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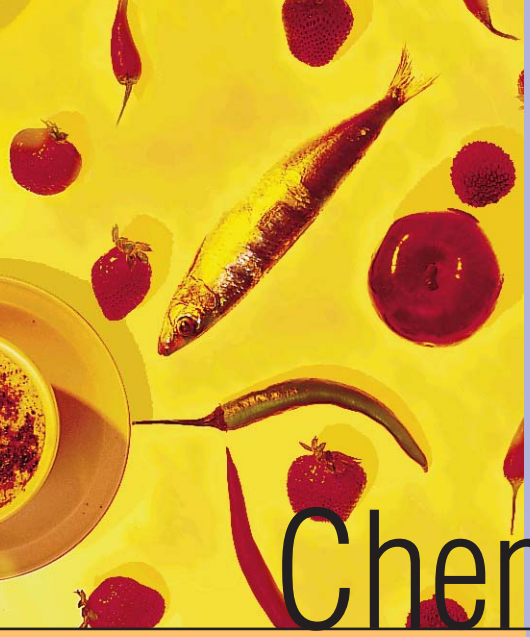

ChemoSense

Editorial

By Graham Bell
g.bell@atp.com.au

Ten Year Anniversary

This is our 40th issue of *ChemoSense*, and with it, we complete ten years of publishing news and reviews on the chemical senses. We are honoured and delighted to carry messages of celebration from Tom Scott, Gordon Shepherd, Hildegarde Heymann, Howard Moskowitz, Nobuyuki Sakai, Tim Gilbertson, Ron Devere, Wayne Silver, Wendy Parr, Isabelle Lesschaeve, Hely Tuorila and Judith Reinhard.

Sensational TRP Channels! In this issue Wayne Silver and colleagues bring to our attention the importance of TRP channels for chemo*sensation*, including forming direct gating for sour tastants, possibly underlying interactions between sweet and bitter compounds, specifying

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TRP Channels and Chemosensation

Wayne L. Silver, Paige Roe, Vajini Atukorale, Winston Li, and Bo-Shan Xiang

Department of Biology
Wake Forest University
Winston-Salem, NC, USA 27109
silver@wfu.edu

The first Transient Receptor Potential (TRP) channel was described in *Drosophila* photoreceptors in the 1970's (Minke, 1977) and cloned in 1985 (Montell et al., 1985). Since then, research on TRP channels has exploded. A quick search for "TRP channel" in Medline turned up over 1700 papers and 345 reviews published since then. As of this writing, at least 28 mammalian TRP channels have been classified into six subfamilies. TRP channels are ubiquitous and are probably found in all mammalian organs and cell types (Talavera et al., 2008A). TRP channels play a role in many diseases, including neuropathic pain, kidney disease, and the severe neurodegenerative disorder, mucolipidosis (Venkatachalam and Montell, 2007). The discovery of TRP channels has been a real boon to sensory biologists. TRP channels are involved in virtually all of our senses, including mechanoreception, photoreception, thermoreception and

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vomeronasal functions, underlying the cold sensation of menthol, and many other chemosensational functions. This article is a "must read" for our widest audience.

Of special clinical importance, for practitioner and patient, is a Flow Chart and Commentary, for diagnosis and treatment of taste and smell disorders, devised by Ron Devere. We are privileged to be first to publish this useful document.

ChemoSensory Science and its important spin-offs for medicine, is progressing in the Land Downunder, no more excitingly than at the National Centre for Adult Stem Cell Research, at Griffith University, Brisbane, led by Alan Mackay-Sim, as described succinctly in this issue.

Griffith University will be the venue for the next AACSS meeting (4-6 December, 2008) ■

ChemoSense turns TEN

CHEMOSENSE TURNS TEN

Nearly a decade ago I was traveling Down Under with my wife and son, and paid a visit to the ebullient Graham Bell in Sydney. That memorable encounter included a 14-km City-to-Surf footrace from downtown to Bondi Beach and an invitation from Graham to contribute a review to his new e-publication: *ChemoSense*. I readily complied, not yet knowing how well Graham's venture would thrive, or that my thoughts would be followed in succeeding years by those of some of our most respected colleagues.

ChemoSense is by parts a scholarly journal, newsletter, advice column, forum for discussion, and platform for commercial advertisements. It lands in my in-box, thankfully interrupting a day otherwise occupied with administrative concerns, as a colorful hybrid that captures my attention, demands my concentration, and surprises me with its nimble transitions. Graham's writing style is intellectual yet lively, radiating energy as palpably in print as its author does in life, and betraying a witty, well-educated mind.

The newsy features of *ChemoSense* give it currency. We're kept up with Australia's wine industry, and advised how to negotiate our chemical environment as our senses inevitably decline. But Graham is also an academic entrepreneur, and *ChemoSense* is his outlet, so we're rarely kept innocent about the virtues of E-Nose, his remarkable olfactometer that serves as chemical sentinel to industry, monitor of the health of farm animals, and defender against a polluted environment. Finally, the seduction: issues of *ChemoSense* seem often to end with aerials of Heron Island and its northward companions that form the archipelago outlining the Great Barrier Reef, scenes that must double the attendance at the AACSS meetings they promote.

While *ChemoSense* is fun, it's also work. The featured articles that lead the news give each issue a worth that warrants its being archived. These are thoughtful, well-documented 2500-word reviews of a quality that matches that of any tightly-refereed journal. They are complemented by Graham's accompanying précis in which he distills the main elements of the author's argument for non-specialists, or those too occupied to linger over the entire piece. The reviews now form a growing repository of knowledge of our discipline—its molecular biology, physiology, anatomy, behavior, psychophysics, clinical application and historical perspective—in about a 2 : 1 ratio of olfaction : taste, similar to the ratio of presentations at ISOT meetings.

Each issue of *ChemoSense* reaches an estimated audience of some 4000, well beyond the scope of most professional journals. Its content and style make it accessible to those beyond the academic community, and so serve our discipline by informing funding agencies and our industry partners of our achievements and worthiness of support. *ChemoSense* is an addendum to our formal scholarly portfolio, yet holds its own worth in scholarship. I have come to anticipate its quarterly arrival.

