

**第4回 アジア太平洋
潜水・高気圧環境医学会**

会 長 川嶋真人 (国際潜水・高気圧環境医学会 特別名誉会員)
日 時 2019年10月25日 (金) ・26日 (土)
会 場 グランプラザ中津ホテル

General session A, Diving medicine & Technology

A-1

Dysbaric Osteonecrosis Severity in the UW Sheep Model After A 24 Hour Dive at 45 FSW Followed by A 15-Min, 30-Min, 45-Min Oxygen Pre-Breathes Before Dropout Decompression

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[INTRODUCTION / BACKGROUND]

After a provocative dive, bubble formation in fatty long bone marrow may lead to a bone compartment syndrome with bone and marrow ischemia and necrosis. We evaluated oxygen pre-breathes (OPB) to determine which would be most likely to provoke dysbaric osteonecrosis (DON) and where DON would occur.

[MATERIALS AND METHODS]

Twelve adult female sheep (89.5 ± 11.6 kg SD) underwent dry chamber air exposure at 45 fsw (2.36 atm abs) for 24 h followed by oxygen (88-92%) pre-breath (15-min, 30-min, and 45-min) before “dropout” decompression 30 fsw/min (0.91atm/min). One month later, bone MRI (GE Signa HD 1.5T scanner) of radii and tibiae were used to detect “hot spots” of remodeling DON lesions.

Alizarin complexone fluorochrome was injected IV to visualize sites of DON repair. Six weeks’ post “dropout” decompression, sheep underwent necropsy to observe DON pathology. Images of long bone gross pathology were taken. Using Scion Image software (Scion Corporation, Frederick, MD), we mapped the areal extent of alizarin complexone deposition as the index of DON severity. DON severity was compared by ANOVA.

[RESULTS]

Alizarin complexone deposition was greater in sheep experiencing 15-min OPB dives than 30-min OPB dives (P<0.05), and sheep DCS incidence was lowest in the 45-min oxygen pre-breathe group. Distal radii accumulated more alizarin complexone in the 15-min OPB group than in the 30-min group (P<0.05). The distal tibia appeared most affected in the 45-min OPB dive group (P<0.05).

[SUMMARY / CONCLUSIONS]

Brief 15-min O2 pre-breath dives show greater DON severity than 30-min and 45-min OPB dives. In humans, DON often may trigger secondary osteoarthritis. These findings indicate that even a 45-min O2 pre-breathing did not prevent DON in decompressed sheep, but enabled “dropout” survival.

General session A, Diving medicine & Technology

A-2

Asymptomatic Dysbaric Osteonecrosis in Japanese Divers

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[INTRODUCTION]

Dysbaric osteonecrosis (DON) is a serious problem amongst divers. We examined bone x-rays

hypertension at annual medical check-up last year, however he had no medical following up. He conducted an air scuba diving which was one-year interval from the last diving, and developed pulmonary edema during dive to 23 msw for 25 min. He became to breathe rapidly and felt difficult to breathe at 5msw depth, and changed to a secondary breathing gas supply, however the situation was getting worse, and he had to performed rapid ascent to the surface. Right after surfacing, he felt dark around and his consciousness declined. SpO₂ was 80% when the rescue arrived 15 min after the surface. His chest X-ray confirmed pulmonary edema.

He was treated with HBO₂ (USNavy table 6) as arterial air embolism with IPE. Soon after reaching 2.8ATA dyspnea had gone and his consciousness fully recovered.

[Second case]

A 23-year-old female had a third scuba diving experience after 2 years interval. After 46min dive to 23.1 msw she got into panic by failing to change her mouthpiece to another one at 10m depth and performed rapid ascent to the surface. Soon after surfaced, she lost consciousness for a short time, and then complained headache and difficulty breathing.

Her initial SpO₂ in hospital was 93% using non-rebreather mask with 10L/min of 100% oxygen. Her chest X-ray confirmed pulmonary edema. USNavy table 6 was started 112 min after the diving accident for headache that we diagnosed as arterial air embolism. After the treatment symptoms were resolved and hypoxemia improved. Third case; a 58-year-old man presented with sudden onset of dyspnea, cough, and hemoptysis after surfacing. He was an experienced diving instructor with a history of moderate mitral valve regurgitation. While IPE was diagnosed and oxygen administered, respiratory symptoms deteriorated, and serum C-reactive protein (CRP) elevated. No evidence of

infection was seen. Three courses of HBO₂ were performed under suspicion of DCS, and symptoms subsequently resolved.

General session A, Diving medicine & Technology

A-4

Deep Pneumatic Caisson Work Using Heliox

Akio Hashimoto

Hyperbaric work support office

A pneumatic caisson method to construct large underground structures was originated in Europe in mid-19 century and developed in USA, but gradually taken over by other methods in mid-20 century. In Japan, on the other hand, after the pneumatic caisson method was introduced from USA to rebuild bridges destroyed by Great Kanto Earthquake in 1923, the method has been used while changing from man-power work to unmanned remotely operated excavators. In the unmanned pneumatic caisson work, engineers have to get inside a pressurized caisson work site to maintain or repair excavators, perform ground bearing testing, and disassemble then remove all machineries after the caisson work is completed at the final depth. When working in a pneumatic caisson work site at the ambient pressure greater than 0.4 MPa, breathing gas must be helium mixed gas by law in Japan. In this presentation, a deep pneumatic caisson work down to 70 meters underground is described. The pneumatic caisson work was employed to construct a large

shaft with 19 meters of outer diameter for sewage treatment water connecting tube at a sewage treatment plant located in Tokyo bay area. Excavation in a pressurized caisson is performed by remotely operated excavators and soil carrying buckets so that the tasks in which caisson workers

have to engage are routine machinery maintenance in the course of excavation, and ground strength testing and machinery disassembling at the final depth reached. Breathing gases used were a mixed gas of O₂ and He (heliox) inside the pressurized caisson site greater than 0.4MPa, air during decompression to 0.09MPa and O₂ from 0.09MPa to the surface. The reason why heliox is utilized rather than a mixed gas of O₂, He and N₂ (trimix) is to avoid the effect of nitrogen narcosis caused by high partial pressure of N₂ which might induce human error during working and to reduce breathing resistance by minimizing the increase of gas density. Decompression procedures were prepared at every 0.05MPa increment up to 0.7MPa with exposure time of 40, 50 and 60minutes. At the pneumatic caisson site, three excavators were employed and 95 times of maintenance work and 30 times of disassembling work, totally 125 times of hyperbaric work were safely performed and no decompression sickness was observed. The hyperbaric work at the final depth of 0.67MPa took 14 days. It could be shortened to 6 days, if a saturation diving method were utilized.

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General session A, Diving medicine & Technology

A-5

Development of ICMM (Immediate Care of Marine Medicine) Course for First Responder in Marine

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ICMM (Immediate Care of Marine Medicine) is developed to provide minimal essential related to marine sports, occupational diving, and work under high pressure environment for medical staff (doctors, nurses, paramedics, etc.). It is the concept of first responder training in acute ocean medicine for citizens. The concept is also important to realize an safe and sustainable society in Japan, which is a maritime nation surrounded by the sea and which requires deep development in a narrowing urban space. The prototype of the ICMM course was designed on Okinawa by the late Masahiro Kohama (Deputy Director, Northern District Medical Association Hospital), who was chairman at the 7th Japanese Association of Clinical Hyperbaric Oxygen and

Diving Medicine (JACHOD) in 2010, Okinawa. It was proposed to raise the level of the first response level of marine medicine in the Okinawa area. From the beginning, a large number of slides and materials for training have been prepared, and ICMM course development review committee (chairperson: Hiroshi Okudera, University of Toyama) promotes development as an education tool. At the 14th JACHOD meeting, instructor courses are held for directors and councilors at the board meeting (2017, Kurume). The first workshop of ICMM was held in Tokyo Medical Association (2018, 6/15) with the 15th JACHOD meeting (Tokyo). The ICMM for a first response to marine medicine is half day course (4 hours, 5 lectures) + BLS (non-attendant, already employed can be omitted), and attends to promote the spread to the general public with provider certification. The "ICMM Guidebook for Immediate Care of Marine Medicine" was published in June 2018 by the ICMM Editing and Course Preparation Committee, in June 2018, as an extra issue of the Journal of Japanese Association of Clinical Hyperbaric Oxygen and Diving Medicine, which is the official journal of the

JACHOD. The basic design of ICMM as training is 1) Basic knowledge of diving medicine, 2) diving and emergency diseases, 3) problems with diving ability, 4) marine bite, 5) Marine bacteria and wound infection, 6) BLS and AED.

Invited lecture 1

Hyperbaric Oxygen for Sports Medicine

Kazuyoshi Yagishita, Toshiyuki Ohara,
Mikio Shioda, Yasushi Kojima, Yumi Niizeki,
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Recently, the applications of hyperbaric oxygen therapy (HBO) for soft tissue injuries are brought into perspective, especially for the athletes with ligament injury, muscle strain and joint sprain. The effects of HBO on sprains, ligament injuries, and muscle strains have been reported in several animal studies. In a dog model of compartment syndrome and in a rat contused skeletal muscle injury model, the significant effects of HBO on the reduction of edema and muscle necrosis have been reported. In basic research, HBO stimulated fibroblast activity to improve the healing process. Oyaizu et al. reported in a rat contused skeletal muscle injury model that HBO reduced muscle wet weight, and decreased the extracellular space and vascular permeability, which resulted in rapid reduction of edema. Therefore, HBO is expected to improve focal edema and pain in the acute phase and accelerate the healing of injured tissue in athletes. HBO is also expected to improve healing process for rapid return to competition. We examined the effects of HBO on professional or semi-professional Japanese rugby players with grade 2 MCL injury that occurred during sports activity, and we reported HBO could have a short-term effect

on pain reduction during the acute phase, and a long-term effect on recovery acceleration with a 25% decreased time to return to play. This presentation aimed to show evidences of the short-term and the long-term effects of HBO on soft tissue injuries in athletes, and to show the HBO for sports medicine.

