use of SDS, NRS & VAS for assessing pain in dogs after surgery.
- Results showed significant **observer variability** –as high as **36%** -with all three scales.

DIVAS (Dynamic and Interactive Visual Analog Scale)

- Use of DIVAS reported by Lascelles *et al.*
- Animals are first observed from a distance undisturbed and then approached, handled and encouraged to walk.
- Finally, the surgical incision & surrounding area are palpated, a final overall assessment of sedation and pain is made
- The DIVAS used to assess postoperative pain in cats, it detected differences between analgesics (meperidine and caprofen) and between treated (with analgesia) and untreated (no analgesia) cats.

The University of Melbourne Pain Scale (UMPS)

- Incorporates objective physiological data and behavioural responses.
- By assigning numbers to each factor, a score between 0 and 27 is derived.
- Tested on dogs following ovariohysterectomy and **it could differentiate between dogs that were anesthetized but not subjected to surgery & those who have undergone surgery.**

BEHAVIOUR

It is now accepted that quantitative measurements of **behaviour** are the most reliable methods for assessing pain in animals and that, if the methodology used to develop and validate these systems is rigorous, they can be more objective with minimal observer bias.The absence of normal behavior is the most striking sign of pain in animals, which is why it is essential to be familiar with the normal behavioral pattern of the species. Normal behavior may include various species-specific actions such as head pushing of goats and general activity and vocalization of pigs. Although there are individual and species variations, some common signs that an animal is in pain include changes in behavioral patterns, appearance, posture, gait, appetite, response to handling, and weight. Behavioural indicators of abdominal pain in large animals includes vocalization, rolling, kicking at abdomen, flank watching, stretching, dullness and depression.

Behavioural indicators of limb & foot includes weight shifting, limb guarding, pointing, hanging and rotating limbs and arched back. Behavioral indicators of dental pain includes head shaking and abnormal bit behaviour. Common indicators of pain in dog are decreased social interaction, submissive behaviour, howling, whimpering, growling, aggression and loss of appetite. However in cat common indicators are reduced activities, loss of appetite, hiding, hissing, stiff gait, guarding behaviour and attempts to escape.

It is appropriate to administer analgesics to prevent pain where it is likely to occur. Accurate selection and dosing of analgesic drugs provide relief of pain without severe respiratory depression.

Transduction is the translation of physical energy (noxious stimuli) into electric activity at the peripheral nociceptor.

Transmission is the propagation of nerve impulses through the nervous system.

Modulation occurs through the endogenous descending analgesic systems, which modify nociceptive transmission. These endogenous systems (opioid, serotonergic, and noradrenergic) modulate nociception through inhibition of the spinal dorsal horn cells.

Perception is the final process resulting from successful transduction, transmission and modulation, and integration of thalamocortical, reticular, and limbic function to produce the final conscious subjective and emotional experience of pain.

Transduction can be obtund by NSIADs as the decrease production of endogenous algogenic substances such as prostaglandins at the site of injury.

Transmission can be abolished by local anesthetic blockade of peripheral nerves or nerve plexuses or by epidural or subarachnoid injection.

Transduction can be largely abolished by use of local anesthetics infiltrated at the site of injury or incision, or by intravenous, post thoracotomy intrapleural, or post laparotomy intraperitoneal injection.

Modulation can be augmented by subarachnoid or epidural injection of opioids and α2-adrenergic agonists.

Perception can be obtunded with general anesthetics or by systemic administration of opioids and α2 - agonists either alone or in combination with tranquilizer sedative.

Pain Management

Balanced or Multimodal analgesia relies on the additive or synergistic effects of two or more analgesic drugs working through different mechanisms of action. Doses of individual drugs can be reduced, thereby decreasing the potential for any one drug to induce adverse side effects. Balanced analgesic techniques appear to offer several advantages in the management of postoperative pain.

Preemptive analgesia refers to the application of balanced analgesic techniques prior to exposing patients to noxious stimuli (surgical manipulations).

ANALGESICS

Five main classes of analgesic are opioids, NSAIDs, local anesthetic, alpha –adrenergic agonist and miscellaneous drugs. Opioids/Narcotic analgesia are ß endorphins-natural antidote for pain, enkaplins -inhibit substance P and dynorphins-neuromodulator in CNS.