Thomas R. Scott
San Diego State University
San Diego, CA, USA
tscott@mail.sdsu.edu

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TRP Channels and Chemosensation

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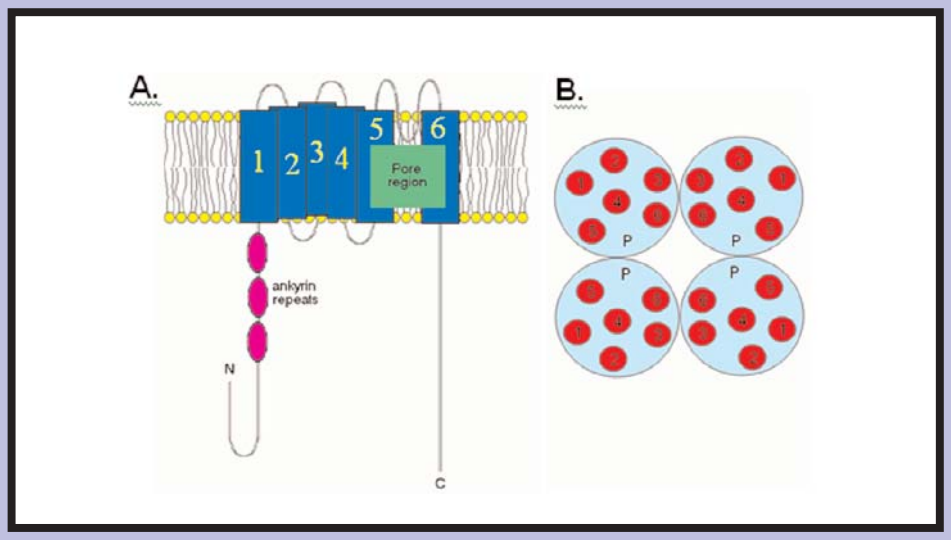

Figure 1. **Structure of generic TRP channel.** A. **Each channel consists of subunits with 6 membrane spanning regions. The pore region (P) is between region 5 and 6. The N- and C- terminals are both intracellular. Some TRP channels have one or more ankyrin repeats on their N terminals.** B. **Functional TRP channels are made up of 4 similar (homomer) or dissimilar (heteromer) subunits from the same subfamily.**

chemoreception. It is their role in chemoreception that we would like to review briefly in this article. Of the six TRP channel subfamiles, five (TRPP, TRPC, TRPM, TRPV, and TRPA) are related to some aspect of chemoreception.

Each of these five TRP channels contains six membrane spanning domains as well as a cytoplasmic C- and N-terminal domain (Figure 1). The pore loop forming the ion channel lies between the fifth and sixth transmembrane segments. All but the TRPM channels contain a number of ankyrin repeats in their intracellular N-terminals. Ankyrin repeats are repeated motifs which are found in a number of proteins and are thought to bind with other proteins or the cytoskeleton (Hoenderop et al., 2003). Ankyrin repeats in TRP channels may play a role in connecting subunits together, since most functional TRP channels contain 4 TRP subunits (Figure 1). Most TRP channels are non-selective cation channels, although some may be more selective for calcium than for other cations (Venkatachalam and Montell, 2007).

In the following brief overview of the chemical stimulation of TRP channels, we focus mainly on non-drug, natural exogenous compounds. Many of the compounds which stimulate TRP channels are found in spices and common household products. Finally, we include TRPM5 and TPRC2 because, while they may not be stimulated by exogenous chemicals, they are found in chemosensory receptor cells.

TRPP

Humans express all three of the TRPP channels found in mammals. The P stands for polycystic kidney disease, in which mutations of some of the channels play a role. Only TRPP3 channels (PKD1L3) have been implicated in chemosensation. TRPP3 channels are found in a subset of taste receptor cells and are suggested to form a functional sour receptor which was shown to respond to citric acid, HCl, and malic acid (Ishimaru et al., 2006).

TRPC

Seven mammalian TRPC channels have been reported, six of which are expressed by humans. The C stands for canonical since the TRPC channels were the first homologs of the original *Drosophila* TRP channel (Venkatachalam and Montell, 2007). Interestingly, the channel that humans do not express, TRPC2, is found in vomeronasal sensory cells in mice (Zufall et al., 2005). They are downstream of the vomeronasal receptors (VRs) and are activated by the second messenger, diacylglycerol (DAG). They are among the first DAG-gated channels reported for the mammalian nervous system. TRPC2 channels are nonspecific cation channels permeable to calcium and other small cations. TRPC2 plays a crucial role in the detection of pheromones by mammals. Indeed, knockout mice lacking TRPC2 display clear behavioral deficiencies in the regulation of sexual and social behaviors (Zufall et al., 2005). That humans do not express TRPC2 lends support to the idea that humans do not have functional vomeronasal organs. There is some evidence that TRPC6, which is also activated by DAG, is found in a subset of olfactory receptor cells and may play a role in depolarizing these cells upon stimulation with odorants (Elsaesser et al., 2005).

TRPM

There are eight mammalian TRPM channels, all of which are found in humans. The M stands for melastatin after the first TRPM channel was found in some melanomic cells and was inversely correlated with their metastatic potential (Venkatachalam and Montell, 2007). TRPM channels do not have ankyrin repeats like the other

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TRP Channels and Chemosensation

continued

TRP channels. Two of the TRPM channels play a role in chemosensation.

TRPM5 channels, like TRPC2 channels are involved in the transduction cascade of chemoreceptive cells – taste receptor cells, solitary chemoreceptor cells, and some olfactory receptor cells – and are probably responsible for the depolarizing currents that arise upon chemical stimulation of these cells. TRPM5 channels are heat activated as well as Ca^{2+} and voltage-gated. In taste receptor cells they play a significant role in the transduction of sweet, bitter, and umami tastes and contribute to the effect temperature has on taste sensations (Talavera et al., 2005). Recently, quinine was shown to inhibit TRPM5 channels in taste receptor cells, which could account for the well-known interactions between sweet and bitter compounds (Talavera et al., 2008B).

Solitary chemoreceptor cells have only recently been reported in mammals. They are modified epithelial cells found scattered throughout the nasal cavity as well as the respiratory and digestive tracts (Sbarbati and Osculati, 2005). In the nasal cavity, they are concentrated posterior to the vestibule and in the vomeronasal ducts. Many of these cells have the characteristics of individual taste cells, not the least of which is the presence of TRPM5 channels (Gulbransen et al., 2008). These cells respond to chemical stimuli, and the activation of TRPM5 channels is thought to lead to an influx of Ca^{2+} and depolarization. Interestingly, TRPM5 channels have also been found in a subset of olfactory receptor neurons (Lin et al., 2007). These receptor cells project to an area of the olfactory bulb that processes socially-relevant odorants.