Presidential lecture

Hyperbaric Oxygen Therapy for Orthopaedic Infection.

Mahito Kawashima, Masayuki Kawashima,
Hiroaki Tamura, Ikufumi Nagayoshi,
Takashi Yamaguchi, Katsuhiko Takao,
Kenji Miyata

Kawashima Orthopaedic Hospital

Osteomyelitis and pyogenic arthritis are bacterial infectious diseases in bones/joints which sometimes become refractory and long-term treatments may be necessary.

Also, gas gangrene and necrotizing fasciitis are bacterial infections in the soft tissue.

It is a dangerous infection which is high risk and turns into a fatal condition and limb amputation. We started using Hyperbaric Oxygen Therapy (HBO) in 1981 and positively apply it in our orthopaedic treatments. We will discuss various treatment cases and results using HBO.

We treated 22 necrotizing fasciitis cases. The results were as follows: cure after necrotomy and/or skin graft without amputation in 10 cases. 3 cases almost cured, minor amputation performed in 4 cases, major amputation performed in 2 cases. 4 cases were transferred to another general hospital due to their general condition worsening. Sixty-four gas gangrene cases were dealt with HBO and other treatments. The results were as follows: 33 cases were cured and their limbs were salvaged, 9 cases were amputated on the foot or toes (Syme amputation), 15 cases were

A-K/B-K amputation, 3 cases died and 4 cases were transferred to other facilities. We performed HBO for 60 minutes at 2.8 ATA (atmosphere absolute) against fatal infectious diseases such as necrotizing fasciitis or gas gangrene.

Depending on the patient's condition, 2 sessions of HBO per day are an effective measure.

We treated 822 osteomyelitis cases and 171 pyogenic arthritis cases with HBO. We performed HBO at 2.0ATA for 60 minutes daily for from 30 to 60 sessions. Many cases finished treatments conservatively, but serious cases needed surgical operations which consisted of washing the bone marrow/internal joints continuously: "closed irrigation therapy". Treatment results of osteomyelitis are:- 533 cases (64.8%) were treated without surgical operations, 437 cases were good. 289 cases (35.2%) were treated with a surgical operation in addition to HBO, 230 cases were good and the other 15 cases (5.2%) were not good enough. 103 out of 171 pyogenic arthritic cases treated conservatively. 101 cases (98.1%) were good and the other 2 cases were not good enough. 68 pyogenic arthritic cases treated with surgical operations in addition to HBO. 67 cases (98.5%) were good and the other case was not good enough.

The effect of HBO for infectious diseases are caused by the oxygen toxicity (oxidative killing) and it increases the leukocyte activity. In addition to it, HBO increases wound healing and enhance the use of antibiotics. HBO is the one of the most useful conservative methods for orthopaedic treatments.

Luncheon seminar 1

Hyperbaric Facility Accreditation: The Key to Continuous Performance Improvement

John S Peters

UHMS

The UHMS Hyperbaric Facility Accreditation (HFA) program is administered by the Undersea and Hyperbaric Medical Society (UHMS), defines evidence and consensus-based standards, require an operational infrastructure, collect high quality data on UHM, and validate compliance with standards through external peer review. A survey of our constituents confirms a high level of agreement that accreditation is regarded as important in improving outcomes through compliance with standards that include continuous quality improvement.

Special invited lecture 1 Hyperbaric Oxygen Treatment of Neurosurgical Infections

Folke Lind, MD, PhD

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Physician Emeritus Karolinska University hospital,
Senior Consultant Hyperbaric Medicine,
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Neurosurgical site infections often require long-term antibiotic therapy, additional surgery, patient misery and high health care costs. Hyperbaric oxygenation treatment (HBOT) is safe and has a role to play in the neurosurgical armamentarium in selected acute or refractory cranial and spinal infections. Cerebral abscess are caused by local or remote infection spreading to the brain (spontaneous) or as a complication to previous brain surgery. Epidural abscess and subdural empyema are also serious hypoxic cranial and spinal infections that result in significant morbidity and mortality.

In conventional open surgery with craniotomy the neurosurgeon opens the skull, creating a large opening to access the brain. The non-vascularized cranial bone flap and other ischemic or otherwise compromised tissues after trauma or repeat

surgery can become infected and turn into a problem osteitis. Infection of implanted hardware is a particular serious complication often causing surgical replacement or removal of the device with loss of treatment benefit for the patient.

These bacterial and fungal biofilm-associated infections are extremely difficult to treat (refractory infections) as the body's repair and microbial defense systems are impaired.

By biofilm formation bacteria and fungus can hibernate safely in a self-made hypoxic/anoxic environment where leukocytes and macrophages are not functional. Antibiotics has sub-optimal efficacy in biofilm and ischemic, hypoxic, acidotic tissues and all repair mechanisms are also O₂ dependent.

Hyperbaric oxygenation of ischemic infected tissues and biofilm improves microbial killing by white blood cells and antibiotics and helps remove biofilm and necrotic tissues by other O₂ dependent cells e.g. macrophages. Anti-inflammatory effects gives an edema reduction. Daily HBOT treatments gives stem cell mobilization and angiogenesis which helps repair microcirculation and tissue oxygenation long-term.

Bone remodeling and tissue repair is also O₂ dependent with possible complete resolution of infection. HBOT improves functional outcome and reduce the need for reoperation to obtain resolution of brain abscesses. HBOT can be used in postoperative cranial and spinal infections without standard surgical removal of infected bone-/acrylic flap or foreign material.

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Oxygen Therapy as adjuvant treatment for hardware-related infections in neuromodulation. *Stereotactic and Functional Neurosurgery*. 2018; 96:100-107

Special lecture 1

Hyperbaric Medicine in a Tertiary Care Hospital in India – A Diary of Interesting Cases

Tarun Kumar Sahni

Apollo Hospital, New Delhi India

The Hyperbaric Treatment Center at the Apollo Hospital New Delhi India was established in the year 2000. This was the first center in the private sector and has been leading the growth of this specialty across the country. Treatment is offered in a Multiplace Chamber which can take up-to 8 sitting/lying patients depending on clinical status of patients. The center has evolved to be able to treat critical ill patients and has published reports in reknown journals and chapters in books. The caseloads include diving accidents referred from dive sites in neighboring countries. Over the years the application of "Hyperbaric Medicine" has become inclusive in "Hyperbaric Intervention" applicable in Compressed air works (Metro development). This presentation will include illustrative case reports of patients treated in the center in the backdrop of the applications of

hyperbaric medicine in the Indian subcontinent.

General session B, Clinical HBO

B-1

Prevalence and Pattern of Cardiac Injury Identified by Late Gadolinium-enhancement of Cardiac Magnetic Resonance Image in Acute Moderate to Severe CO Poisoning with Elevated HighSensitivity Troponin I: Prospective Observational Study

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[Introduction]

Myocardial injury is a frequent consequence of moderate to severe carbon monoxide (CO) poisoning. In addition, long-term mortality is significantly higher in patients who experienced myocardial injury than patients without myocardial injury. No studies have investigated myocardial injury due to carbon monoxide poisoning through cardiac magnetic resonance image (CMR). We want to know whether there are actually cardiac muscle changes identified by late gadolinium-enhancement (LGE) in CMR in acute phase after acute CO poisoning.

[Methods]

This prospective observational study collected data from consecutive patients who were diagnosed with acute CO poisoning and myocardial injury, defined as elevated highsensitivity TnI (hs-TnI) level above the upper limit, at the ED between August 2017 and April 2019. CMR was performed

to evaluate cardiac muscle changes identified by LGE. Patients with coronary artery disease were excluded. We classified the location of myocardial injury into 4 categories (subepicardium, mesocardium, subendocardium, and transmural) and examined the distribution of injured myocardium.

[Results]

Eighty-nine patients were included. Nineteen patients (21.3%) had cardiac injury identified by LGE in CMR. Mesocardium (8 patients, 42.1%) and subendocardium (8 patients, 42.1%) were most common site in patients with LGE positive and there was one transmural damage. In addition, the territory of left anterior descending artery (LAD) (7 patients, 36.8%) and right coronary artery (RCA) (7 patients, 36.8%) were the most common distribution in patients with LGE positive and one patient had global damage distribution, defined as including distribution of all three coronary artery (LAD, left circumflex artery (LCX), and RCA). Out of 7 patients with LAD territory pattern, 6 patients (85.7%) showed damage to the subendocardial area. Patients with damage to the subepicardial area also showed in the RCA territory pattern.

Mean age was significantly older in the positive LGE group than in the negative LGE group

(60.3 years vs. 51.6 years, $p=0.048$). Hypertension and male sex were significantly more in the positive LGE group than in the negative LGE group, respectively ($p=0.003$ and 0.012). Decreased initial mental status was significantly more in the positive LGE group than in the negative LGE group ($p=0.037$). Conclusion: Cardiac injury identified by LGE of cardiac MRI was found in 19 patients (21.3%) in acute moderate to severe CO poisoning with elevated hs-TnI and there were four different patterns (transmural, subepicardial, mesocardium, and subendocardium) of cardiac injury in CMR.