RECEPTOR

It comprised of μ1 receptor-mediates enkaplin & endorphin analgesia, k receptor-sedation via dynorphins and delta receptor-enkaplins-spinal analgesia. Opioids relieve or reduce pain by combining with opioid receptors in the central nervous system and periphery. They are generally considered to be the most effective of all analgesic medications but vary

widely in their analgesic potency and clinical efficacy when used to treat pain .Although increased dosage of opioids can produce nervousness, agitation, increased locomotor activity, dysphoria and occasionally hyperthermia.

Nausea and vomiting and panting are acute phenomena that are frequently observed after intramuscular opioid administration. Opioids are known to stimulate CTZ i.e. chemoreceptor trigger zone and rest thermoregulatory centres in the hypothalamus, resulting in a slight fall in body temperature.

Respiratory System - opioids increase the concentration of carbon di oxide necessary to stimulate rate and depth of breathing (increase respiratory threshold) and depress ventilatory responses to increase the inspired concentrations of carbon dioxide. Clinically, both effects predispose patients to hypoventilation and the development of respiratory acidosis.

Cardiovascular - other than bradycardia and occasional bradyarrhythmias, opioids relatively few if any clinically significant cardiovascular effect in dogs and cats when administered at recommended doses. First degree (prolonged PR interval), second–degree (P-wave not followed by QRS interval), and rarely, third -degree (no relationship between P wave and QRS complexes) atrioventricular block can occur, which attributed to a vagally mediated increase in parasympathetic tone and is therefore responsive to anticholinergic therapy.

2-NSAIDs

They inhibit the production of prostaglandins, prostaglandins produce their algesic, proinflammatory andpyretic effect. Two types of COX exist :COX-1 and COX-2,Although COX-1 is considered be "housekeeping " COX and to be involved in cell signaling and maintaining tissue homeostasis,COX-1 and COX-2 have housekeeping roles in selected tissues.COX-1 inhibition is believed to be responsible for the majority of acute and chronic toxicities of NSAIDs, especially gastrointestinal ulceration, although one theory contends that inhibition of COX-1 or both of the COX enzymes shunts substrate toward the production of leukotriences, increasing the production of LTB_4 and thereby exacerbating mucosal damage.COX-2, often but inappropriately referred to as inducible COX, is the principal enzyme responsible for the overproduction of prostaglandins following acute injury or infection. NSAIDs includes phenylbutazone, flunixin, ketoprofen, carprofen, aspirin, eltenac, vedaprofen and meloxicam may be used frequently in large animals.

3- ALPHA ADRENERGIC AGONIST

Alpha adrenergic agonist activates presynaptic and postsynaptic a_2-receptors in the CNS, producing sedation and analgesia. Activation of a_2-receptors in the brain and spinal cord decreases pain -related neurotransmitters and interferes with sensory transmission. Vomiting is a common side effect in dogs and cats after the intervenous administration of an a_2-agonist because they activate CTZ.

4-LOCAL ANESTHETICS

All the local anaesthetics block the initiation and conduction of electrical impulses in nerves. Local anaesthetics block sodium ion channels in neuronal cells and other tissues, thereby preventing an influx of sodium ions, membrane depolarization, and a decrease in propagated action potentials.

Small-diameter nerve fibres are blocked first in preference to large myelinated fibres, thereby producing a loss of sensation (analgesia) and a varying degree of paralysis (i.e. loss of motor function). The local anaesthetic used to relieve the pain includes bupivacaine, cetacaine, lidocaine, mepivacaine, mexiletine and ropivacaine.

5-MISCELLANEOUS

NUTRACEUTICALS

Various nutraceuticals are available which include glucosamine sulfate, glucosamine hydrochloride, chondroitin sulfate, microlactin and buffered vitamin C. The combination of glucosamine hydrochloride ,low-molecular-weight chondroitin, and manganese has been shown to induce biosynthetic activity in canine cartilage.Glucosamine and chondroitin, administered in patients with OA and combination of Glu/CS has been shown to protect against chemically induced synovitis in dogs also, stimulate cartilage metabolism and to inhibit its degradation. Buffered vitamin C is believed to have chondroprotective, anti-inflammatory mad immuno-responsive effects that may provide pain control for animals with osteoarthritis.

Combination of glucosamine hydrochloride also has a protective effect when administered before an acute joint injury .Patients receiving this combination before joint injury heal more quickly than those administered the combination after injury.