TRPM8 channels were first cloned and characterized in 2002 (McKemy et al., 2002; Peier et al., 2002). These channels responded to cold and menthol. Since then many compounds have been shown to activate TRPM8 channels including eugenol, icilin, and several monterpenes (eucalyptol, geraniol, linalool, menthyl lactate, trans and cis-p-menthane-3,8-diol, l-carvone, isopulegol and hydroxy-citronellal) (Calixto et al., 2005). Stimulation of TRPM8 channels causes an increase in intracellular Ca^{2+} through voltage-dependent gating of the channel. This results in a depolarization and the generation of an action potential (Reid, 2005). TRPM8 channels are expressed in small-diameter primary sensory neurons found in the dorsal root (DRG) and trigeminal (TG) ganglia (Peier et al., 2002).

TRPV

Humans express all of the six TRPV channels found in mammals. The V stands for vanilloid, since the first TRPV channels discovered, TRPV1, responded

Agonist	Source/Function	Agonist	Source/Function
1-chloroacetophenone; (CN)	tear gas	eugenol	cloves
dimethylphenol	used in pesticides	geranial	citrus
2-chlorobenzylidene malononitrile (CS)	tear gas	geraniol	rose oil
acetylaldehyde	ripe fruits, freshly distilled spirits	gingerol	ginger
acrolein	tear gas, cigarette smoke	hydrogen peroxide	disinfectant
ally isothiocyanate	mustard oil	hydrogen sulfide	rotten eggs
allicin	garlic	hydroxy-a-sanshool	Schezuan pepper
benzyl isothiocyanate	papaya	icilin	cooling compound
bromobenzyl cyanide	tear gas	isovelleral	fungal sesquiterpine
cannabichromene	cannabinoid	methyl salicylate	oil of wintergreen
cannabigerol	cannabinoid	methyl-p-hydroxybenzoate	preservative
Carvacrol	oregano	morphanthridine	tear gas
CBD	cannabinoid	neral	citrus
chlordantoin	antifungal	nerol	bitter orange
cinnamaldehyde	cinnamon	o-Cresol	disinfectants, cleaning agents
crotonaldehyde	soybean oils, cigarette smoke	polygodial	dorrigo pepper
delta-9-tetrahydrocannabinol	cannabinoid	propofol (2,6-diisopropylphenol)	anesthetic
diallyl disulfide	garlic	THC acid	cannabinoid
dibenz[b,f][1,4]oxazepine (CR)	tear gas	thymol	thyme
ethyl bromoacetate	tear gas	WIN	cannabinoid

Table 1. Some chemicals compounds that activate TRPA1 channels For the sake of space, references for these data have been omitted. Many can be found in the reviews by Calixto et al., (2005) and Venkatachalam and Montell (2007).

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TRP Channels and Chemosensation

continued

to the vanilloid compound capsaicin (Caterina et al., 1997). TRPV2 is a heat-activated TRP channel, with no known stimulatory ligands; TRPV4 is activated by the semisynthetic phorbol ester, 4a phorbol 12,13-didecanoate (4a-PDD) (Venkatachalam and Montell, 2007). TRPV1-4 are found in DRG and TG neurons. TRPV3 channels have also been found on keratinocytes in the oral and nasal epithelia (Xu et al., 2006). They respond to carvacrol, thymol and eugenol and are suggested to play a role in nasal and oral chemesthesis. TRPV5 and TRPV6 do not respond to chemicals and are not found in neurons.

The discovery of TRPV1 began the explosion of research into TRP channels and their responses to natural compounds. TRPV1 channels respond to numerous chemical stimuli besides capsaicin. These include the vanilloids, gingerol, zingerone, capsiate, eugenol, piperine, and resiniferatoxin as well as allicin, camphor and cyclohexanone (Calixto et al, 2005; Silver et al., 2006; Venkatachalam and Montell, 2007). TRPV1 channels are also affected by low pH, warm temperatures and mechanical stimuli. Stimulation of TRPV1 in peripheral DRG and TG nerve endings leads to the influx of Na+ and Ca2+, depolarization and the release of the neuropeptides substance P and calcitonin gene-related peptide (CGRP). TRPV1 channels are thus involved in neurogenic inflammation.

TRPA

Finally, we come to the TRPA channels of which only one is found in mammals, including humans. The A is for the many ankyrin repeats that are found in this protein. TRPA1 channels are found on DRG and TG neurons and respond to the largest variety of chemicals of any of the TRP channels. TRPA1 channels appear to be expressed in a subset of neurons which also express TRPV1 (Story et al., 2003). Among the diverse chemicals that activate TRPA1 channels are the psychoactive component in marijuana, environmental irritants, and pungent compounds. A list of individual TRPA1 channel stimuli is found in Table 1.

Summary

The discovery of TRP channels has contributed significantly to our knowledge of chemosensation. TRP channels are involved in all of our chemical senses either as receptor proteins or participants in a transduction cascade. By themselves, these receptor proteins are responsible for the detection of many irritating chemicals in the environment.

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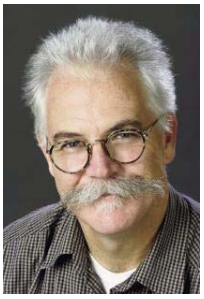
Stems Cells from Adult Olfactory Mucosa: from Naris to Nosology



Alan Mackay-Sim

National Centre for Adult Stem Cell Research
Griffith University, Brisbane, Australia 4111
a.mackay-sim@griffith.edu.au
www.griffith.edu.au/stem-cells

The National Centre for Adult Stem Cell Research was established in mid-2006 with funding from the Australian Department of Health and Ageing. In early 2008 we moved into new laboratories at Griffith University in Brisbane, Australia, and are now a group of over 50 scientists in stem cell biology, developmental biology, systems biology and bioinformatics.

Central to our work are our clinical collaborators in otorhinolaryngology, neurology and psychiatry. In 2005, we demonstrated that stem cells from human olfactory mucosa are multipotent, capable of generating neurons and glia but also many other cells and tissues of the body, either in vitro or after transplantation into the developing chick embryo (Murrell et al, 2005). Olfactory stem cells are accessible through the external naris.

Our focus now is to explore the use of olfactory stem cells for cell transplantation therapies and as cellular models of disease. We recently completed a 3 year Phase I clinical trial of olfactory ensheathing cell transplantation into the injured spinal cord in human paraplegia (Feron et al, 2005; Mackay-Sim et al, 2008). Although not using stem cells, this demonstrated the feasibility of autologous olfactory cell transplantation therapy. We are continuing our work on olfactory ensheathing cell biology and use in spinal cord injury repair in rats.