General session B, Clinical HBO**B-2****Successful Treatment of Delayed Hyperbaric Oxygen Treatment in Patients with Iatrogenic Arterial Gas Embolism**

Jeseop Lee, Yong Sung Cha, Hyun Kim,
Jeongwoo Choi

Wonju Severance Christian Hospital

An arterial gas embolism (AGE) can be categorized as accidental or iatrogenic. An accidental AGE is usually caused by accidental from diving. Most common cause of an iatrogenic AGE (IAGE) is a complication from a central venous catheterization (CVC), which can be from the insertion, manipulation, unintentional disconnection, or removal.

Clinical manifestations include respiratory and hemodynamic disturbances which may cause a cardiac arrest. When high volume of gas enters the venous system and results in the maximum capacity of the pulmonary capillary network, the gas could enter the left heart directly via abnormal anatomic structure and enter the arterial circulation causing end-organ damage, such as hemodynamic instability, or neurological deficits. Hyperbaric oxygenation (HBO₂) is indicated with evidence of cardiopulmonary compromise, or neurologic deficits. Many prior literatures reported pleasing outcomes when HBO₂ is administrated within the first four to six hours after symptom onset. However, we report two cases of successful HBO₂ done more than 24 hours after the symptom onset in the IAGE due to a catheter disconnection. A 48-years-old male diagnosed with a liver failure and post liver transplantation was found with unconsciousness and seizure at the ward with disconnected CVC from his right internal jugular vein at the seventh post-operative date. The mental status was stuporous

and the patient was agitated with left-sided motor weakness. Magnetic resonance imaging revealed the multifocal cerebral infarction of both cerebral cortices and deep gray matter. Because of difficulty of the severe agitation and episodic seizure, HBO₂ was delayed for 30 hours. After eleven consecutive sessions of HBO₂, he was discharged from the hospital with only sequela of left dorsiflexion motor weakness, ambulatory with a cane. After two years, the patient has recovered completely with no sequelae. A 77-years-old female admitted for deep vein thrombosis and pulmonary thromboembolism was found with a sudden mental deterioration in the intensive care unit just after removing CVC from her right internal jugular vein. In both right and left ventricle, a large amount of air bubbles were detected with a limited echocardiography.

Even with a ventilator support and continuous vasopressor applied, stuporous mentality and shock status was not resolved. Therefore, HBO₂ was deferred for 28 hours, because of the unstable hemodynamics. After two consecutive sessions of HBO₂, her mentality fully recovered and the hypoxia was completely resolved, so the extubation was done. Even more than 28 hours from the onset, HBO₂ should be considered for the IAGE.

General session B, Clinical HBO**B-3****Hyperbaric Oxygen Therapy for Intractable Bladder Hemorrhage Caused by Localized Amyloidosis of the Bladder**

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 5) *Department of General Internal Medicine, Tokyo Hikifune Hospital*

Amyloidosis is a disease causing functional disorders that occurs when amyloid, which forms fibrils and has resistance to resolution, deposits in each organ of the body.

Especially the one deposits only in the limited organ is classified as localized amyloidosis.

Vascular fragility and microangiopathy caused by the deposition of amyloid is considered the fundamental mechanism of easy bleeding of this disease. Our patient in this case was 83-year-old male with a chief complaint of gross hematuria and dysuria. Accumulation of blood clots in the bladder, and a number of elevated lesions associated with mucosal bleeding from the right wall of the bladder, including the right ureteral orifice, to the back wall and the trigone of the bladder were observed on cystoscopy. The transurethral biopsy and electrocoagulation were underwent for hemostasis and tissue diagnosis. The patient was diagnosed amyloidosis on the tissue diagnosis and referred to a hospital for collagen disease, in which he was diagnosed localized amyloidosis of the bladder after a thorough examination of his whole body. Although persistent hematuria was subsided after the surgery, intermittent hematuria continued through the subsequent ambulant follow-ups. He did not want to have surgical procedures including total cystectomy and urinary diversion, but only symptomatic treatments. As the symptom did not improve by taking hemostatic agents regularly, the informed consent to perform hyperbaric oxygen therapy (HBOT) was obtained. HBOT consisted of supplying 100% oxygen for 60 minutes at 2.0 atmospheres.

Pressure exposure was performed once a day five times a week, and the procedure was done 20 times in total. Three months after performing HBOT, gross hematuria has disappeared during the ambulant follow-ups. The prognosis of localized amyloidosis of the bladder is relatively good, therefore, HBOT can be considered one of the options to control hematuria as a symptomatic treatment to secure the quality of life of the patients.

General session B, Clinical HBO

B-4

HBOT for Idiopathic Sensorineural Sudden Deafness Treatment in Japan

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 6) *JACHO Saitama, Department of Ear, Nose and Throat.*

Idiopathic Sensorineural Sudden Deafness is nowadays considered not so rare an illness in

Japan. But its treatment still remained controversial and inconclusive. The most common treatments are the Steroid, Circulatory Promotion drugs and hospitalization (admission for bed rest). Two other well received treatments, namely Stellatum Ganglion Blockade and Hyperbaric Oxygen Therapy, are used whenever possible.

As mentioned before, Steroid is the most commonly drug used. But its precise mechanism is still unclear and evaluation by Randomized Trial does not yield conclusive result. Circulatory

Promotion drugs are also commonly administered, banking on the merit of ample supply of oxygen and other nutrients.

Bed rest is the hopeful but is difficult to implement in the ENT clinics with limited admission beds, which are the major and typical type of ENT clinics in Japan.

Ganglion Stellatum Blockade is also the hopeful when administered, but relatively intensive care is needed after blockade, especially for respiration disturbances.

In light of the above we discussed the HBOT for Idiopathic Sensorineural Sudden Deafness.

Though ample supply of oxygen, together with other nutrients, are clearly needed for the damaged tissue recovery, choosing this treatment remains limited in Japan, mainly due to the limited number of apparatus available in multi-place chambers. On the other hand, the numbers of one-man chamber now operating in Japan is not so small, but they are engaged in other diseases, such as decompression illness and gas intoxications.

We report here the circumstances of HBOT in Japan, especially with regard to Idiopathic Sensorineural Sudden Deafness.

Special lecture 2
Effect of Hyperbaric Oxygen Therapy for the Treatment of Delayed Wound Healing After Intracranial Carotid Artery Reconstruction Using a Superficial Temporal Artery

Kojiro Wada
National Defense Medical College

Hyperbaric oxygen therapy (HBO) was used to treat 4 patients who suffered delayed wound healing among 40 patients who underwent intracranial carotid artery reconstruction using a superficial

temporal artery from 2013 to 2014. One patient underwent second open surgery because of head trauma and one patient was treated after irradiation for intracranial tumor. HBO was performed at 2 atmospheres absolute for 90 minutes with 100% oxygen inhalation. The wounds were successfully healed after 5 or 10 sessions of HBO. HBO might be considered as useful for the treatment of wounds which fail to heal.

General session C, Basic research
C-1 Morphological Differences in the Adipose Tissue Between the Human Skin and the Whale Skin

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 Msayuki Kawashima, Mahito Kawashima
Kawashima Orthopaedic Hospital

Human beings can not dive deeply, since they receive the strong water pressure. In addition, the water temperature in the deep sea is considerably low. The whale which is an aquatic mammal, can dive the deep sea. Essentially, the adipose tissue in the skin functions keeping heat and protecting for pressure. It appears significant to elucidate morphological differences in the adipose tissue between the human skin and the whale skin. The human skins were given from cadavers, while the whale skins were used from the adult minke whale which were caught by reason of “2005/6 the second phase of Japanese Whale Research Program under the Special Permit in the Antarctic”.

The samples were investigated by light microscopy using various staining methods and scanning electron microscopy combined with chemical digestion methods. The human skin covers the surface of the body, and consists of two main layers, epidermis and dermis. The epidermis is the

surface epithelium, and the dermis is the dense irregular connective tissue.

Beneath the dermis is loose connective tissue, so-called subcutaneous adipose tissue. The adipose tissue is clusters of fat cells, which are very large and typical spherical in shape.

The adipose tissue was often subdivided into small lobules by thin connective tissue septa.

The whale skin was very different in structure from the human skin. Although the dermis was extremely thin throughout, the subcutaneous adipose tissue was considerably thick, and clusters of fat cells were concealed with dense connective tissue septa.

General session C, Basic research

C-2

Hyperbaric Oxygen Reduces Inflammation, Oxygenates Injured Muscle, and Regenerates Skeletal Muscle Via Macrophage and Satellite Cell Activation.

Takuya Oyaizu, M.D., Ph.D., Mitsuhiro Enomoto, M.D., Ph.D., Naoki Yamamoto, M.D, Masaki Horie, Ph.D., Kazuyoshi Yagishita, M.D., Ph.D.

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Hyperbaric oxygen treatment (HBO) promotes rapid recovery from soft tissue injuries.

However, the healing mechanism is unclear. Here we assessed the effects of HBO on contused calf muscles in a rat skeletal muscle injury model. An experimental HBO chamber was developed and rats were treated with 100% oxygen, 2.5 atmospheres absolute for 2 h/ day after injury. HBO reduced early lower limb volume and muscle wet weight in contused muscles and promoted muscle isometric strength 7 days after injury. HBO suppressed the

elevation of circulating macrophages in the acute phase and then accelerated macrophage invasion into the contused muscle. This environment also increased the number of proliferating and differentiating satellite cells and the amount of regenerated muscle fibers. In the early phase after injury, HBO stimulated the IL-6/STAT3 pathway in contused muscles. Our results demonstrate that HBO has a dual role in decreasing inflammation and accelerating myogenesis in muscle contusion injuries.

