Mucosal Immunology Update
Society for Mucosal Immunology
Officers and Councilors, 2002-2005

President
Warren Strober, MD
wstrober@niaid.nih.gov

President-Elect
Hiroshi Kiyono, DDS, PhD
kiyono@ichr.osaka-u.ac.jp

Secretary-Treasurer
Suzanne M. Michalek, PhD
sue_michalek@micro.microbio.uab.edu

Councilors:
Richard Blumberg, MD
rblumberg@partners.org
Nils Lycke, MD, PhD
nils.lycke@microbio.gu.se
Lloyd Mayer, MD
lloyd.mayer@mssm.edu
Jo Viney, PhD
vineyj@amgen.com

Editor:
Jo Viney, PhD
vineyj@amgen.com

Associate Editors:
Kenneth Beagley, PhD
ken.beagley@newcastle.edu.au
Dean Befus, PhD
deancbefus@ualberta.ca
Paul Garside, PhD
pg3b@clinmed.gla.ac.uk
Edward N. Janoff, MD
janof001@umn.edu
Brian Kelsall, MD
bkehall@niaid.nih.gov
Nils Lycke, MD, PhD
nils.lycke@microbio.gu.se
David W. Pascual, PhD
dpascual@montana.edu
Yoshio Wakatsuki, MD, PhD
wakatsu@kuhp.kyoto-u.ac.jp

Office:
Society for Mucosal Immunology
4350 East West Highway, Suite 401
Bethesda, MD 20814-4410
Tel: (301) 718-6516
Fax: (301) 656-0989
E-mail: smi@paimgmt.com

Table of Contents

Introduction ........................................... 3

Eosinophilia in the mucosa of the airways and GI tract:
separate holes, same response? .......................3-6

Psychological Stress and Asthma .................... 6-9

2003 President’s Report .................. 9-10

SMI News ........................................... 10-11

Cover Art: Reprinted from IMMUNITY,
Vol 17, No 5, 2002; cover image only,
with permission from Elsevier
Introduction

This last issue of 2003 continues with the theme of highlighting lung research in Canada. We have two great articles for you to enjoy over the holidays while sipping your mulled wine! The first focuses on the role of eosinophils in contributing to adverse lung function and highlights the similarities between lung and gut inflammation. The second focuses on the role of stress in altering immune function and contributing to asthma. Enjoy! Next year, MIU will continue to provide you with up to date review articles on a diverse range of topics. Please let us know if you are interested in contributing. Meanwhile, from all of us at MIU, we wish you good health and good cheer for 2004.

—Jo Viney and the MIU Editorial Team

Eosinophilia in the mucosa of the airways and GI tract: separate holes, same response?

Darryl Adamko, MD, FRCP (C) and Redwan Moqbel, PhD, FRCPath
Pulmonary Research Group, 550 Heritage Medical Research Centre, University of Alberta
Edmonton, AB, T6G 2S2, Canada.

Abstract

There are many parallels in eosinophil research between the GI and respiratory tract. In the airways of patients with asthma or allergic rhinitis, the presence of eosinophils and release of their mediators correlates with tissue damage and disease severity. The gastrointestinal tract is a natural homing site for eosinophils as part of normal mucosal defense. However, excessive eosinophilia and active secretion in various compartments of the gut result in disease states. Recent trials of specifically targeting the eosinophil by monoclonal antibody therapy have questioned the importance of eosinophils in human inflammation and disease. This article will review eosinophils in relation to mucosal health and disease of both GI and respiratory tracts, in light of the recent trials of anti-IL-5 therapy.

Shared Embryology of the Respiratory and GI Tracts

The lung and the upper gastrointestinal tract share many common physiologic features relating back to their common origins in embryology (4). The lungs develop from an endodermal bud off the foregut, thus the lung, the esophagus, stomach and proximal part of duodenum share the same embryological tissues. The endodermal lining of the airways turns to a pseudostratified columnar epithelium for its eventual relation to an air interface, while the GI tract turns to stratified squamous epithelium. Both maintain a smooth muscle element layer to varying degrees, the lung for bronchoconstriction, and the esophagus for food bolus propulsion. The neural control of both is largely under vagal or noncholinergic nonadrenergic control (5). In terms of mucosal immunological defense, secretory IgA, complement and luminal macrophages are shared elements. Despite this, the presence of eosinophils in these tissues appears to be distinct depending on the state of health. While a low baseline amount of eosinophils are expected in the GI tract, within the normal, non-allergic airway, eosinophils are few. The reason for the difference is not yet understood, possibly in part to our poor understanding of "normal" eosinophil function.