We are also investigating the use of cell therapies in Parkinson's disease and motor neuron disease. Olfactory stem cells from humans, including a patient with Parkinson's disease, proved to be therapeutic in the parkinsonian rat model, indicating the ability to generate dopaminergic neurons in vivo and in vitro (Murrell et al, 2008). Bone marrow stem cells had a small therapeutic effect after transplantation into a mouse model of motor neuron disease (Morita et al, 2008).

We are also focussing on developing cellular models of disease by obtaining patient-derived, disease-specific stem cells. The Centre now has a bank of olfactory stem cell lines from over 100 people including those with neurological conditions including Parkinson's disease, schizophrenia, motor neurons disease and mitochondrial mutation disorders. We are using a combination of gene expression profiling, proteomics, bioinformatics and functional analyses that we hope may lead to new diagnostics and new drug targets through an understanding of disease-specific alterations in key cellular pathways ■

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Taste & Smell disorders: Diagnosis & Treatment
A suggested Flow Chart

Ronald Devere, M.D.

Taste and Smell Disorders Clinic
Austin, Texas, USA 78734
www.tastesmell.com

Of all the subjects in medicine, the taste and smell system, and its disorders along with its morbidity, seems to be one of the least taught in the United States and Canada. This includes the basics in biology, and undergraduate and post-graduate medical education, including medical specialties of neurology, family practice, internal medicine, geriatrics, and even otorhinolaryngology. Even important fields such as dietary and nutritional specialties, including the private sectors of the culinary and restaurant industry have little knowledge of these disorders.

In my capacity as director of the Taste and Smell Disorders Clinic in Austin, Texas, I have had the opportunity to give many educational seminars in the last ten years to many of these groups. I am always impressed by the feedback and questions asked after a seminar and how eager and interested they are to learn about taste and smell dysfunction and treatment.

Various estimates have suggested there are five to ten million people in the United States alone who have a disorder of taste and smell. And this does not include people who are not aware they have a problem, whether from normal aging or as part of disorders like Alzheimer's disease and Parkinson's disease. It is well known that quality of life can be significantly impaired in patients with taste and smell impairment. This can range from increased safety concerns due to the inability to detect smoke, burned or spoiled food, and even chemical exposure, to weight loss and decreased appetite and a higher incident of depression, just to name a few. It also takes its toll in certain professions: fire fighters, wine tasters, chefs and cooks, and nurses who work in the newborn nursery.

To help people with taste and smell disorders we need to increase education in all of the above-mentioned disciplines. Relying on a handful of Taste and Smell specialty clinics in the country to provide the majority of clinical evaluation and treatment is grossly inadequate. I have received numerous emails and phone calls (as have others I am sure) from people suffering from a taste and smell disorder that has not been evaluated in any detail by smell or taste testing, and who have not been informed of the diagnosis or prognosis, nor offered any compensatory treatment.

I have embarked on an aggressive program of educating private practice neurologists, geriatricians, and dietitians in my hometown of Austin, Texas. Along with my food consultant, we are starting a program to educate the local restaurant associations and culinary schools about these disorders, and how certain changes in food preparation can improve the quality of life in many of our patients.

I know there are many different ways to evaluate patients with taste and smell disorders and I welcome any criticism or other ideas from any of you reading this article. In my own clinical work, I realized there was no simple guide to diagnose and treat taste and smell disorders. I thought a guide like that would be useful to the various disciplines of clinical medicine and the nutritional and dietary fields. I have always liked to use flow charts as a learning tool. With my thirteen years experience running a Taste and Smell Disorders Clinic and trying to keep up with the clinical literature of the field, I have put together a flow chart that can be most useful in evaluating patients with taste and smell disorders. I grant you it is a bit "busy", but if you look at it closely, you will find it covers the basics of the field. In my clinical practice and in the flow chart, I use the University of Pennsylvania Smell Identification Test (UPSIT) or the Brief Smell Identification Test (B-SIT) and for taste testing I use Whole Mouth or Taste Strip Test. However, *any standardized test for taste or smell can be used and easily plugged into the flow chart.*

We begin at the top center box in the flow chart with a patient complaining of a taste or smell symptom or both. This should lead to a very thorough history of the smell and taste complaints, a detailed general

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Taste & Smell disorders: Diagnosis & Treatment
A suggested Flow Chart
continued

medical history with a list of medications and length of time these medications have been used. This should be followed by appropriate medical and neurological examinations with special attention to cranial nerves V, VII, IX and X, which serve the smell and taste system, and should be followed by a thorough examination of the mouth, dentition, tongue, throat and saliva quantity. Smell and taste testing should follow this.

If the smell test is abnormal in the presence of normal basic taste testing, the history often reveals the cause such as a recent viral infection, head trauma or recent use of new medication. If a viral infection or chronic sinusitis is suspected, there should be a referral to an ENT physician for a nasal endoscopy to rule out nasal polyps, tumor, scarring or complication of a sinus infection. CT scan of the nasal sinuses can also be done ahead of time to determine any pathology in this region. If the history suggests trauma to the head and nasal or facial structures, an MRI of the brain should be ordered with special views of the olfactory system in the nose, base of the skull, and medial temporal lobes along with facial views and nasal views. These areas need to be evaluated because of the possibility of injury. As shown on the flow chart, if there are any structural lesions on the MRI of the brain, olfactory system or other bone structures, then referral to a neurosurgeon, neurologist, and ENT physician may be necessary for treatment.

If the cause of the impaired smell is unclear on history and testing, then a full work-up should include CT scan of the sinuses, MRI of the brain and olfactory system, B-12, TSH, metabolic profile, and a Zinc level (especially if there are GI symptoms and weight loss.) If any of these tests are abnormal then the appropriate diagnosis and treatment should be instituted. If the test results are non-specific or normal, then referral to the ENT physician for nasal endoscopy should be done to eliminate any structural changes in the olfactory organ in the nose or nasal pathways.

If medication or toxic exposures are considered a cause of the smell impairment, then the suspected offending medication should be discontinued or toxic exposure eliminated. Offending medications need to be stopped for at least two or three months to see if there is any improvement in the smell disorder. If stopping the medication does not improve the taste and smell symptoms, then on follow-up a full work-up should be done as outlined in the previous section, which again would include a MRI of the brain, B-12, TSH and Zinc level and metabolic profile. This should be followed by nasal endoscopy if these studies are non-specific or normal.