HERBS

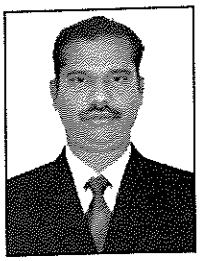
Various traditional herbs are used to treat pain in animals are-

Boswellia carterii	Rheumatoid arthritis in dog
Capsaicin	Topical analgesia
Arnica gel	Osteoarthritis
Comfrey	Joint pain
Devils claw	Joint & muscle pain

CONCLUSION

There are various limitations in using behavioral indicators to assess pain in clinical settings. There is utmost need to develop and provide scoring and assessment tools. There is need of open-ended questions during history-taking with clients to maximize the understanding of each patient's situation. Most effective analgesia is provided by multimodal analgesia. While administration of drug its side effects and toxicity is to be kept in mind. We need to begin the client's awareness of the importance of identifying and treating pain whenever it occurs.

LOW FLOW INHALATION ANAESTHESIA IN CATTLE – A SAFE, ECONOMICAL AND VIABLE DECISION



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The trend towards the use of inhalation maintenance for complicated long duration surgeries in cattle is growing up promisingly. The pros of inhalation anaesthesia like smooth induction and recovery, prolonged use with minimum side effects and minimum post operative complications have outweighed the injectables.

Inhalation anaesthesia is a method of anaesthesia achieved by administering volatile inhalant agents through the respiratory system. The inhalation agents used are either gases (Ex. Nitrous oxide) or vapours (Ex. Isoflurane, halothane etc.,). MAC is defined as Minimum Alveolar Concentration of an inhalant anaesthetic at one atmospheric pressure that produces immobility in 50% of subjects exposed to a supramaximal stimulus. It is equivalent to ED_{50} of Injectable drugs. Generally, 1.5 to 2.0 times the MAC of an inhalant anaesthetic produces immobility and achieve surgical plane of anaesthesia. However, the commonly used premedicants and induction agents exert inhalant sparing effect and decrease the concentration of inhalant required for surgical plane of anaesthesia. The commonly used volatile inhalant agents tend to vapourize significantly beyond the concentration required for clinical application and warrants the use of vapourizers to control the degree of vapourization and deliver anaesthetic vapour at safer concentration. Anaesthetic machine is required to deliver inhalant agent at safe concentration and is composed of Basic Components and a Breathing System. The Basic components of an anaesthetic machine include oxygen cylinder, pressure regulator, oxygen flow meter (rota meter) and vapourizer.

Oxygen Cylinder

Colour coding : Black with white shoulder

Pressure to which refilled : 2000-2200 psi (140-154 kg/cm_2 or 136-150 atm)

Oxygen cylinders and its capacity		
Type	**Approximate Water Capacity (WC)**	**Approximate Oxygen content**
A or E type	4.5 litres	600-660 litres
B type	10 litres	1400-1500 litres
Bulk or G/H type	45 litres	6000-6600 litres

It is important that oxygen content in a cylinder calculated and adequate availability ensured before start of inhalation anaesthesia. The oxygen content can be calculated by the simple formula explained below.

Oxygen (Litres) = Water capacity of the cylinder (litres) x Pressure reading of the cylinder (kg/cm_2)

Pressure regulator

Pressure regulators are designed to decrease the cylinder pressure and deliver gas or oxygen at 60 psi (4 atm) which is the working pressure for any anaesthetic machine. The proper functioning of the pressure regulator must be ensured to have an uninterrupted safe oxygen supply during inhalation anaesthesia.

Oxygen flow meter

Flow meters are used to set the oxygen flow rate (litres per minute) during inhalation anaesthesia. The oxygen flow rate and vapourizer setting are the two major variables that influence the maintenance of inhalation anaesthesia. The oxygen flow rate employed in large animal anaesthesia varies from 10 to 20 ml/kg/minute. The oxygen flow rate employed with the use of non rebreathing system is usually high and not employed in large animals. The oxygen flow rates employed will be comparatively lower when total rebreathing system (Closed POP off / APL valve) or partial rebreathing system (Partially opened POP off/APL valve) is used.

It is important to note that when higher oxygen flow rates are used (>10ml/kg/minute), the POP off/APL valve must be kept partially opened to allow escape of gas from breathing system preventing pressure build-up and barotrauma.

