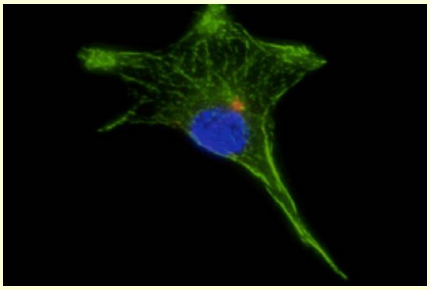
UCDAVIS NEWSLETTER

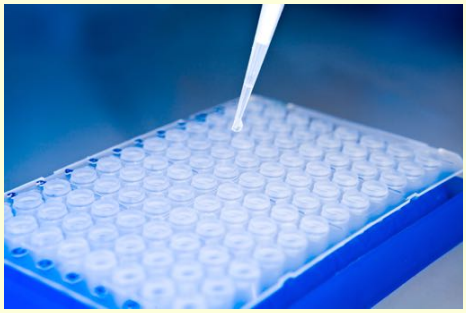
CENTER FOR VOICE AND SWALLOWING

FDA Approves Stem Cell Clinical Trial for Tongue Dysphagia

The US Food and Drug Administration has granted approval for Center for Voice and Swallowing clinicians to proceed with a Phase 1 open label clinical trial evaluating the safety of autologous muscle derived stem cells for patients with dysphagia secondary to tongue injury. This first-in-human clinical trial culminates 5 years of research dedicated to improving the lives of patients with profound oropharyngeal dysphagia.



Preliminary research suggests that the injection of autologous myoblasts (muscle stem cells) is safe and may be effective in improving the strength of the tongue. The FDA has approved investigation into the safety of treatment in 20 patients with swallowing dysfunction secondary to chemotherapy and/or radiation therapy for head and neck cancer.

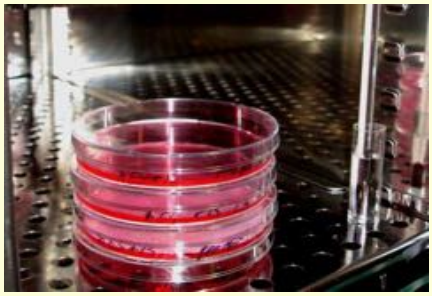


Patients enrolled in the trial will have a small biopsy taken from the muscle of the lateral thigh. The biopsy will be transferred to the lab at Cook Myosyte and 150 - 300 million myoblasts will be cultivated from the specimen. This process takes approximately 2 weeks.

The cells will then be transferred to the Center for Voice and Swallowing where they will be injected into the patient's tongue. Study participants will be monitored for safety, stem cell integration, and improvement in swallowing function.

The primary outcome for the investigation is patient safety. Secondary outcome measures include tongue strength, penetration aspiration scale (PAS), dysphagia symptoms (EAT10), and functional oral intake (FOIS). Patients will be monitored periodically for safety and efficacy throughout the two-year study period.

Dysphagia in head and neck cancer survivors is complex and involves more than just tongue dysfunction. This study, however, is an exciting step in our relentless mission to improve swallowing and quality of life in persons with profound dysphagia.



DYSPHAGIA IN THE OBESE

Obesity is one of the greatest threats to the health of our nation. Over one-third of the United States population meet criteria for obesity. In a review conducted by Center for Voice and Swallowing researchers, 23.8% of people suffering from dysphagia were obese. This is no different from the 24% prevalence of obesity in the general California population. Our team's research suggests that dysphagic patients with obesity are slightly younger and more likely female than non-obese persons with dysphagia. Dysphagia in obese patients is more likely caused by acid reflux and less likely caused by head and neck cancer and progressive neurologic disease.

CHRONIC COUGH IS THE MOST COMMON SYMPTOM IN USA

COUGH SUPPRESSION THERAPY TO THE RESCUE

By Laurie Slovarp, PhD, CCC-SLP, BCS-S

Chronic cough (CC) is defined as a cough that persists more than eight weeks. It is one of the most common complaints for which patients seek medical care. The three most common causes of CC in non-smoking adults are *upper airway cough syndrome* (UACS; also commonly referred to as *postnasal drip*), gastro-esophageal or laryngo-pharyngeal reflux (GERD/LPR), and asthma. Most patients with CC are effectively treated medically; however, up to 10% of patients may not respond to typical medical treatments. Cough in these patients has traditionally been referred to as *nonspecific, unexplained, idiopathic,* or *refractory CC*.

