

The Pressure Point



Henderson Hall News

U.S., Thai Navy work to tackle hyperbaric treatments

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ABHAKORN HOSPITAL, SATTAHIP NAVAL BASE, Thailand (May 9, 2007) – Thai cancer patients at Sattahip Naval Base’s Abhakorn Hospital experienced the healing powers of hyperbaric oxygen therapy May 9 while Thai and U.S. military members trained together during the combined military exercise Cobra Gold 2007.

In continuing their humanitarian assistance in the Pacific region, the U.S. Navy helped its Thai counterparts im-

plement advances in hyperbaric treatments in Royal Thai Naval medical facilities.

Hyperbaric therapy is a treatment in which patients breathe pure oxygen at high pressure levels. The treatment delivers oxygen at levels two to three times greater than atmospheric pressure. When combined with other medical and surgical procedures, the treatment enhances the healing process of many treatable conditions.

The therapy helps increase the



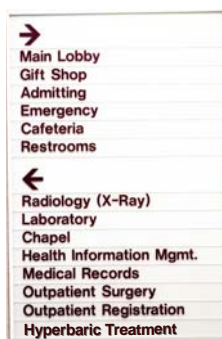
blood oxygen supply, grow new blood vessels and works in killing bacteria through high levels of oxygen.

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New Wound Care Technology Comes to Mercy Medical Center



Mercy Medical Center (701 10th St. SE, Cedar Rapids, IA) is anticipating the delivery of two hyperbaric oxygen chambers on Tuesday, May 8, sometime between 8 a.m. and 10 a.m. The hyperbaric cham-

bers will be the latest additions to the arsenal of treatments to combat wound infection at Mercy’s Wound Healing Center – and the only ones in the Cedar Rapids metro area.

The leading-edge hyperbaric oxygen chambers surround the patient with 100 percent

oxygen at above-normal atmospheric pressure. This increases the amount of oxygen in the patient’s blood and, in the case of wounds, allows red blood cells to pass more easily through the plasma into the wound to heal it from the inside out.

“Simply put, oxygen is food for your cells,” says Penny Glanz, Service Line Administrator for Surgical Services at Mercy. Glanz oversees the Wound Healing and Treatment Centers.

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Anti-Aging Treatment Hyperbaric Oxygen Therapy

by Slavica Gavric

Since the Sumerian's civilisation some 5000 years ago, people have dreamt about staying young and having eternal life. Their king Gilgamesh searched for the plant that can make him young again, if not immortal. Gilgamesh dives into the sea to pick the plant, but loses it later, while bathing, because a snake slithers up and eats it.

Medical Science follows Gilgamesh voyage with more or less success ... challenge to extend human time limit is old as human race and is the base of many serious medical research regarding man and his existence.

Anti-aging medical experts know that many illnesses connected with aging could be avoided or slowed down through optimal cell health. Hyperbaric Oxygen Therapy helps to create the optimal environment for cell essential processes.

Hyperbaric Oxygen Therapy known as HBO therapy or HBOT, has been used since 17th century for treating various medical conditions but is still not accepted by mainstream medicine—some doctors are dismissive, some are even hostile. Nevertheless many doctors do use HBOT along the side of their official medical treatment.

Side effects of oxygen use are broadly studied but practically they have been ignored. Due to such therapeutic characteristics, J. H. Jacobson opened his lecture at The First International Congress for the Use of Hyperbaric Oxygen (Amsterdam, 1963.), by words:

"The use of oxygen under pressure higher than atmospheric, represents a progress which, by importance, may be measured by introduction of blood transfusion and antibiotics in the treatment."

Hyperbaric Medicine, HBOT, is based on only one medicament: the pure oxygen, breathed under the pressure higher than atmospheric, in special equipment - hyperbaric chambers. The origin of the most deceases (or their consequence) is a lack of oxygen: hypoxia or anoxia.

Hyperbaric oxygenation (HBOT), if it is used at the right moment, stops the suffering of cells, tissues and organism in hypoxia or anoxia, leading to the recovery, regeneration and complete restitution if destruction already took a place. The main functions of human system, is to deliver oxygen through blood to all parts of the body. The heart of healthy human pumps daily 8 000 lit. of blood, and the body consumes 368 lit. of oxygen. The highest consumers of oxygen in human body are digestive system, brain tissue, muscles, etc.

We live in a toxic world today – the air we breathe, the food we eat, environmental contamination, stress, depression, alcohol, cigarettes. The latest scientific research suggests that even degenerative diseases do not occur because we get older, but because the lifestyle we follow does not provide optimal conditions for us to blossom.