Vapourizer

The vapourizers deliver the set and safe concentration of volatile inhalant vapours. Precision vapourizers are unaffected by the ambient temperature, pressure and flow rate employed and deliver precise set concentration of inhalant anaesthetics. Non precision vapourizers are not compensated for the above factors and may deliver lower or higher concentration than the set reading. The Breathing system supplies oxygen-anaesthetic gas/vapour mixture to the patient and eliminates CO_2 from the exhaled gas. It includes Y piece, breathing tubes, unidirectional valve, fresh gas inlet, POP off/APL valve, reservoir bag, manometer and CO_2 absorber.

In inhalational anaesthesia the concentration of inhalant anaesthetic delivered from the anaesthetic machine to the patient does not equilibrate the vaporizer setting at the start and it may take several minutes to achieve equilibrium. The time taken for achieving this equilibrium depends on the time constant of the machine and the fresh gas flow employed. The time constant of the machine is dependent on the volume of circle (ie. Volume of the breathing tube, rebreathing /reservoir bag and soda lime canister) and the fresh gas flow rate employed.

The volatile inhalant utilization is the major factor that influences the cost of inhalation anaesthesia. The isoflurane consumption per hour (mL liquid) during inhalation anaesthesia can be calculated from the below formula.

Isoflurane consumption (mL liquid) =3x Fresh gas flow rate (Litres per min) x Vapourizer setting(%)

Low flow anaesthesia

Low flow anaesthesia is defined as an inhalational anaesthetic technique where in the rebreathing fraction at least amounts to 50%. Low flow anaesthesia was first described by Foldes *et al.*, 1952. Modern inhalational anaesthetic agents are metabolized to a small extent only and are largely exhaled unchanged. The use of closed system with carbon dioxide absorption units and comprehensive gas monitoring permits the exploitation of this to

perform economical and safe 'low-flow anaesthesia'. It is carried out with a fresh gas flow rate which is significantly lower than the minute volume. When such low FGF are used, the anaesthetic gases must be conducted to the patient via semi closed or even closed rebreathing systems. The rebreathing fraction increases with the reduction of the FGF whereas the volume of excess gas decreases.

Oxygen uptake during anaesthesia corresponds to basal metabolic rate and during anesthesia oxygen consumption can be regarded as virtually constant. It can be calculated using Brody's formula, $\mathbf{VO_2 = 10 \times BW\ [kg]^{3/4}\ [mL/min]}$. However, for clinical purposes, oxygen consumption can be calculated as $\mathbf{VO_2 = 3.5 \times BW\ [mL/min]}$

Low flow anaesthesia is a simple but highly effective method of cost minimization that can be applied to a large number of patients without any compromise in patient care or safety. Low flow anaesthesia is used in conjunction with equipment for measuring inhaled and exhaled gas concentration. Monitors are already increasingly available with end tidal anaesthetic gas measurement. The efficiency of the anaesthetic gases increases with reduced fresh gas flow rate. Also, exposure for staff to anaesthetic gases in anesthesia workplace drops noticeably with low flow technique. Apart from economic advantage, low flow anaesthesia helps to reduce environmental pollution.

Phases of low flow anesthesia: Adjustment of fresh gas flow rate during low flow anaesthesia can be divided into following three phases,

1. Initiation of low flow anaesthesia.
2. Maintenance of low flow anaesthesia.
3. Recovery

Initiation of low flow anaesthesia

The Primary aim at the start of low flow anesthesia is to achieve an alveolar concentration of the anesthetic agent that is adequate for producing surgical anesthesia (approximately 1.3 MAC). The factors that can influence the buildup of alveolar concentration are classified into;

1. Factors governing the inhaled tension of the anesthetic.
2. Factors responsible for rise in alveolar tension.
3. Factors responsible for uptake from the lungs thus reducing the alveolar tension.

Methods to achieve desired gas and agent concentration:

- ✓ **Use of high flows for a short time**
- ✓ **Prefilled circuit**
- ✓ **Use of large doses of anesthetic agents**
- ✓ **Injection techniques**

Time constant - Time constant is the main characteristic unit of the first order linear time invariant system. In an increasing system the time constant is the time for the systems step response to reach approximately 63.2 % of its final value. For volatile anaesthetic agents the time constant is volume divided by flow. From the standpoint of the anaesthesia circuits the time constant is the volume of the circuits divided by the fresh gas flow rate. From the

standpoint of the lungs the time constant is the volume of the lungs (Functional Residual Capacity) divided by the minute ventilation. It takes 3 time constants for 95% of a concentration change to be achieved. Fresh gas flow is the total volume of gas that flows from the anaesthesia machine into the breathing system per minute. Inhalational anaesthetic agents with a low blood gas solubility coefficient are optimally suited for low and minimal flow anaesthesia.