If you see patients who have disorders like memory loss, Alzheimer's disease, Parkinson's disease, Parkinson's dementia, multiple sclerosis, and even "normal" patients who have weight loss, decreased appetite and increased depression, they should have a thorough work-up. That would include taking a complete smell and taste history with the patient and the care-giver, where appropriate, and thorough taste and smell testing. If the smell and taste testing are normal then nothing further needs to be done, and smell and taste are likely not playing any role in the weight loss and change of appetite. On the other hand, if the smell testing is abnormal, one should strongly suspect their neurological disorder is likely the cause of the smell loss. In certain cases, it may be prudent to do some further testing to be sure that there are no other underlying causes for the smell impairment other than the neuro-degenerative disease itself. Sometimes this might include MRI of the brain and olfactory system, and thyroid and B-12 studies if not previously done. Also possibly the patient should be referred to an ENT physician if there is any suspicion for nasal polyps or other structural lesions in the nose. However, the important point in this section is that the neurological disorders I have already outlined, which can cause cognitive and functional decline, can also directly effect the smell and taste system as part of the disease and often without complaint, but may be associated with weight loss, decreased appetite and increasing depression.

Except for some very treatable conditions like nasal polyps, chronic sinus infections, some medication, toxic exposure, low thyroid, and B-12 deficiency, *the majority of the causes of smell and secondary taste disorders are not specifically treatable*. The primary treatment as outlined in the flow chart (center lower box) is educating the patient about their particular cause and prognosis, and how to improve their quality of life. The latter includes discussing safety issues like using smoke and gas leak alarms, and hygiene issues such as use of deodorant and perfume, and having members of the family alert them to appropriate levels. Also important is education about food preparation, especially emphasizing the normal trigeminal nerve system, which is responsible for appreciation of

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Taste & Smell disorders: Diagnosis & Treatment
A suggested Flow Chart
continued

texture, temperature and spices of our food, and also the presence of normal basic tastants such as MSG, sweet, sour, bitter and salt. Use of MSG, artificial sweeteners, and marinades can be very helpful in improving food taste and increasing eating enjoyment. If the smell loss is only mild to moderate, flavor recognition is usually impaired, but still may be somewhat present. Adding various flavor extracts can improve the flavor of some foods. The use of anti-depressants and counseling may also be necessary in treatment in some patients.

Articles on the prognosis of various smell and secondary taste disorders are showing much more positive outcomes than in the past, especially where patients have been followed for longer periods of time. This is especially true for smell impairment due to head trauma and viral infections, which make up forty-five percent of symptomatic smell loss.

Dysosmia often occurs in traumatic and viral induced olfactory loss and almost always improves with time. A trial of intranasal physiological saline (10 cc in each nostril placed in the head down position three or four times a day) often helps relieve dysosmia. In my experience and that of others (unpublished), the addition of Gabapentin (Neurontin*) or Zonisamide (Zonegram*) can also help some patients with dysosmia.

If the history and taste and smell testing show normal smell and impaired taste, a thorough examination of the mouth for oral and dental hygiene, smoking stains, amount of saliva and appearance of the tongue should be carefully done. Be sure to include a complete list of medications and their length of use since certain medications can cause disturbance in taste. If the examination of the mouth and dental hygiene is normal and there are no probable offending medications, then a further work-up should include a B-12 and thyroid testing, as well as checking blood sugar for diabetes. It is very uncommon for primary taste impairment to come from a neurological cause, but an MRI of the base of the skull with special views of cranial nerves V, VII, IX and X should be considered. If there is any abnormality on the testing, it should be appropriately treated. If medication is considered the cause of the taste abnormality, it should be discontinue for at least two months after consultation with the prescribing physician.

Again, the treatment of primary taste disorders is very much the same as for smell loss in that it begins with education as to the cause of their disorder and prognosis, if known. It is also important to discuss food preparation changes that might improve appetite and eating enjoyment, and help treat depression and reduce weight loss. This should include emphasis on flavor enhancement, and temperature, texture, and spice since the trigeminal system is usually spared. Flavor extracts of many varieties can be added to foods in higher concentrations and spices varying from salsa and Tabasco* sauce to mustard and horseradish can be used in many prepared foods to improve taste. If the taste loss is mild to moderate, it is worth attempting higher concentrations of the basic tastants like MSG and sweeteners in food preparation.

Dysgeusia is not an uncommon symptom in many patients that have primary taste disorders. It can occur in any cause of primary taste dysfunction and usually impairs quality of life. If you look at the flow chart in the left lower box there are a number of treatments that have been successful and reported in the literature. These include the addition of Zinc Gluconate, up to 140 mg a day. I have used Cepacol lozenges with Benzocaine and artificial sweetener to help some patients with this disorder. One percent Xylocaine mouth gel used three or four times a day has also been reported as beneficial. As in dysosmia, the anti-convulsants in the form of Gabapentin (Neurontin*) and Zonisamide (Zonegram*) have also been reported of benefit (unpublished.)

If the patient scores less than five points on the UPSIT or is unable to detect any of tastes in whole mouth taste testing or taste strips, one has to suspect malingering. (The top upper box in the left hand column on the flow chart.) Because the UPSIT is a forced choice test it is very hard to get a score less than five because of the probability of a higher score even just guessing. People who are malingers may come into your practice with taste and smell symptoms. I found this to be more common following automobile accidents or job injuries where medical legal issues are occurring, and there is often an underlying secondary gain.

Our clinic has identified many recipes. Some were given to us by patients to share with others. But many were developed in our clinic during a small study (unpublished) conducted with several of our patients and normal controls. These recipes provided for patients consultation with our food consultant. In most cases, our patients have found these recipes and other food preparation changes to be