Most of what is called aging – from sagging skin and falling hormone levels to raised cholesterol and blood pressure – is premature and preventable. Many of today's illnesses as well as premature aging

are caused by lack of oxygen.

The body accumulates a certain amount of toxic waste from food. When food is metabolized and broken down in the body, it leaves certain residues, which give way to either alkaline or acidic potentials of pH. These residues appear to most strongly influence body pH levels and can lead to serious health problems, weight gain, poor athletic performance, low energy levels and premature aging if continuously too acidic or too alkaline.

Without enough oxygen, human body does not function properly and it cannot get rid of free radicals, uric acid, fungal and bacterial infections. When the pH of

the body becomes too acidic it results in tiredness, stress, fatigue, excess weight, poor digestion, aches and pains, and disorders that are even more serious. The body becomes imbalanced and overly acidic because of eating too many acidifying foods like processed sugar, meats, dairy, coffee, alcohol, etc... As the body becomes more and more acidic,

bad bacteria, yeasts and other microforms proliferate in the body.

The body uses many systems in order to buffer acids including breath, mineral reserves, and fat. HBOT helps reduce acidic build-up and rebalance pH by buffering these residues and removing them from the body, helps the cleansing and repair of tissues, helps maintain proper insulin production and use. Hyperbaric chambers assist the body in helping itself and in getting rid of all harmful toxins within.

HBOT is very successful in cosmetic and spa treatments, such as rejuvenation, anti-aging,

**“Hyperbaric Oxygen
Therapy known as
HBO therapy or
HBOT, has been used
since 17th century for
treating various
medical conditions”**

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Neuroprotective effect of hyperbaric oxygen therapy following experimental brain contusion

Neuroprotektiver Effekt der hyperbaren Sauerstofftherapie auf experimentelle Hirnkontusionen C. Voigt - Klinik für Neurochirurgie, Universität Leipzig A. Foerschler - Klinik für Radiologie, Universität Leipzig M. Jaeger - Klinik für Neurochirurgie, Universität Leipzig J. Meixensberger - Klinik für Neurochirurgie, Universität Leipzig L. Küppers-Tiedt - Klinik für Neurologie, Universität Leipzig M. U. Schuhmann - Klinik für Neurochirurgie, Universität Leipzig

Text Objective: Previous experimental research showed a positive effect of hyperbaric oxygen therapy (HBO) on infarct size in models of focal brain ischemia. In this pilot study we evaluated the effect of HBO on experimental brain contusions in rats using MR imaging. Clinical TBI studies from the last 15 years had repeatedly reported a possible clinical benefit from HBO therapy.

Methods: 10 SD rats were investigated 24h and 72h after Controlled Cortical Impact injury. 5 rats were

treated with 100% oxygen at 2.5 atmospheres absolute, 5 were kept at normobaric room air for 60 min, beginning 1h after CCI. MRI scanning (Philips Intera, 1mm slice, T2, DWI) was performed 24h and 72h after injury in all animals. Lesion size was determined in T2 weighted MRI scans. The relative change of ADC values in the area of contusion was determined in comparison to the contralateral side.

Results: Lesion volume in T2 images decreased in the HBO animals within 24h (63.1±16.5 mm³ vs. 87.4±13.8 mm³, p<0.05). This decrease in contusion size continued in HBO animals till 72h, while there was a trend to even larger contusions in controls at this time (46.8±17.8 mm³ vs. 92.5±13.1 mm³, p<0.01).

In addition, T2 hyperintensity within the contusion area was clearly milder in the treatment group. This was reflected in ADC mapping. The mean relative ADC increase at 24h of 26.8±2.3% in controls, was strongly attenuated after HBO ther-

apy. 3 animals even showed a decrease in ADC values, resulting in a mean relative ADC change of 2.3±12.2% (p<0.01). 72h after the HBO, induced attenuation of relative ADC values was less compared to 24h, however still significantly lower than in controls 10.1±14.8% vs. 32.8±11.2%, p<0.02).

Conclusions: A 60-minute exposure to hyperbaric oxygen starting 1h after controlled cortical impact injury significantly attenuated the induced lesion size and the relative increase of ADC values in the contused area.

Thus, HBO after trauma seems to have neuroprotective effects on contused brain and its penumbra as previously observed in models of focal brain ischemia. The effect of HBO in ischemia is thought to be mediated through improved oxygen supply to the tissue at risk, increased BBB integrity, attenuated vascular basal lamina degradation, down regulation of COX-2, reduced excitotoxicity, alterations in inflammation and apoptotic regulators affecting late neuronal damage.