Maintenance of low flow anesthesia

- ✓ Maintenance of steady alveolar concentration of respiratory gases.
- ✓ Addition of the anesthetic gases to match the uptake and providing oxygen for the basal metabolism. In Closed circuit anesthesia, this would be directly equal to the uptake. In low flow anesthesia, the amount of gas which is vented is also added to the circuit to maintain steady state anesthesia.

Termination of low flow anaesthesia

- ✓ Use of High fresh gas flow rate - Towards the end of the anesthesia, the circuit is opened and a high flow of gas is used to flush out the anesthetic agents, which accelerates the washout of the anesthetic agents. This has the obvious advantage of simplicity but would result in wastage of gases.
- ✓ Use of activated charcoal - The second method is the use of activated charcoal which when heated to 220°C adsorbs the potent vapors almost completely. Towards the end of the anesthesia, the gas is directed through the activated charcoal canister. This results in rapid recovery and at the same time, reducing theatre pollution.

The duration of the initial phase of low flow anaesthesia, in which comparatively high flow of fresh gas has to be applied, must be adapted to the rate to which the flow is reduced, to the composition of the carrier gas, to the maximum output of the agent specific vapourizer and to the individual gas uptake. The duration of initial phase of low flow anaesthesia is aimed to achieve desired anaesthetic gas composition within the entire gas containing system, adequate depth of anaesthesia and denitrogenation. Too early reduction of fresh gas flow rate results in gas volume deficiency and must be avoided.

High fresh gas flow rate during inhalation anaesthesia can cause hypothermia and dehumidification of the patient. Structural and functional damage of the respiratory epithelium can occur when ventilating patients with cold and dry gas that eventually affects mucociliary clearance resulting in infection and atelectasis. Inspiration of cold and dry gas may result in increased release of inflammatory mediators TNF – α, IL- 6, IL – 8.

The fresh gas flow rate employed during inhalation anaesthesia determine the amount of inhalant anaesthetic agent used, and hence the cost of anesthesia. Use of closed circuit with leak proof system and higher fraction of inspired oxygen (FiO_2) minimizes the cost of anaesthesia as well render the protocol safe. Also, closed circuit administration decreases the cooling and drying effects which cause deleterious consequence on ventilation. Any change in anesthetic concentration requires temporarily altering the vapourizer setting and increasing the gas flow to speed equilibration. As the fresh gas flow increases, times to equilibration of changes in inhaled anesthetic concentration are faster, but the patient is exposed to cooler and drier gasses potentially compromising their pulmonary function, and more agent and inhaled gases are wasted.

Requirements for low flow anaesthesia

- ✓ Leak free anaesthetic machine components and connections
- ✓ Returning the exhaust sample gas from gas measurement back into the breathing system
- ✓ Robustness and precision of oxygen, carbon dioxide and anaesthesia gas measurement in a humid environment
- ✓ Precise performance of the anaesthetic vaporizers

Ecological concerns – "Greenhouse effect"

- Remission of emission of anaesthetic gases should be reduced to an unavoidable minimum. Unused anesthetics should be reused.
- Low flow and minimal flow anaesthesia meet these demands
- Consistent use of the minimal flow method results in a threefold consumption of the soda lime the associated costs are negligibly small in the cost to benefit analysis

Employing low flow anaesthesia with high FiO_2 in cattle ensures adequate supply of oxygen to meet the metabolic oxygen demand rendering the protocol safe. Effective utilization of potential inhalant during low flow anaesthesia reduces the cost of anaesthesia making it economically viable and ecologically safe.