General session C, Basic research

C-3

Hyperbaric Oxygen Therapy Promotes Muscle Regeneration Via Angiogenesis by Reactive Nitrogen Species in Muscle Contusion Injury of Rat.

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[Introduction]

Contusion injury of muscle causes vascular disruption which leads to delayed delivery of nutrients, oxygen and factors necessary for tissue recovery which may reads to the loss of function. For early and complete recovery of motor function, promotion of angiogenesis appears to be crucial. In previous reports, HBO is useful for circulation disorders by promoting angiogenesis, and after muscle injury, angiogenesis is necessary for muscle regeneration. But the mechanism of HBO on angiogenesis is not known. The purpose of this study was to investigate the effects of HBO on

angiogenesis and muscle regeneration after skeletal muscle contusion injury.

【Materials and Methods】

A muscle contusion injury of the right calf was performed in rats using the drop mass method and rats were then treated with HBO or not treated (NT).

The HBO protocol was at 0.15 MPa for 120 minutes with 100% oxygen inhalation 1 time in a day, for 5 days. To determine whether reactive nitrogen species (RNS) have a role in HBO-induced angiogenesis, HBO-treated rats was also treated with LNAME, a nitric oxide synthase inhibitor. Rats were treated (i.p.) with LNAME before contusion and daily following contusion until the end of the study. We evaluated vascular endothelial growth factor (VEGF) by ELISA, endothelial cells proliferation with Tie2 and Ki67 showing growth phase, and angiogenesis with Tomato Lectin showing blood vessels and Laminin showing basement membrane. HBO only 1 time immediately after contusion (HBO 1-time Day 0 group) were also evaluated in comparison of normal HBO 5 Times group and the NT group.

【Results】

HBO promoted VEGF increasing at 3 hours, accelerated endothelial cell proliferation at 1 day, angiogenesis of immature vessels at 3 days and mature vessels at 5-7 days after contusion. Inhibition of RNS suppressed the effects of HBO on angiogenesis and muscle regeneration. In addition, angiogenesis and muscle regeneration promoted by 1-time HBO in early phase were almost equal to 5 times HBO.

【Conclusion】

RNS appears to be crucial mediators of HBO on angiogenesis and recovery of muscle function. 1-time HBO in early phase is also effective for muscle regeneration via angiogenesis.

General session C, Basic research

C-4

Characteristics of Self-evaluation of Trainees in ICMM (Immediate Care of Marine Medicine)

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ICMM (Immediate Care on Marine Medicine) course is designed to learn basic knowledge of marine medicine for medical staff to provide the necessary first aid. The course consists of half-day course (6 module lectures, 3-4 hours) + BLS. The providers are certified as provider candidate in order to promote widespread use to the public.

In order to study learning effect of the ICMM that has been held five times since 2018, we conducted a questionnaire survey on the participants of the two most recent ICMM courses held. The questionnaire used a questionnaire prepared for the purpose of enabling easy evaluation before and after the training and as an opportunity for students to continue learning. Since the ICMM is composed of six modules, the survey items are: "basic knowledge of diving medicine, "diving and emergency disease", "problem about diving appropriateness", "marine bite disease", "marine bacteria and wound infection", and "BLS and AED". Questionnaires were distributed to all participants, and the survey was conducted completely unnamed. We fully requested that consent was obtained by submitting the questionnaire, and that there would be no disadvantage if not filled in, and we requested submission of the questionnaire. Among

57 subjects, there were 22 physicians (38.6%), 16 diving instructors (28.1%), 9 fire and ambulance crews (28.1%), 3 nurses (5.3%), 3 rescue crews (5.3%) and others (maritime personnel, clinical engineers, etc.) (7.0%). Among physicians, the basic knowledge of diving medicine was the most important (50.0%). Among diving instructors, basic knowledge of diving medicine " shows 37.5% of attendant, who could respond by themselves after taking the course. There was a difference in knowledge before attendance depending on the occupation, but a certain learning effect was recognized in all occupations by attendance. There was an opinion that continuous learning was necessary after attending this course, and we think that showed significance of this course.

We will continue to improve the contents of this training through free description analysis and self-evaluation using questionnaires.

General session D, High pressure technology

D-1

Microcoating of Drugs with Enteric Polymers Using High Pressure Technology

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Enteric coating microencapsulation technology has attracted considerable attention in the field of medicines specially for oral administration due to their ability to prevent dissolution in the gastric environment. However, conventional coating methods often require toxic organic solvents or

surfactants so it is difficult to apply to the human body. Therefore, microcoating methods without a nontoxic solvent are desired. In this study, formation of microcapsules of phenylalanine as model drug substance with pH-responsive polymers was performed by particles from gas saturated solution (PGSS) method with supercritical carbon dioxide (scCO₂) solution. This method has less environmental load than conventional methods and the produced microcapsules are biocompatible because it uses only CO₂. Microcapsules consist of phenylalanine as drug, porous calcium carbonate as carrier, and an anionic copolymer based on methacrylic acid and methacrylate - Eudragit L100 having a pH response functional polymer as coating material, which are not harmful. Into the high pressure cell, calcium carbonate carrying the drug, polymer dissolved in ethanol, and carbon dioxide were placed and mixed under high speed stirring of 940 rpm at a pressure of 10 MPa and a temperature of 323 K. From the nozzle, the sample highly dispersed was sprayed onto the Teflon sheet and recovered. The structure of the microcapsules was observed by SEM equipped with an electron probe microanalyzer

(EPMA) devices. Particle size was measured by dynamic light scattering (DLS) method.

Furthermore, Sustained release rate of phenylalanine from pH-responsive microcapsules was measured using a UV detector.

General session D, High pressure technology

D-2

Modified Gas-saturated Solution Process for Masking Microcomposite Particles of Alpha Lipoic Acid/Hydrogenated Colza Oil in Supercritical Carbon Dioxide

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Alpha lipoic acid (ALA), which has high antioxidant properties, is attracting attention as an active substance in anti-aging products and dietary supplements. However, ALA has an unpleasant taste and needs to be masked with edible polymers to eliminate it. In the past, even with the use of supercritical carbon dioxide (scCO₂) technology, microcomposites could not be formed with masking materials due to the high viscosity of ALA molecules.

The purpose of this study was therefore to investigate and develop a new method for producing ALA microcomposite particles of hydrogenated rapeseed oil (HCO). ALA/HCO microcomposite particles were prepared using a novel Gas Saturated Solution (PGSS) process where the solid dispersion method is used in conjunction with Stepwise Temperature Control (PGSS-STC). Here, the solid particles of ALA and HCO are dispersed in scCO₂ at low temperature, and the temperature is gradually changed to mix ALA and HCO melted in scCO₂. As a result, uniform dispersion of ALA droplets in molten HCO saturated with CO₂ is obtained at high temperatures. After the saturated solution expands rapidly through the nozzle, ALA/HCO microcomposite particles with a diameter of a few micrometers are obtained. The particle distribution

of microcomposite particles produced by PGSS-STC was measured by dynamic light scattering method. As a result, ALA/HCO microcomposite particles showed a particle size distribution that was clearly smaller than that of MC-50F, which is generally sold. Further, the color tone judgment and particle surface state of the collected microcomposite particles were carefully observed with SEM (Scanning Electron Microscopy).

General session D, High pressure technology

D-3

Application of medical materials with using high pressure technology

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Fukuoka university

Micro-composite materials for medical applications can be obtained with high pressure technology as the interfaces between different materials such as medicine, polymers and solutions can be controlled. High pressure techniques such as pressure-induced phase separation using supercritical carbon dioxide (scCO₂) and scCO₂ with ultrasound irradiation can produce microcomposite particles small as micro- to nano-sizes. Medicine, such as Levofloxacin and various coating materials was dissolved in scCO₂ with co-solvent at high pressures, where pressure was slowly decreased to atmospheric pressure resulting in the formation of microcapsules within the high pressure cell. Discussions on the experimental parameters on the morphology, particle size and chemical structure of the microcapsules will be discussed. Results and details of a novel method for producing and quantifying micro- and nano- bubbles by a specially designed high pressure cell with

an ultra sonication horn will be also introduced. Micro phase separation between the high pressure gas and liquid interphase through direct sonication were critical for the formation of micro- and nano-sized bubbles. The characterization (particle size and concentration) of the micro- and nano- bubbles revealed that this novel method was superior to conventional methods.

General session E, Clinical HBO & Basic research

E-1

Hyperbaric Oxygen Improves Functional Recovery of Rats After Spinal Cord Injury Via Activating SDF-1/CXCR4 Axis and Promoting Neurotrophic BDNF Expression

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[Aims]

The current study aims to elucidate the underlying mechanism of hyperbaric oxygen (HBO)'s protective effect for spinal cord injury (SCI) induced neurological defects in rat via exploring SDF-1/CXCR4 axis and neurotrophic BDNF expression.

[Methods]

Acute spinal cord injury rat model was performed in Sprague-Dawley rats with the Allen methods.