Further research has to clarify the role of HBO and the mechanisms of neuroprotection after traumatic brain injury.

(Continued from page 1) **US, Thai Navy**

Patients receiving this treatment are placed inside a large metal cylinder where pressure is increased enabling the healing process.

Some of the recent U.S. advances include limiting the amount of time patients spend in these giant pressurized tubes. In the past, patients spent up to 36 hours in the chamber. U.S. Navy researchers found this dangerous and suggested decreasing the amount of time to no more than 22 hours inside the chamber per treatment.

This advancement has substantially improved the way Thai medical personnel use hyperbaric therapy, according to Royal Thai Navy Capt. Kajit Autsaneesawat, doctor of underwater medicine at the hospital.

The hyperbaric chamber at Abhakorn is one of three official treatment facilities in Thailand, according to Royal Thai Navy Lt. Cmdr. Doo Nitran, Underwater Treatment Division commander. It is used quite extensively for its many health benefits.

“Our department is on call all the time,” Nitran said. “We are open 24 hours a day, seven days a week.”

Hyperbaric treatment, which is also used to treat decompression sickness, is vital technology in Thailand, a country with a vast diving industry.

“...hyperbaric therapy could potentially be used to treat military members during exercises involving amphibious operations such as Cobra Gold”

According to an article written by the Thai Tourism Authority, Thailand has one of the world’s more frequented dive destinations with more than 550,000 diving tourists a year.

Royal Thai Navy Chief Petty Officer 1st Class Cholchai Chaiprasitt, a

hyperbaric chamber nurse, said hyperbaric therapy could potentially be used to treat military members during exercises involving amphibious operations such as Cobra Gold.

“This treatment is important to the public and the military,” Chaiprasitt said. “I am happy that we can improve it.”



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Similar but not the same:

normobaric and hyperbaric pulmonary oxygen toxicity--the role of nitric oxide

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ABSTRACT: Pulmonary manifestations of oxygen toxicity were studied and quantified in rats breathing greater than 98% O₂ at 1, 1.5, 2, 2.5 and 3 ATA to test our hypothesis that different patterns of pulmonary injury would emerge, reflecting a role for CNS excitation by hyperbaric oxygen.

At 1.5 ATA and below, the well-recognized pattern of diffuse pulmonary damage developed slowly with an extensive inflammatory response and destruction of the alveolar-capillary barrier leading to edema, impaired gas exchange, respiratory failure and death; the severity of these effects increased with time over the 56 h period of observation. At higher inspired O₂ pressures, 2 to 3 ATA, pulmonary injury was greatly accelerated but less inflammatory in character, and events in the brain were a prelude to a distinct lung pathology. The CNS-mediated component of this lung injury could be attenuated by selective inhibition of neuronal nitric oxide synthase (nNOS) or by unilateral transection of the vagus nerve. We propose that extrapulmonary, neurogenic events predominate in the pathogenesis of acute pulmonary oxygen toxicity in hyperbaric oxygenation, as nNOS activity drives lung injury by modulating the output of central autonomic pathways.

The Breast Implant



Scuba Diving Connection

By Trev Albinez

Although it may seem harmless at first, there is much danger to be had when speaking of the breast implants scuba diving connection. Many people don't immediately recognize the danger of breast implants when placed deep within water with hundreds of pounds of pressure applied to them . However, they have the potential to cause severe harm.

If you are interested in scuba diving but have breast implants, it is imperative that you study and com-

pletely understand what the breast implant--scuba diving connection may be and what precautions, if any, you can take to protect yourself and ensure a healthy and enjoyable dive!

Breast Implant Scuba Diving Study

There have been several tests conducted to show the potential hazards of the breast implant scuba diving connection. However, the type of materials used in breast implants can range vastly and this study is strictly pertaining to the silicone, saline/silicone implants only.

With that said, the breast implant scuba diving study began by acquiring several breast implants and inserting them in a hyperbaric chamber to observe the results. Before disclosing the results of this specific test it is imperative to recognize that these were con-

ducted outside of a living body and there is quite a difference between being out in the open and being within a body that is sustaining many pounds of pressure from the water directly over the head.

The first major observation in the breast implant--scuba diving study was that the bubbles in the implants grew considerably, in fact, up to four per cent! It is important to note that they did not grow large enough to rupture the breast implants and the bubbles worked themselves out after a period of time in the hyperbaric chamber.