Eosinophils and Infections

The function of eosinophils in host defence against parasitic infection is well documented, especially in association with helminths that have part of their lifecycle in the GI tract. Although, parasitic elimination has been demonstrated in the mouse model (6), this ability is impaired. Thus, the prevailing dogma regarding normal eosinophil function in humans is that eosinophils may have been retained in evolution because on balance they contribute to adaptive immunity within the GI tract associated with...
both innate and acquired immune response against helminth infection (7).

Beyond this, the role of the eosinophil in defense of any organ system is much less established. A role in viral clearance by eosinophils has been proposed. Respiratory Syncytial virus (RSV), like many of the more virulent human airway viruses, is composed of single stranded RNA. One of the granule proteins produced by eosinophils is the potent RNAse, eosinophil-derived neurotoxin (EDN), which in vitro, appears to decrease RSV replication (8). In HIV infected patients, an increase in blood eosinophils has been noted. In studying this association, human eosinophils in vitro have demonstrated the capacity to inhibit HIV replication via eosinophil peroxidase (EPO) and subsequent production of hypobromous acid (9). In our lab, we are further pursuing this anti-viral capacity of EPO to specifically inhibit airway viruses via hypobromous acid (10).

Eosinophils and mucosal diseases

In contrast to mucosal defense, research on the association of eosinophils with clinical disease has received greater attention, especially in asthma. Release of eosinophil mediators including cytotoxic granule proteins and cytokines, have been related to airway mucosal damage, bronchial hyperresponsiveness, and neuronal dysfunction (11). Similar findings are seen in eosinophilic GI tract conditions (3). Gastroesophageal reflux disease (GERD) is associated with increased intraepithelial eosinophils (12,13), that are cleared with anti-reflux therapy (14). Eosinophilic esophagitis, distinct in its etiology from GERD due to its allergic basis, also responds to such anti-eosinophil therapy as systemic corticosteroids (15), topical corticosteroids (16,17) and montelukast (18). Similar eosinophil associations are seen in inflammatory bowel disease (19). Despite these clinical associations, the exact role of eosinophils remains unclear if not more confusing considering confounding research in animal models and more recently, work in humans using anti-IL-5 therapy in asthma.

Monoclonal antibody (mAb) therapy in humans

Humanized mAb’s are attractive therapeutic strategies (20). The expression of IL-5, a cytokine essential in eosinophil maturation, terminal differentiation, survival and function, is increased in the bone marrow and airways within 24 hours after antigen exposure of sensitized asthma patients (21). This increase can be blocked by inhaled corticosteroids, suggesting a communication between the lung and the bone marrow (22). Increases in IL-5 correlate with blood eosinophilia and an increase in the number of BAL eosinophils in the late asthmatic response (23). Thus targeting IL-5 was expected to produce significant clinical benefit for patients with asthma. However, ablation of blood and sputum eosinophils with the humanized recombinant mAb to IL-5 Mepolizumab did not improve clinical outcomes of mild asthmatics, including airway hyperreactivity (24). As a result, it was concluded that eosinophils may not be critical in asthma (i.e., it became unclear whether the eosinophil was an effector or a bystander cell). An excellent review by O’Byrne and Inman (25) rebutted the data showing many shortcomings in design of the Leckie study, including a lack of the main outcome measure, airway hyperreactivity (AHR), in the positive control. Flood-Page et al. having reviewed the biopsies found that the anti-IL-5 mAb depleted less than 50% of bronchial tissue (26). In addition, eosinophil progenitors appear unaffected by anti-IL-5 mAb (27).