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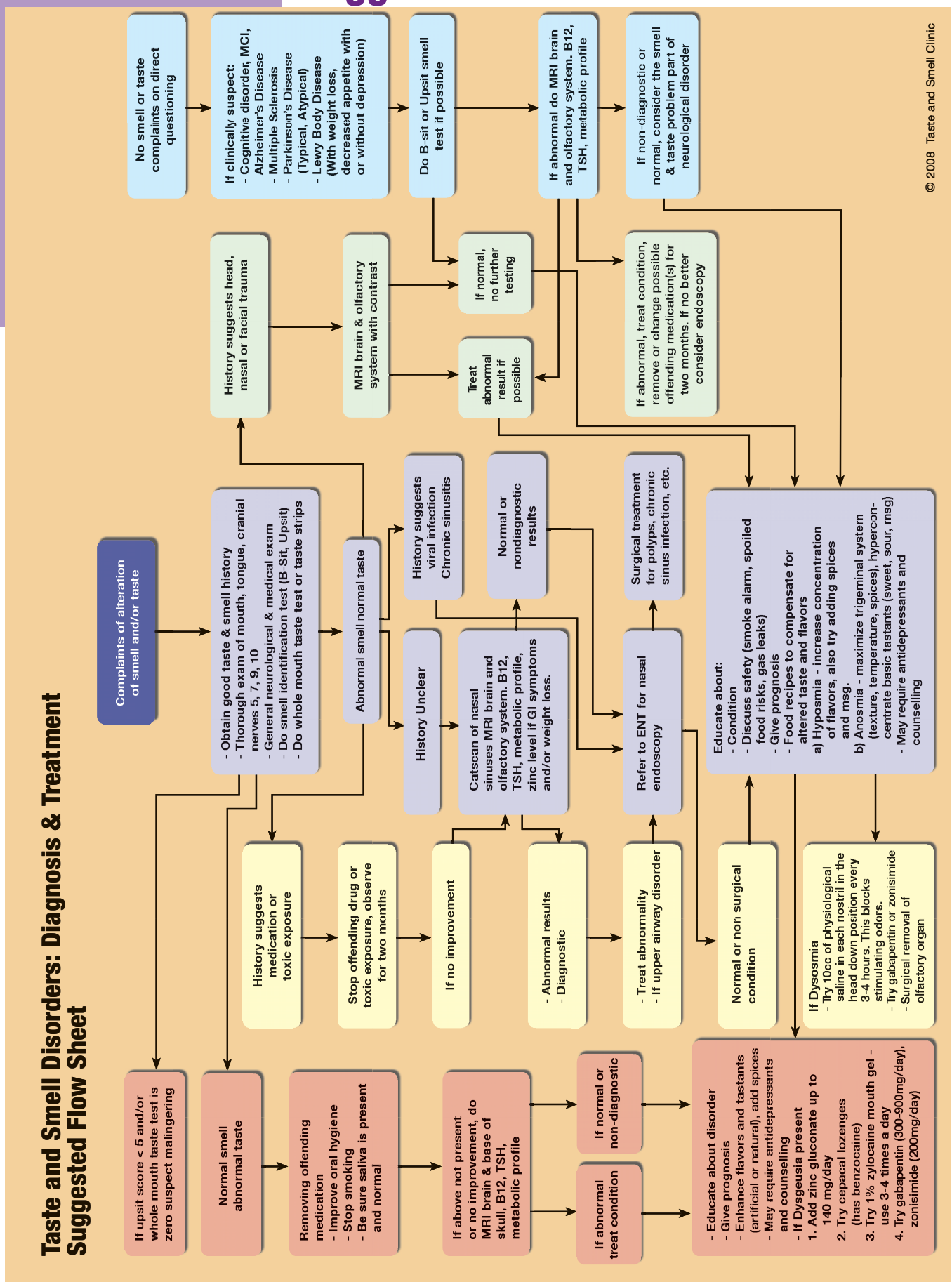
Taste & Smell disorders: Diagnosis & Treatment

A suggested Flow Chart continued



TENTH ANNIVERSARY SPECIAL EDITION

ChemoSense turns TEN

continued

"No other publication...

Congratulations ChemoSense on your 10th anniversary. I think ChemoSense is an outstanding publication. For ten years it has presented original information by the leaders in the chemical senses. The editors and authors have been able to present and distill complicated and cutting edge research into scientifically accurate but still highly accessible, readable, and understandable material.

In addition to the articles covering the basic science of chemoreception, I have been impressed with the way ChemoSense integrates the applied aspects of chemical senses research. Several years ago I taught a course entitled Food, Culture and Nutrition in Japan. Articles from ChemoSense were required reading for the course.

I often recommend articles from ChemoSense to students and others who want to learn more about the chemical senses.

There is no other publication that provides "lay readers" such superior introductory information about the field. The fact that it is available on line only increases its value to the chemical senses community and to anyone wanting to learn about the chemical senses.

ChemoSense and Graham, keep up the good work!

Wayne Silver, Ph. D.

Department of Biology
Wake Forest University
Winston-Salem, NC, USA 27109
www.wfu.edu/~silver/

ChemoSense Guides a Revolution

The past ten years have been revolutionary for olfaction and taste. *ChemoSense* has played a leading role in this revolution: by communicating syntheses of the new research results from the discoverers themselves, by providing new insights into the personal and social dimensions of these senses, and by leading the way in showing how to make the translation from the laboratory to real-life applications in industry and society. *ChemoSense* provides a means for communicating those advances within the fields of olfaction and taste in ways not available in mainstream publications. Graham Bell deserves our gratitude for taking these initiatives and assembling them into this attractive format. We look to *ChemoSense* to continue to guide us in the next ten years!

Gordon M. Shepherd
Department of Neurobiology
Yale Medical School
New Haven, CT 06510 USA.
gordon.shepherd@yale.edu

Inspiring, Infuriating, Challenging Enjoyment

I have been following the evolution of *ChemoSense* with great interest. In the early days I looked forward to receiving the hardcopy and since 2003, through the advent of the internet, in its digital form. The research related articles have frequently been the first glimpse into some cutting edge work – allowing a quick publication with some real-time responses from the readers to actually, in some cases guide the further work prior to publication in peer reviewed journals. I also enjoy reading *ChemoSense* for the profiles of researchers, either as retrospectives (Lloyd Beidler, Rose Marie Pangborn, come to mind) or as descriptions of their current work (Leigh Francis and Kate Lattey, come to mind). Additionally, it allows us an outlet for 'conversations' about sensory science, in its widest sense – a real luxury that does not exist in any of the peer reviewed journals. *ChemoSense* has inspired me, at times infuriated me, challenged me and has always been an enjoyable read. Please keep up the good work.

Hildegarde Heymann
UC Davis,
Davis, Ca., USA
hheymann@ucdavis.edu

Sensory Food Science and *ChemoSense*: Congratulations to the 10-Year-Old!

For a sensory food scientist, every new issue of *ChemoSense* is a truly refreshing e-mail gift. The review paper starting on the first page is exciting and comprehensive. *ChemoSense* does not have an impact factor, but based on the name of author, we know that the review is updated and scientifically interesting. Even if (or particularly because) the text deals with the perception and chemical senses in general, rather than with applied sensory and consumer science, it supports and expands our professional expertise.