“The first major observation... the bubbles in the implants grew considerably, in fact, up to four per cent!”

(Continued on page 5)



(Continued from page 4) Breast Implant



The silicone implant has become a popular choice despite controversy

Most people don't realize when understanding the breast implant—scuba diving connection that silicone is heavier than water and when implanted within the walls of a human being and can potentially cause an alteration in buoyancy. It goes without saying that the larger the breast implants, the more of a factor they play in the breast implant—scuba diving connection.

“...the larger the breast implants, the more of a factor they play in the breast implant—scuba diving connection.”

In closing it is imperative to note that if you have breast implants and are contemplating taking up scuba diving, it is essential that you visit your doctor and get professional guidance as to how you may be able to overcome these issues to ensure a safe dive.

essential that you visit your doctor and get professional guidance as to how you may be able to overcome these issues to ensure a safe dive.

(Continued from page 1) New Wound Care Technology at Mercy Medical

Approximately five million Americans suffer from chronic open sores that can become seriously infected, gangrenous and, in some cases, require amputation. Most complications are a result of limited blood flow to the wound area, which prevents healing. Hyperbaric oxygen treatments increase circulation and encourage growth of healthy tissue.

Jeffrey Clark, MD, Linn County Anesthesiologists, PC, is medical director of Mercy's Wound Healing Center. He and a team of area physicians will monitor patients who are treated with the new technology, which is done on an outpatient basis.

“Hyperbaric oxygen therapy offers the possibility of healing chronic wounds that have, in the past, been unresponsive to more traditional therapy,” says Clark. “We are very optimistic about the potential benefits to patients from this technology.”

Each hyperbaric chamber is approximately the same size as a tanning bed. Featuring glass tops and electronic ports, the units al-



Monoplace chambers allow for single person therapy

low patients access to television and music. A speaker system also allows patients to converse with others outside the chamber.

Unlike much larger chambers where as many as six patients sit alongside each other wearing oxygen hoods, these chambers offer individual privacy and comfort. Patients receive daily treatment for 20-40 days, depending upon the type of wound and rate of healing.

Types of wounds frequently requiring additional care include: diabetic skin sores, pressure sores, radiation necrosis, vessel disease wounds, surgery incisions, spinal injury wounds and chemical wounds.

(Continued from page 2) Anti-Aging Tx



weight loss, skin toning, banishing cellulite, wrinkles reduction, detox, and stimulation of the immune system, as well as for longevity. Skin disorders such as eczema, psoriasis, rosacea, or proper vascularization of tissue flaps, fat grafts, tissue grafts, show heightened healing, especially after any surgery. Other perks include increased collagenation, increased chances of hair follicle growth after re-implantation, and help with the digestive tract — increased nutrient absorption, allergy and IBS resolution and numerous other conditions.

Oxygen deficiency creates dirty and toxic blood and fluids within the

body. Cancer is a build up of toxins within the body. Cellulite, skin disorders, food intolerance, etc, also indicate an imbalance of toxins. No healing can begin until these toxins are removed from the body.

The central therapeutic problem in the origin of many diseases, injuries, and intoxications is hypoxia (reduced partial pressure of oxygen in tissues) or anoxia (complete lack of oxygen in tissues). The struggle against hypoxia is the struggle for the life of the cell, tissue or organism in whole. HBOT effectively increases level of anti-oxidative protection of the body, increasing production of superoxide dismutase, catalase and peroxidase.

“The central therapeutic problem in the origin of many diseases, injuries, and intoxications is hypoxia”

In that way, HBO decreases mutation of chromosomes, slows the process of growing old and has anti-carcinogenic and anti-stress effects. If toxins are present within the body, oxygen and the body's "food supply" cannot efficiently reach cells to supply needed nutrients, nor can the cells function properly.

So far, the only medically documented method for increasing oxygen in the skin, and thus nourishing it and protecting it from premature aging, is by the use of hyperbaric oxygen chambers. Today's hectically-paced lifestyle requires more than just the essentials. With Hyperbaric options, you will be glad to have all the help you can get.



Neurobiological effects of intraventricular propionic acid in rats:

Possible role of short chain fatty acids on the pathogenesis and characteristics of autism spectrum disorders

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Abstract

Clinical observations suggest that certain gut and dietary factors may transiently worsen symptoms in autism spectrum disorders (ASD), epilepsy and some inheritable metabolic disorders. Propionic acid (PPA) is a short chain fatty acid and an important intermediate of cellular metabolism. PPA is also a by-product of a sub-population of human gut enterobacteria and is a common food preservative. We examined the behavioural, electrophysiological, neuropathological, and biochemical effects of treatment with PPA and related compounds in adult rats.