The term ***cough hypersensitivity syndrome*** (CHS) has been proposed to describe the most likely underlying cause of this persistent cough.

There is evidence that patients with CHS have more sensory receptors and lowered sensory thresholds to cough stimulants placing them in a heightened state of arousal.

There are several common symptoms reported by patients with CHS. The most common trigger of the cough is an upper respiratory tract infection (URI) that begins with a severe cough. Although the URI resolves, a dry unproductive cough persists. Patients with CHS frequently identify specific cough stimulants such as perfume, smoke, pollution, certain air temperatures and crumbly foods. Even speaking, laughing, or a increase in rate of breathing can trigger spasmodic coughing.

Cough Suppression Therapy (CST) has evolved into a primary treatment for most patients with CC and CHS. CST is administered by a licensed speech and language pathologist and is based on "*use it or lose it*" principles of neuroplasticity. All cough is suppressible to a certain degree. By volitionally suppressing the cough over a period of time, the cough sensory threshold returns to normal and the cough stimulus diminishes.

"The less a patient coughs, the less the neural signal that elicits coughing is reinforced and eventually the airways return to normal function."

- Laurie Slovarp, PhD

Causes of Chronic Cough

- ACID REFLUX
- ALLERGIC RHINITIS
- ASTHMA
- POST-VIRAL NEUROPATHY
- EOSINOPHILIC BRONCHITIS
- COUGH HYPERSENSITIVITY
- ATYPICAL MYCOBACTERIA
- BRONCHIECTASIS
- LUNG CANCER
- PNEUMONIA
- HABITUAL COUGH

There are four primary components of CST: 1) education on CHS and cough triggers, 2) training in cough suppression and relaxation techniques, 3) instruction in vocal hygiene, and 4) psycho-educational counseling to improve internalization and cough control.

With this 4-step program, patients experience significant cough reduction in 2-4 weeks!!

By the time patients initiate CST, they have typically seen numerous physicians, had countless tests, and have failed treatment with several different medications. By employing CST earlier in the treatment algorithm, patients can often avoid unnecessary tests and medications and get back on their feet sooner!

CAN ALLERGY AND POLLUTION CAUSE CHRONIC LARYNGITIS?

Dust mites are invisible insects that hide in our pillows, blankets, carpets, drapes, and sweaters. They feed on our dead skin. Thankfully, unlike spiders, ticks, and other pests, they do not burrow into our skin, bite or transmit disease. Unfortunately, these little buggers are a major source of allergy.

Established symptoms of dust mite allergy include runny nose, nasal congestion, itchy eyes, and asthma. The effect of dust mite allergy on the larynx has not been adequately investigated. We hypothesize that dust mite allergy may be responsible for some people's chronic throat symptoms such as throat clearing and itching, intermittent hoarseness, throat pain, and the sensation of post nasal drip.

Dermatophagoides farinae
- a.k.a. -
The American House Dust Mite

Pollution is a major threat to public health. Nearly half of the United States population lives in an area with unsafe levels of environmental pollution. Risks associated with high levels of pollution include asthma and other breathing difficulties, heart disease, birth defects, and premature death. The effect of pollution on the larynx and throat symptoms has not been adequately investigated.

IS EOSINOPHILIC LARYNGITIS A DISTINCT CLINICAL ENTITY?

Eosinophilic esophagitis (EoE) is a distinct clinical entity responsible for dysphagia and food impaction in both children and adults. It is thought to be secondary to a food allergy (milk, nuts, soy, egg, meat, wheat).

Similarly, eosinophilic bronchitis (EB) is a distinct clinical entity responsible for bronchial inflammation and chronic cough. ***Eosinophilic laryngitis has not been previously described.***

Chronic laryngitis (CL) is common and costly. Symptoms include hoarseness, throat clearing, cough, globus, and excessive throat mucus. Established causes of CL include tobacco, voice abuse, and laryngopharyngeal reflux (LPR).

We hypothesized that allergy and environmental pollution may cause CL and set out to evaluate the role of allergy and pollution in the development of eosinophilic laryngitis.