Animals were randomly divided into four groups, including sham (SH), SCI, SCI treated with HBO, and SCI treated with both HBO and AMD3100 (an inhibitor of SDF-1/CXCR4 axis). HBO treatment was performed in rat twice per day for 3 days and thereafter once per day after surgery for up to 28 days. Following surgery, neurological assessments were performed with Basso-Bettie-Bresnahan (BBB) scoring system on post operation day (POD) 7, 14, 21, and 28. Meanwhile, spinal cord tissues were harvested to assess expression of SDF-1, CXCR4 and BDNF at mRNA, protein, and tissue levels, using qRT-PCR, western blotting, and histopathological analysis, respectively.

[Results]

1. SCI model and BBB score

BBB scale is a valid and predictive measure of locomotor recovery able to distinguish behavioral outcomes due to different injuries and to predict anatomical alterations at the lesion center. To elucidate HBO's effect on functional recovery in SCI injured rats, we assessed BBB scores for all SH, SCI, SCI+HBO, and SCI+ HBO+AMD groups at various time points postsurgery. The sham(SH) group demonstrated a baseline BBB score(greater than or equal to 20 points)before and after operation, while all SCI injured(with or without treatment) groups showed complete paralysis of both lower extremities with a BBB score of 0 to 1 at early time points (POD 7 and POD 14), suggesting neurological damage due to SCI. Intriguingly, at later time points (POD 21 and POD 28), unlike SCI only and SCI+HBO+AMD groups, SCI+HBO animals demonstrated significantly improved BBB score over time and close to the baseline level of SH group ($P < 0.05$ vs. SCI only and SCI+HBO+AWD groups). Such gradual functional recovery initiated solely by HBO at later time points further validated that HBO possessed protective effect in chronic phase following SCI

injury. Interestingly, co-treatment with AMD3100, a well-established of SDF-1/CXCR4 axis inhibitor, significantly inhibited HBO's protective recovery of BBB scores at all time points after SCI injury (grey line) ($P < 0.05$), further revealing mechanistic evidence that SDF-1/CXCR4 axis might be a major pathway in HBO's therapeutic effect.

2. HBO promotes recovery in tissue after SCI

Histological characteristics were detected after treatment in four groups by HE sections. As expected, SH and SCI+HBO groups were proved to be shown better histological characteristics. In contrast, the SCI group showed prominent edema, haemorrhage, neutrophil infiltration, and disordered tissue structure. The pathological features of tissues from animals in the HBO+AMD were similar to SCI groups, also been disordered structure of tissues.

3. HBO treatment increases mRNA levels of SDF-1, CXCR4, BDNF

RT-qPCR results indicated that HBO treatment resulted significant elevation of SDF-1 mRNA expressions in SCI+HBO groups when comparing with other three groups at POD 7, 14, 21, 28 ($P < 0.05$). Meanwhile, similar pattern regarding CXCR4 mRNA expressions was also observed with slightly varied time points POD 7, 14, 21 ($P < 0.05$). The chemokine receptor antagonist (AMD3100), co-administered with HBO, effectively inhibited such HBO induced activation SDF-1 and CXCR4 as shown in a relatively low level in SCI+HBO+AMD group. Meanwhile, at most time points, mRNA expressions of SDF-1 and CXCR4 in SCI group were not significantly different from SH groups, whereas dramatically lower than SCI+HBO group. Consistently with our behaviour results in Figure 1, the synaptic plasticity markers BDNF also shown to be greatly promoted by HBO treatment when compared to other groups at POD 14, 21, 28. To this point, we illustrated, at mRNA level,

the mechanistic involvement of SDF-1, CXCR4, and BDNF in the therapeutic function of HBO treatment in the pathological process of SCI.

4. HBO treatment increases the protein levels of SDF-1, CXCR4, BDNF

Subsequently, we explored the expression of SDF-1, CXCR4 and BDNF in spinal cord tissues at protein level. The normalized protein level of SDF-1/ β -actin was highest in SCI+HBO groups at most time points, such as POD7, POD14, POD21, compared to SH, and SCI SCI+HBO+AWD groups. Such phenomenon was more prominent for CXCR4/ β -actin expression when HBO significantly promoted CXCR4 expression at all time points post SCI injury, compared to other groups. The coherent trending between CXCR4 and SDF-1 further supported the involvement of SDF-1/CXCR4 axis. In contrast, the co-treated chemokine receptor antagonist (AMD3100) lead to decreased CXCR4 and SDF-1 levels in SCI+HBO+AMD groups, compared to SCI+HBO groups at all time points post-surgery. Similar to SDF-1 and CXCR4, the neurotrophic factor BDNF detected by western blotting demonstrated moderately elevation in SCI+HBO group compared to SCI group, whereas showed a significant increase when compared to SCI+HBO+AMD groups. As expected, HBO promoted BDNF expression after HBO treatment, benefiting the regeneration and neurological function recovery of SCI.

5. Effects of HBO treatment on the expression of SDF-1, CXCR4, and BDNF in spinal cord tissues

To clarify these interesting proteins at tissue level, immunohistochemistry was applied to determine the SDF-1, CXCR4, BDNF in spinal cord tissues from SH rats. The distributions of SDF-1 were found to locate in white matter and grey matter. Meanwhile, BDNF-positive cells were identified primarily in white matter. Moreover, CXCR4, a chemokines receptor, was then found

in the inflammatory cells scattering in spinal cord tissues with less abundance. Besides, we stained the BDNF and SDF-1 to compare their levels in spinal cord tissues from the rats subjected to both SCI and HBO treatment at POD 14, 21, and 28. Consistently with our findings at mRNA and protein level, it was visually distinctive that HBO treatment resulted the increases of SDF-1 in white matter. In addition, HBO treatment also increased expressions of BDNF.

Our study not only provided a clue that hyperbaric oxygen may benefit recovery after SCI and but also elucidated mechanistic support that such protective function might be mediated through enhancing SDF-1/CXCR4 axis and promoting neurotrophic elements such as BDNF. Therefore, we might be able to deduct that HBO might synergistically inhibit neurodegeneration. The dynamic and longitudinal changes of these proteins (SDF-1/CXCR4/ BDNF) at various time points after SCI and HBO treatment not only confirmed our hypothesis in supporting HBO's translational therapeutic function, but also raised a serial interesting scientific questions for future investigation.

Although our study provided fundamental behaviour and mechanistic support for HBO, there are more research efforts to be carried out to clarify detailed molecular mechanism regarding drug action and SCI pathogenesis. Several study demonstrated that TGF- β , AKT, WNT signalling pathways involved in SDF-1/CXCR4/BDNF conducting cell migration or differentiation. Since, SDF-1/CXCR4/BDNF had been confirmed to benefit recovery after SCI. Future study would be taken the focus on monitoring the levels of SDF-1 or CXCR4 or BDNF in the peripheral blood from patients with SCI and assisted the clinicians predict the outcome of hyperbaric oxygen treatment.

In conclusion, our study indicated the HBO

treatment, a clinically translational approach, significantly improved functional recovery after SCI in rats for up to 28 days. In addition, we also demonstrated that such promising effect of HBO might be associated with endorsed SDF-1/CXCR4 axis and promoted BDNF (synaptic plasticity markers) expression at mRNA, protein and tissue levels. These data lay a solid pre-clinical foundation in translating HBO into a safe and effective clinical treatment of SCI, warranting further and more in-depth investigations.

General session E, Clinical HBO & Basic research

E-2

HBO Therapy in Acute Traumatic Ischemic Diseases

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Evidence-based indications: The use of HBO for all kinds of traumatic diseases has potential beneficial results, about 15% trauma patients has improved or beneficial outcomes. The HBO center or unit was built in trauma hospital or center in many country such as The Trauma Hospital in Maryland in U.S. and Murnau trauma center in Germany.

Acute traumatic peripheral ischemia (including crush injuries and suturing of severed limbs) when loss of function, limb, or life is threatened and HBOT is used in combination with standard therapy. Crush injury and skeletal muscle-compartment syndrome (SMCS) are two related conditions that arise as a consequence of trauma. Common features include ischemia and hypoxia at the injury site, a gradient of injury, and the potential for self perpetuation of the injury. Convincing laboratory

studies and clinical researches show statistically significant reduction, in loss of muscle function, metabolites associated with muscle injury, edema and muscle necrosis with HBO. With HBO there is often restoration of function of the injury, ischemia, undemarcated (living vs. dead) muscle after fasciotomy.

In addition, HBO accelerates demarcation of live and dead muscle, which makes debridements and grafting established more easily. This makes HBO a logical intervention for the SMCS.

The benefits of HBO on compromised skin grafts and flaps arise from a systemic elevation in oxygen tension rather than a local effect. In addition, HBO therapy prevents neutrophil adherence and subsequent vasoconstriction following ischemia.

A compromised flap is allowed to progress over the days following surgery until visible signs of necrosis obviate the use of HBO; delayed treatment with HBO cannot revive dead tissue. HBO therapy for compromised flaps should be based on the type of flap, classification of ischemia, and effects of treatment of HBO, which decided HBO therapy regimen.

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General session E, Clinical HBO & Basic research

E-3

The Effects of Hyperbaric Oxygen (HBO) on Brain Dysfunction After Cardiopulmonary Resuscitation (CPR)

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【Background and objective】

Hyperbaric oxygen (HBO) has been shown a

beneficial effect in improving survival or neurologic outcome in patients who are comatose after cardiac arrest. The aim of the study was to obtain information about the opinion of the Chinese Emergency Medicine Group and representatives of Hyperbaric Medicine Group members regarding the best clinical practices using hyperbaric oxygen therapy treatment for the brain dysfunction of patients after cardiopulmonary resuscitation.