Intraventricular infusions of PPA produced reversible repetitive dystonic behaviours, hyperactivity, turning behaviour, retropulsion, caudate spiking, and the progressive development of limbic kindled seizures, suggesting that this compound has central effects. Biochemical analyses of brain homogenates from PPA treated rats showed an increase in oxidative stress markers (e.g., lipid peroxidation and protein carbonylation) and glutathione S-transferase activity coupled with a decrease in glutathione and glutathione peroxidase activity. Neurohistological examinations of hippocampus and adjacent white matter

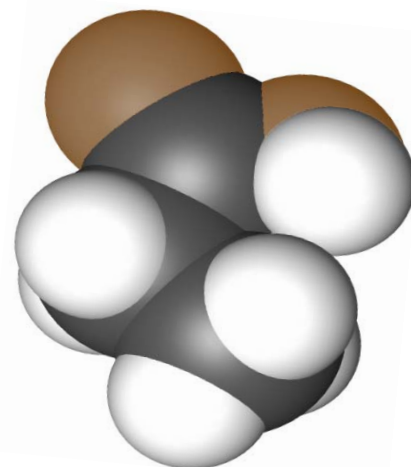
(external capsule) of PPA treated rats revealed increased reactive astrogliosis (GFAP-gial fibrillary acidic protein—immunoreactivity) and activated microglia (CD68 immunoreactivity) suggestive of a neuroinflammatory process. This was coupled with a lack of cytotoxicity (cell counts, cleaved caspase 3 immunoreactivity), and an increase in phosphorylated CREB (cellular response element binding protein) immunoreactivity. We propose that some types of autism may be partial forms of genetically inherited or acquired disorders involving altered PPA metabolism. Thus, intraventricular administration of PPA in rats may provide a means to model some aspects of human ASD in rats.

Keywords: *Locomotor activity; Seizures; Dystonia; Kindling; Animal model; Oxidative stress; Neuroinflammation; Glutathione; Clostridia*

Excerpts from this paper:

1.5. Propionic acid (PPA)— a possible environmental factor in autism?

Propionic acid (PPA) is an intermediary in cellular fatty acid metabolism found in high



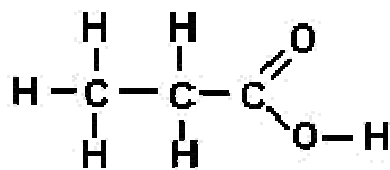
Propionic Acid Molecule

“Intraventricular infusions of PPA produced reversible repetitive dystonic behaviours, hyperactivity, turning behaviour, retropulsion, caudate spiking, and the progressive development of limbic kindled seizures”

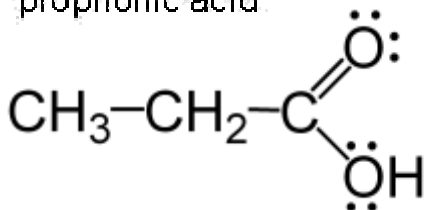
levels in the gut, along with a number of other short chain fatty acids, such as acetate and butyrate, each of which are a major metabolic end product of enteric bacteria [81]. In addition to its endogenous synthesis from amino and fatty acids [165], PPA is also present naturally in a variety of foodstuffs [187] and is commonly used as a food preservative that is added to refined wheat and dairy products [22].



PPA may play a role in the behavioural, neuropathological and biochemical abnormalities observed in autism. There are a series of inherited and acquired conditions which lead to



propionic acid



elevations of PPA and other short chain fatty acids and these are related to developmental delay, seizure disorder and gastrointestinal symptoms, resembling some aspects of ASD [27,173]. Thus, PPA may be a putative link between dietary or enterobacterially derived metabolites along with genetic predisposition, and subsequent features of ASD.

Being a weak organic acid, PPA exists in ionized and non-ionized forms at physiological pH allowing it to readily cross lipid membranes, including the gut-blood and blood-brain barriers [86]. In addition, PPA and related short chain fatty acids are taken up by monocarboxylate receptors in the gut lumen [163] and cerebrovascular endothelium [13], as well as neurons and glia [101,127] where they are thought to comprise a major energy source in brain metabolism, particularly during early brain development [136].