ANAESTHESIOLOGY SESSION

ANS 01

EVALUATION OF PROPOFOL AS GENERAL ANAESTHETIC AGENT IN ATROPINIZED GOATS (CAPRINES)

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Six healthy non-descript goats of either sex weighing between 20-25 kg were taken to evaluate propofol (5mg/kg I/V) as general anaesthetic agent in atropinized (0.04 mg/kg I/M) goats. Animals became ataxic immediately after propofol administration and fell down to lateral recumbency after onset of anaesthesia (0.52±0.50 minutes). Transient apnoea was observed immediately after propofol induction which lasted for 60-70 seconds. Swallowing reflex, corneal, palpebral conjunctival and panniculus reflexes were sluggish throughout the period of anaesthesia. The anal pinch and pedal reflexes were sluggish but were not fully abolished.Response to pin pricks at the base of tail was diminished but persisted at abdominal skin, ribs, periosteum, base of horn and fetlock. The duration of anaesthesia was 16.31±1.29 min. and complete recovery occurs within 27.33±2.04 min. which was smooth with no excitement. Heart rate and respiration rate significantly ($p<0.05$) decreased upto 60 minutes of observation. There was no major variation in rectal temperature, haematological and biochemical parameters except serum glucose which was significantly increased after propofol administration.

ANS 02

CLINICO-PHYSIOLOGICAL RESPONSE TO DETOMIDINE-PROPOFOL AS ANAESTHETIC COMBINATION IN ATROPINIZED GOATS

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The study was conducted on six healthy non-descript goats of either sex weighing between 20-25 kg by administrating atropine sulphate (0.04 mg/kg I/M) followed by detomidine (15 µg/kg I/M) and 10 min. later followed by induction of anaesthesia with propofol (5mg/kg I/V). There was decrease in spontaneous activity with marked sedation as well as lowering of head after detomidine administration was observed in all the animals. After administration of propofol, there was rapid and smooth onset of anaesthesia (0.46±0.51 min). Transient apnoea was observed immediately after propofol induction which lasted for 40-50 seconds. This was followed by loss of swallowing reflex, corneal, palpebral and conjunctival reflexes were abolished within 3 min which remained throughout the period of anaesthesia. The anal pinch and pedal reflexes were also fully abolished. The muscle relaxation was excellent. Complete analgesia at fetlock, base of tail, abdomen, ribs, periosteum and base of horn was observed. The duration of anaesthesia was 52.50 ± 8.44 min and complete recovery occurs within 91.66 ± 14.24 min. which was smooth with no

excitement. Heart and respiration rate significantly decrease upto 60 min. after detomidine propofol administration. There was non-significant decrease in the rectal temperature was observed. It can be concluded that detomidine-propofol combination may be safely used for longer duration anaesthesia in atropinized goats.

ANS 03

HAEMATO-BIOCHEMICAL RESPONSE TO DETOMDINE-PROPOFOL COMBINATION IN ATROPINIZED GOATS

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The study was conducted to evaluate the effect on various haemato-biochemical parameters in response to detomidine-propofol anaesthesia in six healthy non-descript goats of either sex weighing between 20-25 kg. Detomidine (15 µg/kg I/M) was given 10 min. later followed by propofol (5mg/kg I/V) anaesthesia. Prior to this atropine sulphate (0.04 mg/kg I/M) was injected. There was non-significant decrease in Hb and PCV. There was significant increase in neutrophils with significant decrease in lymphocyte. There was significant increase in serum glucose level with slight alternation in serum urea, creatinine, AST and ALT. It is concluded that detomidine-propofol combination produced no deleterious effect on vital organs and changes remained within physiological limits, thus can be safely used in atropinized goats.

ANS 04

EFFICACY OF KETOFOL AS A GENERAL ANAESTHETIC IN MEDETOMIDINE PREMEDICATED GOATS

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The study was conducted on six healthy non-descript goats of either sex weighing between 20-25 kg by administrating atropine sulphate (0.04 mg/kg I/M) followed by medetomidine (10 µg/kg I/M) and 15 min. later followed by induction of anaesthesia with ketofol (5mg/kg I/V). Marked sedation with protrusion of tongue from buccal cavity, profuse salivation was noticed after onset of anaesthesia (0.78±0.02 min.) Eyes remained partially closed throughout anaesthesia. The corneal, palpebral and conjunctival reflexes were sluggish. The anal pinch reflex was abolished completely. Extent of muscle relaxation was excellent. The duration of anaesthesia was 85.42 ± 2.31 min. and recovery was smooth, free from excitement which occurs within 132.85± 3.24 min. Rectal temperature showed a non-significant decrease in the rectal temperature. A significant decrease in heart rate and respiration rate was observed up to 30 min. and 60 min. respectively. There was non-significant decrease in Hb, PCV and TLC. Neutrophils showed significant increase with