With the little notes on recent research, books and other updates, *ChemoSense* reminds us of issues of importance. *ChemoSense* also reminds us of the wonderful, luxurious meetings that you sensory people organize at the Australian Great Barrier Reef every third December. In our darkness at the other side of the world, we genuinely envy you of those.

Dear Graham, thank you for raising up so well this baby called *ChemoSense*. Let's hope she (and you) will survive the teenage years well!

Hely Tuorila
Sensory Food Science
University of Helsinki
Finland
hely.tuorila@helsinki.fi

An Invaluable...Much Treasured Resource

In 1991, Linda Buck and Richard Axel discovered both the family of transmembrane proteins that were believed to be the receptors for odour molecules. This was a seminal breakthrough in our potential understanding of the olfactory system. Until early 1998, however, there was no direct proof that functionally these were actually odour receptors. Only in January 1998, it was demonstrated that specific odorants triggered increased electrical activity in the neurons carrying these receptors, thus delivering the final proof. In 2008, ten years on, olfactory research has grown exponentially and our understanding of the chemical senses and chemoreception has been transformed by a wealth of discoveries. Odorant receptors in worms, flies, moths, bees, fish, mice, rats, birds and humans have been characterised. Signalling pathways and olfactory memories have been elucidated, connections between molecules, neurons and behaviour have been made. In these ten exciting years, *ChemoSense* has kept us up to date with research developments in the field, from novel food flavours and wine aromas to insect pheromones, from bird olfaction to clinical issues and electronic noses. Only 10 years

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TENTH ANNIVERSARY SPECIAL EDITION

ChemoSense turns TEN

continued

old, *ChemoSense* has become an invaluable and much-treasured source of information on all things "smelly" – I certainly look forward to every new issue and to the next decade's discoveries, succinctly reviewed by the authors of *ChemoSense*.

Judith Reinhard
Queensland Brain Institute
University of Queensland
Brisbane, Australia
j.reinhard@uq.edu.au

Celebrating Taste and Smell 'Down Under'

What signals the health of a science? Is it the journals, the High End of High Science? The conferences? The popularized reportage of one's research for a not-so-academic world? Or is it the published adverts for 'stuff', of 'off-the-shelf' technology that was once lovingly crafted by the artisan, and now manufactured for more popular application? The correct answer, of course, is all of the above. And, what better witness to it all than the 'Down-Under', charming and enchanting newsletter, *ChemoSense*?

ChemoSense is celebrating ten years of publishing. Ten years in most sciences is a mere eyeblink. It's a bit more, however, when it comes to the chemical senses when we realize that this science of ours just reached the 'big time' in the 1960's, and from then began its unstoppable growth, towards a Nobel Prize on the one hand, and significant industrial interest and application on the other.

So...what's special about *ChemoSense*? Why take note of this quarterly newsletter in a world awash with information? It's simple – *ChemoSense* is, in some respects, THE marker of our field. Read the contents -- not just the 'stories', really articles popularized. Go beyond that. Read outside the stories, look at the adverts, think about what's going on here, and get a sense of our buzzing world of taste and smell. Your curiosity will be well rewarded. Look at what's being sold – from technology that 'measure' smell electronically (always fun if you're in the business of finding taints and spoilage), to announcements about upcoming courses in basic and applied sciences, and finally to service offerings by practitioners. You'll be amazed at the vibrancy, revealed so well, even perhaps innocently, in this ten year old record of chemosensory sciences in its full, spring bloom. If you haven't done so, dip back into your old issues, skip around, dip in again, and see how the decade since that first issue in 1998 has developed. Its great fun....and will give you a most delightful, charming, quite revealing snapshot of this science we love so much.

Howard Moskowitz
Moskowitz Jacobs, Inc.
White Plains, NY USA
mjihrm@sprynet.com

OMEDETO: *ChemoSense* and AACSS

I offer my heartiest congratulations to the editor and readers of *ChemoSense*. It was at the end of 1998 when I first took a copy of *ChemoSense* in my hand. In that year, I completed a PhD. degree in behavioral neuroscience on associations of taste with odor and visceral information, and had just started my professional life as a post-doctoral fellow. I was studying hard and struggling to start studies about human eating and smelling. I still have a black-and-white photo-copy of the first issue of *ChemoSense*. I guarantee that I was the most avid reader of *ChemoSense* in Japan at that time, but that now readers of *ChemoSense* are found in every Japanese laboratory studying the chemical senses. Of course, this trend is a result of the academic significance of the *ChemoSense* and the annual meetings of the Australasian Association for ChemoSensory Science (AACSS). I am proud to have made my contributions to both, by attending the wonderful AACSS scientific meetings in 2002 and 2005 at Heron Island, the abstracts for which were published in ChemoSense. Citations of *ChemoSense* articles can be found in my articles in The *Japanese Journal of Taste and Smell Research* (official journal of JASTS). AACSS notices often feature in messages for the Behavioral Science Group on Chemical Senses (a division of the Japanese Psychological Association) and on my homepage. I look forward to further development of, and prosperity for, *ChemoSense* and AACSS, and to fruitful and increasing collaborations between members of AACSS and JASTS. I congratulate *ChemoSense* for its important role over the past ten years, in fostering, internationally, strong ties between individuals and institutions.

Nobuyuki Sakai
Kobe Shoin Women's University
Shinohara Obanoyama 1-2 -1
Nada, Kobe, Japan.
nob-sakai@shoin.ac.jp

A Hidden Jewel in the Chemical Senses

I'd like to congratulate Graham, Brian and Jodi on the 10th Anniversary issue of *ChemoSense*. Despite busy schedules and

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TENTH ANNIVERSARY SPECIAL EDITION

ChemoSense turns TEN

continued

the explosion of online publications, I always make the time to read the latest issue of *ChemoSense*. As our field has grown and with it *ChemoSense*, it has become increasingly difficult to keep up with the innovations and advances in taste and smell research. *ChemoSense* always seems to find that seminal topic that merits coverage. The authors, combined with Graham's deft editing, do a great job in presenting information in a visually interesting and, importantly, understandable format to those outside the specific topic area. Of particular note in many articles is the willingness of authors to speculate about the implications of their research above and beyond the data, something not always possible in more conventional peer-reviewed journal articles. One of the real strengths of *ChemoSense* lies in its ability to bridge the basic animal and human research with the practical benefits of these studies to the corporate world. I, like many of my colleagues, will look forward to the next 10 years of *ChemoSense* and I encourage all my colleagues to discover, as I have, a real hidden jewel in the chemical senses.