Center for Voice and Swallowing Center scientists used an established animal model of CL to evaluate the

"Although pollution is a major threat to public health, the role of airborne pollution in the development of chronic laryngitis is unknown."

- Peter Belafsky, MD, PhD

effect of house dust mite allergen (HDMA) and the pollutant iron soot on the development of laryngeal eosinophilia. HDMA is an allergen ubiquitous to our environment. It is found in our carpets, drapes, and pillows. Carbon black soot is one of the most prevalent environmental airborne pollutants and is produced as a byproduct of internal combustion engines, boilers, fires, and incinerators.

In an animal model of CL, the combination of HDMA and iron soot resulted in laryngeal eosinophilia. The data supports the notion that factors other than reflux and tobacco may cause chronic laryngitis. Further investigation into eosinophilic laryngitis as a distinct clinical entity caused by exposure to environmental allergen and pollution is warranted.

THE **FEES**IBILITY OF FEES IN DOGS

Dogs suffer from profound swallowing problems. Causes of dysphagia in canines include cricopharyngeus muscle dysfunction, acid reflux disease with peptic stricture, hiatal hernia, Myasthenia Gravis, cancer and idiopathic megaesophagus. Diagnostics used to evaluate swallowing dysfunction in dogs include a clinical "bedside" examination, swallowing fluoroscopy, esophageal manometry, pH testing, and esophagoscopy.

Center for Voice and Swallowing clinicians partnered with UC Davis Veterinary Specialist Dr. Stanley Marks to evaluate the feasibility of the Flexible Endoscopic Evaluation of Swallowing (FEES) in dogs.

Six healthy large breed canines with no history of swallowing problems underwent an endoscopic swallow evaluation to evaluate safety and tolerability. The procedure was completed successfully in all animals without any adverse events. A dynamic view of the pharynx and larynx revealed normal swallowing biomechanics similar to humans. Further research is required to evaluate the ability of FEES to assist in the diagnosis and management of dogs with dysphagia.

Malnutrition Caused by Congenital Megaesophagus

DDTP - JUST WHAT THE DOCTOR ORDERED

The *Deaf and Disabled Telecommunications Program* (DDTP) is a state-mandated program of the California Public Utilities Commission (CPUC), providing Californians who are deaf or disabled with specialized telephone equipment and relay services **FREE** of charge. The California Telephone Access Program (CTAP) makes available specialized telephones, speech generating devices, specially-trained communications assistants and speech-to-speech services for people with communication disabilities.

RESOURCES

DDTP home page: http://ddtp.cpuc.ca.gov/homepage.aspx

CTAP equipment: http://www.californiaphones.org/Products-Speech.php

California Relay Service: http://ddtp.cpuc.ca.gov/relay.aspx

Speech to Speech: http://ddtp.cpuc.ca.gov/default1.aspx?id=1489

Speech Generating Devices: http://www.cpuc.ca.gov/SGD/

CRICOPHARYNGEAL WEBS ARE THE MOST UNDER-DIAGNOSED CAUSE OF DYSPHAGIA

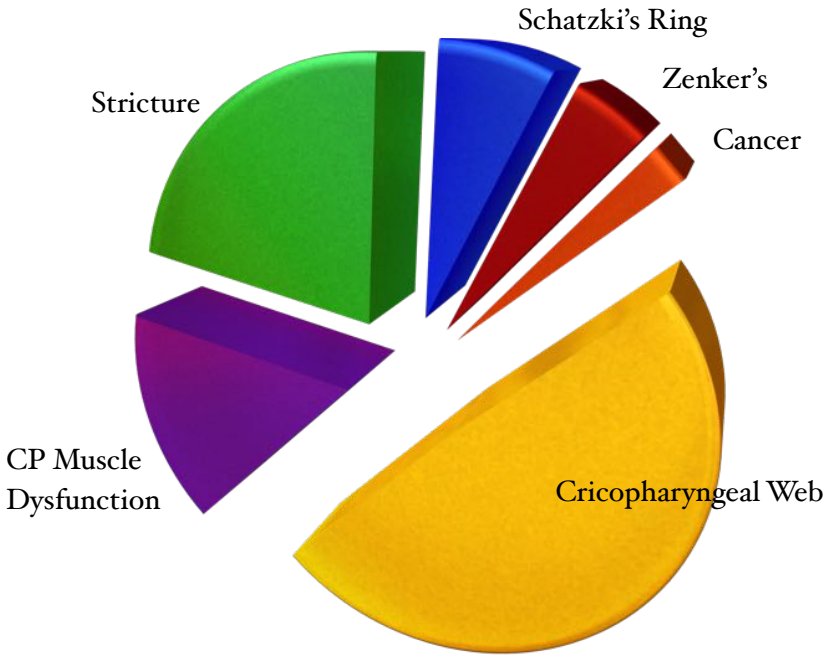
Cricopharyngeal webs (CPW) are one of the most commonly missed causes of solid food dysphagia. CPWs tether the cricopharyngeus muscle to the hypopharyngeal mucosa of the posterior aspect of the cricoid cartilage. They can be differentiated from cervical esophageal webs which are typically located 2cm distal to the CP muscle. Their etiology is unknown but a potential cause involves mucosal trauma and adhesion formation caused by the passage of food and repetitive movement of the cricoid cartilage against the cervical spine.