PPA has a number of direct effects on gastrointestinal physiology. Along with acetate and butyrate, PPA is known

to reduce gastric motility and increase the frequency of contractions, presumably via a reflex that involves direct contact of these short chain fatty acids with the terminal ileum [51]. In addition, PPA increases contraction of colonic smooth muscle [103], dilates colonic arteries [108], activates mast cells [85] and increases the release of serotonin from gut enterochromaffin cells [104]. Thus PPA is in a position to interfere with normal gastrointes-

tinal peristaltic activity and cause inflammation that is to some degree reminiscent of the gastrointestinal dysfunction observed in some patients with ASD [76].

The manner in which increased systemic PPA levels may influence the central nervous system are unknown. In vitro and animal studies suggest that increased levels of PPA affect diverse processes, including Na⁺, K⁺-ATPase activity [183], NMDA receptor activity [57], cytoskeletal phosphorylation [55], intracellular calcium levels [110], scavenging of reactive oxygen and nitrogen species [10,81], and modulation of gap junctions [143].

Increased PPA levels may interfere with overall cellular metabolism. One of the mechanisms by which this might occur is via the uncoupling of mitochondrial function, via direct inhibition of oxidative phosphorylation [20]. Other effects could include sequestration of carnitine [19] and increasing the levels of propionyl coenzyme A levels which could result in an inhibition of short chain fatty acid oxidation. Ele-

vated PPA could also produce sensitivity to oxidative stress which could result in an increase in damage caused by other environmental toxic factors (e.g., hydrocarbons, metals) or infectious agents [173].

Elevated PPA may also modulate immune function by stimulating the release of pro-inflammatory cytokines such as interferon (IFN)-gamma [39]. This immune system modulation may also occur via the direct activation of G-protein coupled receptors specific to short-chain fatty acids on polymorphonuclear leukocytes and neutrophils [24,92]. Activation of these receptors leads to alterations in intracellular calcium levels and cellular motility [24] which may promote the migration of immune cells to areas, such as the digestive tract, where PPA levels are high. However, it is unknown whether a similar immune system activation by PPA occurs in the CNS. Evidence from in vitro studies suggest that a variety of cells in the gut [58], the immune system [24], and the CNS [143] can concentrate PPA and other weak organic acids leading to intracellular acidification, a phenomena which can be exacerbated with additional minor reductions of pH in the extracellular environment [86]. This may raise the possibility that in clinical conditions of elevated PPA, serum levels might not be reflective of intracellular PPA levels.

“...PPA is also present naturally in a variety of foodstuffs and is commonly used as a food preservative that is added to refined wheat and dairy products .”

(Continued on page 8)



(Continued from page 7) PPA and Autism

One interesting effect of PPA is its ability to reversibly reduce intercellular electrotonic coupling via the closure of gap junctions, presumably by inducing intracellular acidification [67,143]. Gap junctions are intercellular channels composed of connexin proteins which are gated by a number of factors that are elevated by PPA including dopamine [142,146,172], calcium [130], nitric oxide [114] and cytokines [87]. Gap junctional coupling is integral for the synchronization of neural electrical activity within discrete functional groups [93], and this coupling is more extensive during early brain circuit formation and development [127]. In addition, gap junctions are extensive between glial cells forming a functional neuroprotective syncytium [2,129,140] which protects neurons during periods of increased metabolic stress by the uptake and intercellular diffusion of glutamate and potassium.

Gap junctional communication is involved in neurotransmission in those areas implicated in seizure development and movement disorder, including the basal ganglia [119], prefrontal cortex [142], nucleus accumbens [120] and the hippocampus [107,142]. Intrastratial injections of known gap junction blocking agents, such as carbenoxelone and anandamide, produce stereotypical movements, increase locomotion and disruption of motor sequencing in rodents [107]. Additional studies of gap junction knockout mice show abnormal brain development [68], exaggerated responses to neurotoxic insults [111], and abnormal behaviour [66].

1.6. PPA and enteric bacteria

The human digestive tract is host to a wide variety of intestinal bacterial flora, both harmful and protective, that produce a number of metabolic products capable of entering the systemic circulation in both normal and pathological conditions [184]. Many of these bacteria produce a number of short chain fatty acids, such as acetate, butyrate, and PPA, via the breakdown of carbohydrates, and amino acids [52].