Tim Gilbertson
Professor & Associate Head - Biology
Associate Director, Center for Advanced Nutrition
Utah State University, Logan, UT USA
tag@biology.usu.edu

A Clinical Assessment: Prognosis Favorable

Congratulations on your 10th anniversary in publishing *ChemoSense*. My first contact with your journal was in 2000. Some how I got on your mailing list at that time and I have been an avid reader of the journal ever since. I have been impressed with many of the written articles which cover basic physiology and clinical disorders in taste and smell. The colors and format of the journal make easy reading. My wife and I are members of a wine tasting club and we appreciate the section "Wine Sense", which offers interesting information.

Your section on "News" is very informative and offers information that I would never know about unless I read your journal.

Your section on upcoming events is very thorough and covers the most important meetings in the field.

Since you started this journal online, I find it very easy to read and can download and print some articles of interest. I am in the process of completing a book on Taste and Smell Disorders for the public and I found many articles on *ChemoSense* very useful as a reference. I can't say enough how much I enjoy the format and articles in *ChemoSense*. Congratulations again on your 10th year anniversary of the journal. I look forward to reading every issue. Keep up the good work.

Ron Devere, M.D.
Neurologist
Director, The Taste and Smell Disorders Clinic
Austin, Texas
rdevere@austin.rr.com

Ten years of *ChemoSense*: A Wine Sensory Scientist's Perspective

In 1999, as cognitive psychologist and a newcomer to the field of sensory science, I lacked a solid background in its fundamentals. *ChemoSense* came to the rescue. There were relevant articles by established researchers, and it introduced me to "upcoming events" in the field, and in particular to those of the Australasian Association for ChemoSensory Science (AACSS). Even the advertisements are highly relevant and useful to someone new to the field.

ChemoSense has retained a consistency of quality in the articles and the range of topics. As a wine sensory scientist, articles on general phenomena such as retronasal and orthonasal smelling (Halpern, Vol. 6, 2004 and Vol 10, 2008), provide a substantial overview of an issue, and are particularly helpful. The section termed "WineSense" has covered a range of topical, important and controversial issues. For example: the question of wine closures (cork versus screw-cap or plastic stopper) was addressed by Leigh Francis of the Australian Wine Research Institute (Volume 6, 2004); while the influence of global climate change was addressed in a recent Issue (reporting on a conference presentation by Richard Smart, "the flying vine doctor", Volume 10, June 2008).

Finally, the most important legacy of *ChemoSense's* first 10 years from a wine sensory scientist's perspective, is that it established wine as a key topic of interest to sensory scientists, while also raising the profile and awareness of sensory science in the wine industry.

Wendy V. Parr
Lincoln University
Canterbury, New Zealand.
wendyparr@xtra.co.nz

ChemoSense: "in vino veritas..."

What an appropriate way to celebrate *ChemoSense's* 10th anniversary with a little note on wine. For the last 11 years, I have conducted applied research on factors affecting sensory evaluation of wine and have found interesting articles in several issues of ChemoSense that enhanced my understanding of human sensory physiology.

I have always considered sensory evaluation as a critical tool to bridge the production and marketing functions in winery operations. However, sensory scientists suffer from "expertise deficient trauma": sensory panelists are not wine experts, who have run the wine world for centuries, even though their science and practice are not widely accepted and adopted in the wine industry. Studies have shown that wine experts differed from novices in their way to describe wine, which tends to be prototypic and idiosyncratic; however no clear evidence exist regarding the superiority of the expert's sensory skills. So what's next? I expect more research to be conducted on the perception and cognitive basis of wine expertise that could clarify the respective roles of sensory panelists and wine experts. I hope *ChemoSense* will continue to be a great medium to review such outcomes, as it reaches scientists and professionals from different fields, all of whom are interested in the latest news on chemosensory perception.

Isabelle Lesschaeve, Ph.D.
Associate Professor, Sensory and Consumer Sciences
Brock University
St Catharines, Ontario Canada
ilesschaeve@brocku.ca

10th Scientific Meeting of

The Australasian Association for ChemoSensory Science (AACSS)

- Neurobiology of Chemoreception
- Evolutionary Genetics of Olfaction
- Chemoreception of Marine Animals
- Psychology of Human Olfaction
- Food Flavours and Wine Aromas
- Industrial Applications

The Conference will take place at Griffith University - nestled in subtropical bushland, only minutes from Brisbane's city centre

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4 - 6 December 2008
Brisbane, Australia

To register and for further information contact: Judith Reinhard (j.reinhard@uq.edu.au)

Upcoming Events

15-19 November 2008	**Society for Neuroscience** Annual Meeting Washington DC, USA Contact: www.sfn.org
30 Nov -3 December 2008	**Australian Physiological Society (AuPS)** Annual Meeting Melbourne University, Melbourne Contact: www.apps.org.au
4-6 December 2008	**Australasian Association for ChemoSensory Science (AACSS)** Annual Scientific Meeting Griffith University, Brisbane Contact: j.reinhard@uq.edu.au
27-30 January 2009	**ANS 2009** Australian Neuroscience Society Annual Meeting National Convention Centre Canberra, ACT Contact: www.sallyjayconferences.com.au
15-17 April 2009	**ISOEN 2009** International Symposium on Olfaction and Electronic Nose University of Brescia, Italy Contact: www.isoen.org
22-26 April 2009	**AChemS XXXI Annual Meeting** Hyatt Sarasota, Florida, USA Contact: www.achems.org
28-30 April 2009	**EcoForum Conference and Exhibition** Australian Technology Park, Sydney Contact: www.ecoforum.net.au
19-25 July 2009	**Summer School on Human Olfaction** Dresden, Germany Registration deadline: 1 May 2009 Contact: thummel@mail.zih.tu-dresden.de Also: www.tu-dresden.de
6-9 September 2009	**19th CASANZ Conference** "Air Quality and Economic Development" Perth Convention Centre Perth, Western Australia Contact: www.iceaustralia.com/casanz2009
December 2009	**Australasian Association for ChemoSensory Science (AACSS)** Annual Scientific Meeting Heron Island, Great Barrier Reef, Australia Contact: g.bell@atp.com.au

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Production Team
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Coming up in ChemoSense

Images and Palatability
High End Sensory
Elephantine Smell

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