Tissue versus blood eosinophilia

There appears to be important differences in eosinophils after they migrate into tissue. Marked reductions in the expression of mRNA for surface IL-5 receptor are seen in BAL compared with blood eosinophils (28). Unlike blood eosinophils, those from BAL do not release eosinophil derived neurotoxin (EDN) when treated with IL-5. Lee et al. recently demonstrated that eosinophils instilled into the trachea of IL-5 knockout mice not only survive in the absence of IL-5, but in concert with CD4+ T-cells, migrate back into lung, and reconstitute the asthma phenotype of wild-type antigen challenged animals (29). Therefore, while IL-5 may be essential in maturation and differentiation of eosinophils in the bone marrow (30), the recruitment to tissues and function within tissues may be IL-5 independent. Eosinophils can release in an autocrine fashion GM-CSF (31,32), which is stored in association with eosinophils granules (33). Other eosinophil-derived and stored cytokines (e.g. IL-4 (34), IL-13 (35) and chemokines (e.g. RANTES (36)) may further amplify the inflammatory milieu. Thus, local production of such eosinophil factors may be important in tissue eosinophil activity than IL-5.

Eosinophils and tissue nerves

Given the response of patients to β2-agonists, the smooth muscle has been the focus for the etiology of AHR. Whether the airway muscle is intrinsically more hyperresponsive to stimulation remains unclear (37). AHR measured by inhalation of methacholine or histamine (PC20) involves sensory nerve stimulation of the smooth muscle via the vagus efferent nerves (38,39). In human and animal models of AHR these neural pathways are abnormally sensitive (40-42). In the GI tract, nerve dysfunction and close association with of degranulating tissue eosinophils is described (43-47). Similarly, in patients with asthma, positive staining for eosinophils and released eosinophil major basic protein

continued on page 5
continued from page 4

(MBP) has been demonstrated around the lung ganglia (48). In guinea pigs (GP) that are antigen sensitized and challenged (49) or antigen sensitized and virus infected (50), eosinophil MBP causes neural dysfunction and hyperreactivity. Eosinophils appear in closer proximity to the airways of sensitized animals (51) and increased binding to antigen sensitized nerve cultures is mediated via increased ICAM-1 expression (52). In antigen sensitized GP, depletion of CD8+ T-cells before virus infection prevents eosinophil mediated neuronal dysfunction, via a mechanism related to virus-induced eosinophil degranulation near airway nerves (51).

Activation and release

While sensitization alone causes increased tissue eosinophilia (51), airway dysfunction does not occur unless the GP are subsequently virus infected or antigen challenged. Thus, there are regulated receptor-stimulus coupling events that must be established before mediator release. The movement of stored eosinophil products from intracellular to extracellular compartments is extremely complex (53). Eosinophil exocytosis, including in vitro models of piecemeal degranulation (54) involve the mobilization of mediator-containing small secretory vesicles from cytosolic sites to the plasma membrane. Mediator release may also involve the expression and mobilization of the tetraspanin molecule, CD63 (55). Docking of such vesicles as well as granules is regulated by a SNARE fusion complex (56,57). Thus, eosinophils store in mobilization of the tetraspanin molecule, CD63 (55). Docking of such vesicles as well as granules is regulated by a SNARE fusion complex (56,57). Thus, eosinophils store in mobilization of the tetraspanin molecule, CD63 (55). Docking of such vesicles as well as granules is regulated by a SNARE fusion complex (56,57). Thus, eosinophils store in

What's next?

Respiratory and gastrointestinal research are linked by the association of eosinophils to parasympathetic nerves, the release of free extracellular MBP in tissue, and the positive responses to anti-eosinophil therapy. Yet still, correlation between disease and eosinophilia is not always consistent, which suggests that evidence for their effector function remains circumstantial. Interestingly, a key stimulus for developing eosinophilia in the esophagus may not always be food antigen, but inhaled aeroallergen (58,59). The mechanism of this surprising observation is not known but may relate back to the shared embryologic origin of these two systems. Unlike the airways’ poor response to anti-IL-5, it appears that in eosinophil esophagitis patients, anti-IL-5 therapy causes improvements in swallowing with lowering of blood eosinophils and reduction of esophageal eosinophilia (Rothenberg, personal communication). Understanding the shared features or differences in eosinophilic responses within the lung and GI tissue will be a fertile source of innovative eosinophil research and therapy.