Of particular interest are the Clostridia, a family of heterogeneous anaerobic, spore forming Gram-positive rods. Clostridia are major gut colonizers in early life and many of which are producers of PPA and other short chain fatty acids [159]. *Clostridium difficile* is known to be a major cause of severe gastroenterological diseases such as pseudomembranous colitis, but may also be a major cause of antibiotic associated diarrhoea, both pre- and post-natally [61]. This pathogen is known to produce an enterotoxin A, primarily responsible for gastrointestinal symptoms through mucosal damage and lymphocyte infiltration, and cytotoxin B. However, the exact mechanism by which this gut pathology is produced is unknown [61]. Antibiotic resistant clostridial strains play a role in a wide variety of hospital and community acquired infections [102] in adult patients, but their role in paediatric diarrhoea related to antibiotic treatment has not been extensively studied [61]. Spore forming anaerobes and microaerophilic bacteria, particularly from clostridial species, have been shown to be elevated in late-onset autistic children but absent in controls [64]. As well, PCR analyses of stool samples from patients

with regressive autism have revealed increases in clostridial species including *C. difficile* [157]. The eradication of the pathogen with oral vancomycin treatment has improved symptoms in some patients [157].

PPA is also produced by propionibacteria of the intestinal tract, largely from bovine sources [81], as well from endogenous bacteria in skin [189] and oral mucosa [18]. It is intriguing to speculate about the possible interaction of both environmental and genetic factors which could increase PPA over the developmental time span and play a potential role in the development or exacerbation of autism or other neurodevelopmental disorders.

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Short-term benefit from oral vancomycin treatment of regressive-onset autism



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“Improvement in 8 of 10 children... results indicate that a possible gut flora-brain connection warrants further investigation...”

To help test this hypothesis, 11 children with regressive-onset autism were recruited for an intervention trial using a minimally absorbed oral antibiotic. Entry criteria included antecedent broad-

spectrum antimicrobial exposure followed by chronic persistent diarrhea, deterioration of previously acquired skills, and then autistic features.

Short-term improvement was noted using multiple pre- and post-therapy evaluations. These included coded, paired videotapes

scored by a clinical psychologist blinded to treatment status; these noted improvement in 8 of 10 children studied. Unfortunately, these gains had largely waned at follow-up.

Although the protocol used is not suggested as useful therapy, these results indicate that a possible gut flora-brain connection warrants further investigation, as it might lead to greater pathophysiological insight and meaningful prevention or treatment in a subset of children with autism.

Abstract: In most cases symptoms of autism begin in early infancy. However, a subset of children appears to develop normally until a clear deterioration is observed. Many parents of children with "regressive"-onset autism have noted antecedent antibiotic exposure followed by chronic diarrhea. We speculated that, in a subgroup of children, disruption of indigenous gut flora might promote colonization by one or more neurotoxin-producing bacteria, contributing, at least in part, to their autistic symptomatology.

[Vancomycin is a broad-spectrum antibiotic and often used after treatment with other antibiotics have failed. It acts by inhibiting cell wall synthesis in Gram-positive bacteria.]

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Microbes and You: NORMAL FLORA

By David Oliver, SciCreativeQtrly

Microbes are everywhere.

They populate the air, the water, the soil, and have even evolved intimate relationships with plants and animals. Without microbes, life on earth would cease. This is due mainly to the essential roles microbes play in the systems that support life on earth, such as nutrient cycling and photosynthesis. Further, the physiology, nutrition and protection of plants and animals (including humans) is dependent on various relationships with microbes. And as we will see the relationships between microbes and humans relationships are key factors that determine whether or not we live healthy lives.

Microbes and You

You are covered in microorganisms! In fact, there are approximately 10 times as many prokaryotic cells (mainly bacteria) associated with your body than there are eukaryotic cells, but this is a good thing.

Microbes that colonize the human body during birth or shortly thereafter, remaining throughout life, are referred to as normal flora [1-2]. Normal flora can be found in many sites of the human body including the skin (especially the moist areas, such as the groin and between the toes), respiratory tract (particularly the nose), urinary tract, and the digestive tract (primarily the mouth and the colon). On the other hand, areas of the body such as the brain, the circulatory system and the lungs are intended to remain sterile (microbe free).

A Closer Look:

Braving Stomach Acid

What kind of organism would live in a highly acidic (pH 1-2) environment like the stomach? Not surprising there aren't many organisms that have adapted to life in this environment. One organism that has been discovered living in the human stomach is the Gram negative bacterium called *Helicobacter pylori* [4]. How can it survive? Well, it creates a less acidic microenvironment. The bacteria achieve this by burrowing into the stomach's mucosal lining to a depth where the pH is essentially neutral. In addition, *H. pylori* produce an enzyme called *urease* to convert urea produced by the stomach into ammonia and carbon dioxide.