【Materials and methods】

A four-round nominal group technique was carried out for developing consensus. There were 3 categories for the strength of recommendation (strong, weak, and no specific recommendation).

【Results】

Hyperbaric oxygen therapy can be suggested for patients suffering from cognitive impairments after cardiac arrest especially patients who have acute global ischemia/anoxia such as hanging, near drowning, electric shock, air embolism, and carbon monoxide poisoning; The pressure was recommended between 2.0-2.8ATA. The optimal time for hyperbaric oxygen therapy is soon after ischemia, possibly as late as the return of spontaneous circulation (ROSC), is highly beneficial in positive outcomes. Basic cardiopulmonary resuscitation equipment, technician, physician, and nurse staffing should be available in the hyperbaric chamber for patients after ROSC. HBO is likely ineffective for comatose survivors of cardiac arrest whose neurological assessment predicts very poor neurological outcome.

General session E, Clinical HBO & Basic research

E-4

Two-cases Report: Early Rehabilitation Intervention in Peri-hyperbaric Oxygen Period for Infants with Neonatal Encephalopathy

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Neonatal encephalopathy (NE) is a clinically defined syndrome characterized by neurologic function disturbed in the earliest days of life in an infant born at or beyond 35 weeks of gestation.

Major goals of treatment include the maintenance of physiologic homeostasis and treatment of the outward manifestations of cerebral injury. Infants with moderate to severe NE are more likely to develop long-term neurologic morbidity. Fetal or neonatal brain injury can result in lifelong neurologic disability. The hyperbaric oxygen treatment may significantly play a favorable role in improving brain metabolism and the ability to modulate the sequelae of neuronal cell insults or the ability to repair brain injury, so HBO2 is described as valuable neuroprotector.

[OBJECTIVE]

To observe neurodevelopment evaluation for 2 infants with NE following rehabilitation intervention in the peri-hyperbaric oxygen period over one year.

PATIENTS AND METHODS: Test of Infant Motor Performance (TIMP) was evaluated before, after 10 sessions HBO2. Cerebral MRI was imaged on 3-month-old. The protocols of therapy were included rehabilitation intervention for 20min in

the peri-HBO2 (before and after HBO2 therapy) for 10 sessions. Then there was 5days break after 10 sessions in order to avoid oxygen poisoning for infant. The scheme of each HBO2 was 8min to compression, 25-30min at the1.6ATA isobaric pressure and 8min to decompression, 1 session every day, 5 days each week.

[Case 1]

14-day-old female infant with Hypoxic Ischemic Encephalopathy (HIE) when delivered

(01/10/2018, first born at the 41 weeks of gestational age) was admitted to HBO2. Cerebral MRI on 10 days after birth presented Bilateral temporal lobe, cerebellar hemisphere hemorrhage.

TIMP and cerebral MRI were evaluated again after 50 sessions therapy. TIMP and cognition were close to normal children of the same age. Cerebral MRI image was normal and original hemorrhagic signs were disappeared. The evaluations of neurodevelopment, speech for this female infant are normal level.

[Case 2]

3-month-old male infant with HIE caused by fetal intrauterine distress (12/28/2017, G4P2, at the 35 weeks of gestational age) was admitted to HBO2. Cerebral MRI on 5 days after birth presented acute ischemia and hypoxia changes in the border area of the left occipital occipital lobe. Before HBO2, the infant could not raise his head and turn over, with poor eye coordination and high muscle tension for upper limb. after 50 sessions therapy.

TIMP and cognition were close to normal children of the same age. Cerebral MRI image (09/06/2018) presented that original signs were disappeared after 40 sessions. The evaluations of neurodevelopment, speech for this male infant were close normal standard at the same age.

TIMP evaluation for two infants and eye sights have been observed for 1-year. No signs for ROP occurred.

[RESULTS]

Rehabilitation intervention in the Peri-HBO2 period for newborn baby with NE could significantly improve neurodevelopment of infant as much as possible. HBO2 therapy is the safe and effective intervention for newborn infants.

General session E, Clinical HBO & Basic research

E-5

Changes in the Gut Microbiota During and After Commercial Helium-Oxygen Saturation Diving in China

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[Objective]

Saturation diving is widely used to accomplish long time subsea work nowadays, and is reported to have adverse effect on divers' health. Appropriate diet has the potential to alleviate many of the health concerns. However, the guideline for saturation divers' diet is limited.

Gut microbiota plays a key role in host health

and can be easily affected by recent diet and environment exposure. Chronic exposure to the confined, hyperoxic, hyperbaric environment during saturation diving may have influence on diver's gut microbiota. This study is to assess the influence of commercial helium-oxygen saturation diving on divers' gut microbiota, in order to provide suggestion on divers' diet from a new angle.

[Methods]

Fecal samples of 47 divers were collected before (T1), during (T2), and after saturation diving (T3). Their living and excursion depths were 55-134 meters underwater with the saturation duration 12-31 days and ppO₂ 38-65 kPa. The fecal samples were examined through

16s rDNA amplicon sequencing based on Illumina sequencing platform to analyze changes of the bacteria composition in divers' gut.

[Results]

Although the α and β diversity of the gut microbiota which represents the diversity within and among individuals respectively did not change significantly, we found that living in the hyperbaric environment of helium-oxygen saturation decreased the abundance of genus Bifidobacterium, an obligate anaerobe, from 2.43% \pm 3.83% at T1, to 0.79% \pm 1.23% at T2, and 0.59% \pm 0.79% at T3. Besides, abundance of some short-chain fatty acid (SCFA) producing bacteria such as Fusicatenibacter, Faecalibacterium, rectale group, and Anaerostipes showed a decreased trend in the order of before, during and after diving. On the other hand, the abundance of species such as Lactococcus garvieae, Actinomyces odontolyticus, Peptoclostridium difficile, Butyricimonas virosa, Streptococcus mutans, Porphyromonas asaccharolytica, Actinomyces graevenitzi and so on showed an increased trend, most of them were pathogens.

[Conclusions]

Occupational exposure to high pressure of

helium-oxygen saturation environment decreased the abundance of some probiotics and increased the risk of pathogenic bacteria infection. Supplement of probiotics or prebiotics in divers' diet during saturation diving might prevent these undesirable changes.

Invited lecture 2
Current Status of Hyperbaric Oxygen Therapy in Korea
 (The Toxicokinetics & clinical spectrum after CO poisonings)

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More than 300 hospitals were estimated to have HBO₂ chambers for the treatment of carbon monoxide (CO) poisoning between in the late 1970s and the 1980s because of the Ondol heating system by briquettes in South Korea. Gradually changes heating system from briquettes to gas at apartment and CO poisoning patients rapidly decrease in South Korea. So many hospitals abandoned the continuous operation of the chambers due to a lack of patients and increase in reimbursement. In South Korea, an expanded knowledge base and formalized education in HBOT do not exist, and numerous HBOT devices are old and nearing the cessation of operation, although HBOT has undergone refinement, with an increased understanding of mechanisms of action and clinical applications.

Furthermore, there is no specific board certification of HBO competence for emergency, critical care, and surgical physicians and technicians in South Korea. But the Korean Academy of Undersea & Hyperbaric Medicine (KAUHM) was established in Oct. 2014, we are setting a well-organized educational program for medical doctor (MD) /non-MD course and operating 6 mutiplace

chambers and 16 monoplace chambers (level 1 or 2) in civilian hospitals in Korea. The application of HBOT is covered by public medical insurance within the indication including CO poisoning, decompression sickness, air or gas embolism, gas gangrene, idiopathic sudden sensory hearing loss, delayed radiation injury, thermal burns, compromised grafts and flaps, arterial insufficiencies, necrotizing soft tissue infections, crush injuries, refractory osteomyelitis, severe anemia and intracranial abscess. We have to plan for certification and medical training.

The toxicokinetics of CO poisoning was due to cellular hypoxia, oxidative damage, excitatory neurotransmitter release and immunologic dysfunction related to hemeproteins.

An estimated 5,000 to 6,000 patients occurred in the South Korea each year as a result of CO exposure. Persistent or delayed neurologic sequela have also been reported and treatment of choice for moderate and severe poisonings are HBOT.

Invited lecture 3
Deep-sea challenge: Man-machine-environmentsystem Design of Deepsea Manned Submersibles Cockpit

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Deep-seamanned submersible technology is a cutting edge and one of the most advanced deep sea technologies. The Deep-sea manned submersibles have been playing an increasingly important role in deep sea environment research, deep sea biological research, deep sea resource study, as well as in the emerging field of hadal ecological study. In June 2012, the "Jiao Long" manned submersible completed the 7000m sea test mission successfully. It marks the great-leap-forward development of China's deep-sea equipment technology and joins the club of international deep-sea developed countries.

It cannot be separated from the progress of marine heavy vehicle equipment in studying and exploring ocean. "Jiao Long" can bring our marine scientists into the field of abyss science, but for abyss science, reaching 7000m is only the beginning. Full Ocean Deep Manned Submersible is indispensable deep-sea diving equipment in the research of hadal trench. Key technologies of full ocean deep manned submersibles including quick diving, human factors engineering, buoyancy material, batteries with large capacitance, communication and positioning etc. We were in charge of the human factors engineering branch project "Design and Research of Man-machine-environment for Full Ocean Deep Manned Submersible". We used the main task measurement method, physiological measurement method and subjective evaluation method to design and evaluate the Cockpit environment layout, man-machine interface layout and main driver's seat in Full Ocean Deep Manned Submersible.