In a recent Center for Voice and Swallowing Center investigation, CP webs were identified in 25% of all video fluoroscopic swallow studies. They appear to be slightly more common in women and significantly more common in individuals with gastroesophageal reflux disease.

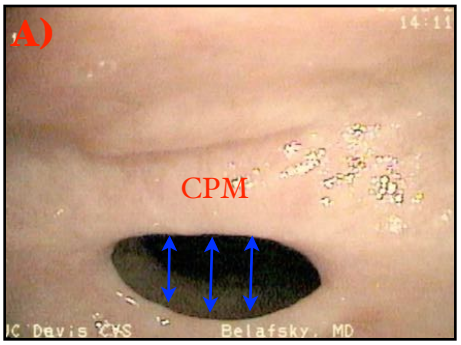
"Videofluoroscopy, the gold standard swallowing diagnostic, can significantly underestimate the degree of pharyngo-esophageal obstruction."

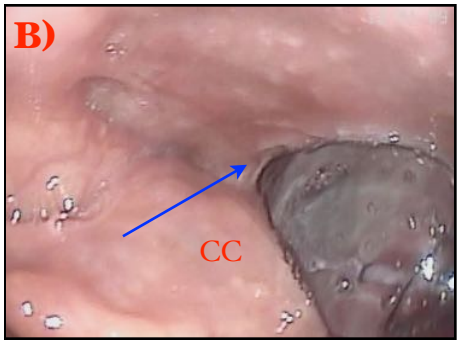
-Maggie Kuhn, MD

Although video-fluoroscopy is the gold standard diagnostic used to identify CPWs, their presence can be frequently missed and their effect on disrupting bolus flow under-appreciated. Video capture rates of 30 frames per second and high definition recording equipment with slow motion frame-by-frame analysis are necessary to reliably identify the site of obstruction.



Causes of Obstructive Dysphagia





A) CP web (blue arrows). The CP muscle (CPM) is tethered to the back of the cricoid cartilage.

B) CP web (blue arrow) best seen during dilation with a 20mm radial expansion balloon. CC = posterior cricoid cartilage.

C) CP web (blue circle) from (B) whose obstruction was grossly under-estimated on fluoroscopy.

All of us have been impacted by dysphagia and its devastating consequences. Swallowing problems account for a large percentage of death in persons with ALS, advancing age, Parkinson Disease, stroke, muscular dystrophy and head and neck cancer. We have dedicated our professional lives to improve the health and quality of life in persons affected by profound dysphagia. The status quo is not acceptable. We must work together to do better. Through passion and innovation we will make a difference in the treatment of dysphagia in our lifetime. This is our mission.

Please join us in our **EAT NOW!** campaign and support dysphagia research. *Send your philanthropic donation payable to UC Regents to ...*

UC Davis EAT NOW!
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Appointments

To schedule an appointment at the UC Davis Center for Voice and Swallowing please contact our CVS coordinator Traci Piazza at 916-734-8763 or tipiazza@ucdavis.edu.

Make a difference

We need your help. Much of our research is funded by philanthropic gifts from grateful patients. Your support will directly help the millions of individuals suffering from complex disorders of voice and swallowing worldwide. Join the movement of hope and help make a difference now. Please contact the Center for Voice and Swallowing Director of Development Sharon Schauer at 916-734-1053 or sschauer@ucdavis.edu.

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