Small Intestine vs. the Colon

Compared to the stomach, the small intestine is a relatively hospitable environment [5]. However, the small intestine presents microbes with a new challenge—high flow rates. This makes it difficult for bacteria to colonize the small intestine because they get washed out very quickly. As a result the concentration of bacteria in the small intestine remains relatively low (106 bacteria per ml) and human enzymes carry out most of the digestion processes.

Minimizing the concentration of bacteria in the small intestine may be a strategy that our bodies have

Figure 1: Location of normal microbial flora. Each of these areas of the body contain their own microenvironments and various inhabitants of microbes.

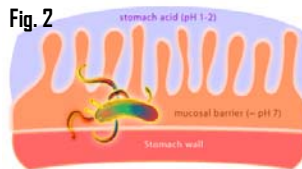
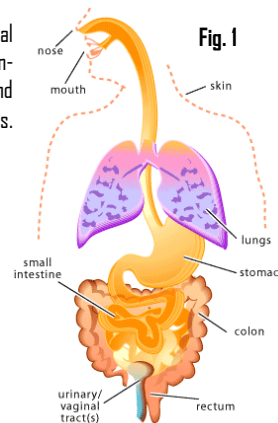
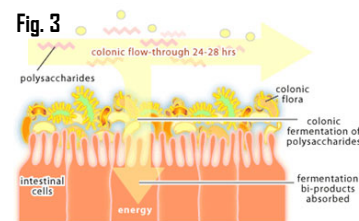


Figure 2: *H. pylori* creates its own microenvironment by burrowing into the mucosal lining of the stomach. Within the lining, the microbe is then able to avoid pH levels that would normally kill it. Here, it may also produce ulcers.

Figure 3: A Colonic Habitant. Microbial flora within the colon are able to digest polysaccharides that float by, which would otherwise be indigestible.



adapted in order to avoid microbial competition for high value nutrients such as simple sugars and proteins.

In the colon, things slow down. While it takes about 3-5 hours for food to move through the small intestine, it takes 24-48 hours for food to travel through the colon. This slower flow rate gives bacteria in the colon time to reproduce so that they reach very high concentrations (10¹²-10¹³ bacteria per ml). Bacteria packed into the lumen account for about 35-50% of the colon contents and for around 2 lbs of total body weight in an adult. The colon is a holding tank for bacteria that participate in the end stages of food digestion. For it is here that bacteria are presented with polysaccharides that cannot be broken down by human enzymes.

The process of polysaccharide degradation in the colon is referred to as colonic fermentation. These polysaccharides are derived from plant material (eg. cellulose, xylan and pectin) and from human cells (eg. the polysaccharides that glue intestinal cells together) and are readily degraded by colonic bacteria. Polysaccharide fermentation results in the production of acetate, butyrate and propionate, which are used as a source of carbon and energy by mucosal cells of the colon. Thus, the colon can be considered an organ of digestion where bacteria do the majority of the work.

In the developed world, where nutrients are plentiful, colonic fermentation is not essential for survival. However, in areas where diets are high in plant polysaccharides and easily digestible nutrients are scarce, colonic fermentation could mean the difference between life and death. There is also evidence that *E. coli* within the colon produce vitamin K, which the human body requires for the process of blood clotting. The colon is a very complex microbial environment that we are only beginning to understand.

(Continued on page 12)



"Mundo vitam dare"



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(Continued from page 11) Microbes and You: Normal Flora

Bringing it All Together

1. Bacteria perform physiological, nutritional and protective functions in the human body.
2. Maintaining a balance is crucial. Normal flora consists of communities of bacteria that function as microbial ecosystems. If these ecosystems are disrupted the consequences can be unpredictable. *Antibiotics, tissue damage, medical procedures, changes in diet, and the introduction of new pathogens are examples of changes that can affect your normal flora.*
3. We are only beginning to appreciate the complexity and function of normal flora in the human body. Our understanding of microbial communities has been limited by our ability to culture microbes in the laboratory environment. It is thought that less than 1% of bacteria will grow on standard laboratory media. That means that we have yet to explore greater than 99% the microbial world. Today, new technologies such as the polymerase chain reaction (PCR), high-throughput DNA sequencing and DNA microarrays are starting

to provide glimpses into these microbial ecosystems.

Researchers have suggested that it is now time to embark on a “second human genome project [6]” where the genomic sequences of the microbes making up our normal flora are determined. Advancing our understanding of normal flora will provide us with fundamental information about who we are.

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