It is suggested that a tractable movable baffle should be designed in the Cockpit to meet the physiological characteristics of the co-pilot's sitting posture and observation position; the red/grey combination of display screen foreground color and background color could improve the performance of interface operators; the key information, important

information and minor important information of man-machine interface should be located in different areas; the suggested backrest angle of the main driving seat is 105°, which can not only meet the requirements of long time sitting comfort and reduce fatigue, but also ensure normal operations. Finally, according to the comprehensive integration measurement data, we also established the Industry Standard for Manned Submersible.

【Funding】

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Special lecture 4 Hyperbaric Oxygen Therapy (HBO) for Conditions Other Than Diving Pathology: Origin, Historical Evolution and Present Activity Round The World

Jorge Pisarello

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The use of hyperbaric oxygen for the treatment of conditions other than diving related diseases has a relatively brief history. Following initial publications by Osorio de Almeida circa 1935, the use of HBO became generalized only twenty years later. Clinical use of HBO was summarized in 1963 by Boerema (1). From that summary the only application that is currently utilized (2014) is the treatment of CO poisoning (2), demonstrating the dynamic evolution of this technology. HBO is considered an adjunct therapeutic intervention,

consequently the justification for its clinical use is dependent on the development of alternative simpler therapeutic methods. HBO is justified in clinical situations that do not resolve or improve without the use of HBO and where there is evidence of HBO efficacy. Identification of new possible uses of HBO is based on serendipity followed by systematic evaluation. The current worldwide use of HBO, with the possible exception of China, follows a pattern of two schools, with some overlap, as a result of recent increase in ease of communication:¹⁾ Recommendations generated in the US (UHMS) and the European experience (Consensus committee) and²⁾ The Soviet Union experience, later transmitted to Cuba and associated regions under their influence. These respective approaches are based on partially differing scientific conceptions and both resulted in a large collective clinical experience. Despite a growing number of scientific contributions dealing with oxygen biology and medicine, the logic behind the use of HBO in general pathology continues to rest on confirmation by quality clinical research.

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Invited lecture 3 Molecular Mechanisms of Hyperbaric Stress in Deep Diving

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Diving is used for a wide variety of purposes including recreational activities, fishing, scientific

research, commercial use, military operations, etc. Depending on the purpose, diving methods and diving apparatus are selected. Among those saturation diving is one of very specialized type of system diving aimed at offshore oil field drilling, salvage work, and submarine rescue. It can reach very deep undersea and deep diving record at chamber depths to 2,300 feet (701 m) was established by the COMEX in 1992. At that time we a project team of the Undersea Medical Center, Maritime Self Defense Force at Yokosuka, Japan were involved in finding biomarkers for deep diving stress. Deep diving stress may cause a wide range of medical problems including high pressure nervous syndrome, arthralgia, organ dysfunctions and so on. In the analysis of peripheral blood samples from saturation divers, we first discovered that extremely high pressure condition causes immunological changes, namely a decrease in T cell subset especially in CD4+ T cell subpopulation. The magnitude of immunosuppression of this type depends on diving depth and compression speed, and it seems to be similar to HPNS patterns. We could successfully attenuate the immunosuppression of saturation divers by rescheduling the diving protocol. We also found that deep diving has an effect to stimulate heat shock protein responses such as Hsp72/73 and Hsp27, which is now considered to be caused mainly by accumulated oxygen stress during diving. Recent report by other group showing that genes related to immune response and Hsp signaling pathway are up-regulated in divers supports our hypothesis. Also our recent analysis of plasma proteome in saturation divers has revealed that anti-oxidant proteins are up-regulated during deep saturation diving and it may have unique coincidence under hypobaric hypoxia. These our research approaches may help understand molecular mechanisms of hyperbaric stress in deep diving.

Luncheon Seminar 2 Space Medicine to the moon and Mars - What about osteoporosis? -

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TSUKUBA KOKEN, ex. JAXA

In 2018 we began to hear announcements from space agencies that they are to send humans to the moon again. They also announce that their scope includes the exploration to Mars. Are we ready for its aerospace medicine support? NASA lists space radiation on the top of the problem list for deep space exploration, including Artemis lunar program.

However, if it is a commercial or individual adventure, magnitude of probable adverse health effects from irradiation should be much lower on the list. Issues of deep space radiation, which are different from low-earth-orbit International Space Station (ISS) environment, are ion particle effects (larger LET) and potential big solar flares. These threaten in violating national radiation worker standards. But if you compare the threats with risks in climbing Himalayan mountains, they are much smaller. Neurological changes from longer weightlessness stay are not well understood. Recently we were surprised to find apparent changes in the eye and brain morphology. Up to one year, they seem to be generally manageable with current physiological countermeasures, though¹⁾. Still, if an astronaut suffers from reduced visual acuity during a mission, it is a direct risk for survival, in addition to a difficulty in rehabilitation. There also are definite health threats in other physiology domains²⁾. Musculoskeletal system is one of them. We do not have enough data to be sure that successful surface activities on Mars and satisfactory rehabilitation back on the earth can be guaranteed. Associated with skeletal system involvement is the possible urinary lithiasis.

This happened in the past (luckily spontaneously passed), and USSR ground controllers had a bad time. We hope to see a better pharmacological countermeasure for these two issues (hopefully at the same time), as exercise countermeasure which works well on ISS is not possible with current large machines. For deep space human exploration, we need to consider Artificial Gravity (AG) in addition to exercise and pharmacological countermeasure, as AG may solve most of weightlessness health issues. Before the end of mission of ISS in 2020's, AG should be verified on orbit³⁾.

References

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Special invited lecture 2 Medical Evacuations of Recreational Scuba Divers Assisted worldwide by Divers Alert Network in the 2014-2018 period

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【Background】

Underwater diving is a popular recreational activity with growing participation, especially in the Asia-Pacific region. Divers are exposed to dive-related injuries and other medical emergencies associated with traveling, which sometimes requires a higher level of medical care than what may be

available in remote destinations.

Divers Alert Network, a not-for-profit organization, provides 24/7 call center for emergency assistance to traveling divers worldwide, which for DAN members also includes evacuation and repatriation services.

【Objective】

We review five years of DAN Call Center data and insurance claims data and analyzed cases of emergency evacuation and repatriation.

【Method】

DAN Call Center records all calls it receives, including data about the geographic origin of the call, demographic data of injured or ill divers, details about a medical condition, the steps involved in management, disposition of injured divers, and outcomes. We searched for cases involving medical evacuation or repatriation for diving and nondiving emergencies.

【Results】

In the observed five-year period, the Call Center received 17,259 requests for assistance with post-dive symptoms, 55% coming from DAN members, eight percent of which were assisted with air evacuation or repatriation. Most evacuation started in the Caribbean, followed by Asia-Pacific and Mexico. Dive specific injuries made 34% of cases, trauma 30%, and the rest were other medical causes. Seventy-two percent of evacuee were 50 years or older. Repatriations followed a similar pattern. When evacuation requires an air-ambulance pressurized to normal atmospheric pressure, the cost may be exorbitant.

【Conclusion】

Severe injuries and acute medical conditions that cannot be treated at destinations are not uncommon among traveling divers. Risk of acute medical conditions increases with age. Travelers to remote locations who intend to dive should receive proper pre-trip consultation and advise how to mitigate

their risk and prepare for emergencies.

Special lecture 5

Hyperbaric Oxygen Preconditioning Protects Against Liver Ischemia/Reperfusion Injury by Heat Shock Protein 70 Overexpression

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【Objective】

Many clinical situations such as hepatic trauma, hepatic transplantation, hypoperfusion shock, or partial keratectomy for liver tumors cause ischemia/reperfusion (I/R) injury of the liver. We assessed whether hyperbaric oxygen preconditioning (HBO2P) in rats induced hepatic heat shock protein (HSP) 70 overexpression and whether HSP70 antibody (Ab) preconditioning attenuates hepatic I/R injury.

【Methods】

Daily treatment with one-dose HBO2P (60 min, 2.0 ATA) was brought about for male Sprague-Dawley rats for five days before an I/R injury of the liver.

【Results】

One dose of HSP70 antibody was administered one day before an I/R injury of the liver. Significant ($P<0.05$) up-regulation of hepatic HSP70 after five days of HBO2P coincided with significant ($P<0.05$) reduction in lethality, hepatic injury, hepatic lipid peroxidation, hepatic myeloperoxidase activity, and hepatic overproduction of proinflammatory cytokines. Inhibiting hepatic HSP70 with HSP70 antibody reversed both hepatic HSP70

overexpression and hepatic I/R injury.

[Conclusions]

Our results indicate that HBO2P diminishes hepatic I/R injury in rats with up-regulating hepatic HSP70. HSP70-mediated HBO2P may protect against hepatic I/R by inhibiting hepatic inflammation and oxidative stress. The application of HBO2P applied in clinics and preventive health will be discussed.

[Keywords]

Ischemia-reperfusion injury; liver; heat shock protein 70; hyperbaric oxygen; inflammation

Special lecture 6

Hyperbaric Oxygen Therapy (HBOT) for Necrotizing Fasciitis Not Responding to Conventional Treatments and Development of Hyperbaric Medicine in South Korea

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Necrotizing fasciitis is a disease of fulminating septic process that involves not only the full layers of the skin but all underlying structures, including muscular structures. It has a very high rate of mortality and amputation unless promptly recognized and aggressively treated.

Early medical and surgical treatments are classic standard treatments, but hyperbaric oxygen therapy (HBOT) is a valuable adjunct in the treatment of this rare but serious disease, which allows more rapid control of the infectious process, a reduction in morbidity, and facilitation of earlier closure. HBOT has been approved by the Undersea and Hyperbaric Medical Society as an adjunctive treatment for necrotizing soft tissue infections. I report a 63-year-old diabetic man transferred from

university hospital not installed with a chamber whose necrotizing fasciitis condition did not improve after 2 months of admission treatment. Multiple incisions and debridement were done. After 2 weeks admission, HBOT treatment was stopped for 1 week due to acute gastric ulcer bleeding. After stabilization of infection process, battery-operated negative pressure wound dressing was applied to the wound bed for coverage. He had an excellent outcome with classic methods and HBOT.

No amputation was required. The mechanism for HBOT of this acute infectious process is proposed as follows: 1) oxygenation of hypoxic tissue, 2) neutrophil oxidative killing, 3) suppression of bacteria multiplication, 4) augmentation of antibiotic effectiveness, 5) enhanced fibroblast function, 6) angiogenesis, and 7) decrease of edema and ischemiaperfusion injury. In addition, I present a brief historical development and current overview of HBOT in South Korea. In South Korea, underwater and hyperbaric medicine was introduced in the early 1950s after the Korean War, by the Korean Navy in order to treat for decompression illness. In public health domains, hyperbaric oxygen therapy was applied in the late 1960s in order to treat carbon monoxide poisoning, which was very common due to the widespread use of coal as the primary fuel for cooking and heating. However, HBOT for illnesses other than diving-related diseases began to develop only in the late 2010s, after Samcheonpo Seoul Hospital installed a multi-place chamber in 2013.

Certain clinical diseases use HBOT as a useful adjuvant and good results have been shown.

General session F, Clinical HBO

F-1

Treatment Effect of Normobaric Oxygen Therapy Right After Physical Therapy for Pain and Numbness Caused by Cervical and or Lumbar Spondylosis

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Normobaric oxygen therapy (NBO) can increase alveolar oxygen over 90% by inhalation of pure oxygen using non-rebreathing mask, and is a life-saving treatment of acute hypoxemia, et al. Group of 49 patients average 68 years old complaining of pain and numbness by spondylosis and/or radiculopathy was treated by five executive NBO, 60 minutes right after physical therapy for the period of approximately one month. For the control group of 21 patients of approximately same age and symptoms was received five physical therapy for the same period. Amelioration of the symptoms was better in physical therapy plus NBO group than physical therapy only group. NBO seems relaxing and comforting effects during oxygen inhalation and thereafter.

General session F, Clinical HBO

F-2

Combined Traditional Chinese Medicine and HBO Treatment for Refractory Osteomyelitis

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[Foreword]

Chinese herbal medicine treatment of osteomyelitis has a history spanning two

millennium with positive results. HBO treatment of osteomyelitis also has proven effects.

Combination of the two methods can generate better results.

Case 1. [Description]

Male, 56 years old. Rhinitis radiotherapy caused lower jaw putrescence, osteomyelitis, multiple sinuses, Temporomandibular joint disorder. Loss of jaw function. Can only drink milk with liquid food. Three suicides attempts caused by persistent and severe pain. Admission time: September 10, 2011. Bacterial: *Pseudomonas aeruginosa* and *E.coli* mixed infection.

[Method]

Débridement, sequestrectomy, Kawashima continuous cleaning, one-stage suture incision. HBO treatments 20 times.

[Result]

Pupil and incision first phase closure. Successful return of jaw functions. Eight years following up period with no recurring osteomyelitis.

[Conclusion]

Débridement followed by the combined methods of HBO and Kawashima continuous cleaning was a successful treatment strategy.

Case 2. [Description]

Female, 8 months. Congenital heart disease treated with transsternal approach heart surgery. Post-surgery sternal osteomyelitis with multiple sinuses. Anemia. Hypoproteinemia. Admission time: December 15, 2004. Operation time: December 30, 2004. Six times débridement in two months period. Intravenous vancomycin.

[Method]

Termination of antibiotics treatment. Oral usage of Zhongjing Dazao Pills, 1 capsule daily, 9g per grain, mixed into milk.

[Result]

Treatment for 1 month, sinuses closure. Followed up for 13 years, Osteomyelitis did not recur.

[conclusion]

Chinese herbal medicine can successfully treat MRSA and osteomyelitis.

Case 3. [Description]

Male, 48 years old. Open fracture of the humerus postoperative osteomyelitis, glomerular purpura. Urinary protein (+++) , urine granule (+++) . Daily intake of 12 prednisone tablets. MRSA. After admission: conventional debridement and skin grafting plus continuous cleaning. Conditions deteriorated 3 weeks after surgery. Expert consultation opinion: steroids were the key factor. Without it the patient' s life may be in danger. The continuous usage of it would prevent effective treatment of osteomyelitis.

[Method]

Gradual termination of both antibiotics and steroids treatment alongside oral intake of Zhongjing Dazao Pills, 6 capsules daily for 45 days..

[Result]

Successful sinuses closure. Successful treatment of osteomyelitis. Symptoms of glomerular purpura disappeared. Urine test: urine blood (-) , urinary protein (-) , particle tube type (-) . 19 years following up period with no recurrence of osteomyelitis and glomerulus nephritis.

[Conclusion]

Zhongjing Dazao Pills are effective for both MRSA osteomyelitis and allergic glomerular purpura nephritis.

Case 4. [Description]

Male, 2 years old. Right Femur ang tibia acute blood-borne osteomyelitis.

6 operations with a highly swollen knee joint, destruction of articular cartilage, articular cartilage necrosis.

[Method]

Stop using antibiotics. Oral intake of Zhongjing Dazao Pills, 2 capsules daily, 6g per capsule. Use

Jiawei Jinhuang Powder to soak lower limb, twice a day, 30 minutes each time, add 50g of powder each time, water temperature 35°C~ 39°C .

[Result]

Sinus closure, knee swelling reduced, bone healed. Followed up for one year and a half, osteomyelitis did not recur.

[Conclusion]

Traditional Chinese medicine oral and external washing proved to have positive effect while avoiding repeat operation.

Case 5. [Purpose]

Female, 68 years old. Lower extremity arterial occlusive disease, install 6 brackets, lower leg large area ulcer, unite type II diabetes.

[Method]

Oral intake of Zhongjing Dazao Pills, 3 capsules daily, 6g per capsule; use Jiawei Jinhuang Powder to soak feet, 2 times a day, 30 minutes each time, 50g per dose.

[Result]

Treatment for one and a half months with successful wound closure.

[Conclusion]

Applying this therapy can avoid big flap and amputation.

[Advantages of this therapy]

1. Proven effective for diverse range of bone and joint infection.
2. Failure of previous treatments can be corrected.
3. No poison and side effect; suitable for elderly patients and children with low functioning immune systems.
4. Can treat other comorbidity at the same time.
5. No resistance.
6. Lower cost.

[Zhongjing Dazao Pills prescription]

Huangqi, Huangqin, Huanglian, Pugongying, Zihuadiding, Baitouweng, Bailian, Renshen, Baizhu, Fuling, Ziheche, Tusizi, Buguzhi, Gusuibu, Bajitian, Roucongrong, Lurong, Yinyanghuo, Danggui,

Heshouwu, Shudihuang, Gouqizi, Huangjing, Shihu, Niuxi, Yuanzhi, Muxiang, Dingxiang, Wujiapi, Shanzha, Maiya, Shenqu

【Jiawei Jinhuang Powder prescription】

Huangqi, Huangqin, Huangbo, Dahuang, Jianghuang, Baizhi, Mufurongye, Bailian, Fupenzi, Tiannanxing, Chenpi, Cangzhu, Houpo, Gancao, Banxia, Yanhusuo, Tianhuafen, Xuejie, Bingpian

General session F, Clinical HBO

F-3

Treatment of Osteomyelitis with Sternotomy Myocutaneous Flap---HBO in ERAS

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【Objective】

To summarize the clinical experience of sternotomy myocutaneous flap in the treatment of osteomyelitis-HBO in ERAS, improve the cure rate, reduce the recurrence rate, and accelerate the rehabilitation surgery.

【Methods】

A retrospective analysis of 312 cases of sternal median incision and deep sternal incision infection (Deep Sterna Wound Infection/DSWI) was performed in China from February 2017 to February 2019 in China's Hebei Yanda Hospital and Beijing Wangfu Hospital of Integrated Traditional Chinese and Western Medicine. The patients, including acute DSWI with cerebral infarction in 18 cases, chronic DSWI in 93 cases, all patients underwent general anesthesia intubation, thorough debridement, pectoralis major or combined rectus abdominis flap for sternal defect repair, wound suture. HBO therapy was performed on 18 patients with acute DSWI complicated with cerebral

infarction and 50 patients with chronic DSWI 10 days after surgery.

Results: Eighteen patients with acute DSWI complicated with cerebral infarction recovered rapidly. The 50 patients with chronic DSWI had no recurrence of osteomyelitis after 6 months of follow-up. Conclusion: The sternotomy myocutaneous flap is used for the treatment of sternal osteomyelitis. For patients with cerebral infarction and chronic sternal osteomyelitis, HBO therapy can achieve rapid recovery of brain and reduce the recurrence rate of chronic sternal osteomyelitis.

【Key words】

sternal incision; sternal osteomyelitis; HBO; the acceleration of the rehabilitation surgery;