References

Psychological Stress and Asthma

Harissios Vliagoftis¹ and Paul Forsythe²
¹ Pulmonary Research Group, University of Alberta, Edmonton, AB T6G 2S2, Canada.
² The Brain-Body Institute, St. Joseph’s Healthcare Hamilton and Department of Pathology & Molecular Medicine, McMaster University, Hamilton ON L8N 3Z5, Canada.

Introduction
The association between stress and asthma was made early in the history of the disease. Moses Maimonides in his treatise on asthma (1198) stressed the “importance of emotional and psychological processes” in asthma. Until the inflammatory basis of the disease was described in the latter half of the 20th century, asthma was considered purely or primarily psychogenic, and was referred to as “asthma nervosa”. Today asthma is recognized as an inflammatory disease of the airways. A number of cells and mediators play a role in the development of this, primarily eosinophilic, airway inflammation (1-5). However, epidemiological data suggest that stress may still play an important role in the development of asthma symptoms and in allergic sensitization.

Stress Response
Stress can be defined as the psycho-physiological reaction of the body to a variety of stimuli that threaten homeostasis (6,7). Stress may be physical in origin, arising from heat, cold, trauma or infection or may arise from emotional and psychological factors. Although physical and psychological stressors activate many similar pathways, psychological stressors have a distinct negative impact on inflammatory diseases including asthma.

When the body is challenged physically or psychologically, short term activation of the neuroendocrine and autonomic nervous systems promote adaptation and survival. This has been termed allostatic, literally ‘re-establishing stability through change’ (8). During allostatic physiological systems operate at higher or lower levels than during ‘normal’ homeostasis. Providing allostatic responses are shut off when they are no longer needed, the body is able to adapt to and survive the immediate challenge without long-term consequences. However, if the same response systems are activated over a longer period of time, or remain active when no longer needed, these adaptive changes may cause damage or exacerbate disease processes.

Stress and the Immune System
Communication between the brain and the immune system is bi-directional involving signaling pathways that interconnect the central and peripheral nervous systems with endocrine and immune responses. Stress can modulate the immune response through activation of the Hypothalamus-Pituitary-Adrenal (HPA) axis and the sympathetic nervous system (SNS) leading to release of cortisol and catecholamines that can influence cell trafficking, proliferation and function including cytokine and inflammatory mediator production (9-11). In return, cytokines are potent mediators of immune-brain communication in response to pathogen exposure or injury. Activation of these cytokine-brain signaling pathways results in subsequent activation of the HPA axis; the resultant increase in serum corticosteroids suppresses cytokine release to prevent excessive inflammation.

Stress and Asthma Severity: Clinical Data
Between 20 and 35% of asthmatics experience exacerbations of their disorder during periods of stress (12). Mental health of asthmatic children is an important predictor of asthma morbidity (13). Psychological distress is associated with difficult to manage asthma (14), more frequent and lengthier admissions to the hospital (15) and increased functional disability (16). Psychological morbidity has been linked to asthma mortality in children (17,18) and adults (19).

A stressful stimulus induces an increased state of vigilance, but also increases anxiety and worrying. Stress effects on asthma depend on the coping mechanism of the individual. When the stressful stimulus precludes any alternative response that can eliminate or decrease the threat to the organism it is more likely to result in a response that is detrimental to an individuals health. Concordantly, passive and avoidance coping strategies have been associated with increased severity of the disease (20), while the development of active coping mechanisms decreases the effects of stress on asthma (21,22). 


Corresponding author: Redwan Moqbel
Email: redwan.moqbel@ualberta.ca
continued from page 6

**Stress and Development of Asthma**

Maternal stress, through the release of corticosteroids in the maternal circulation, which could then cross the placenta (23,24), and the release of corticotropin releasing factor (CRF) synthesized by the trophoblast cells into both maternal and fetal circulation (25), can affect the development of the immune system of the fetus. Interestingly, CRF production in the placenta is up regulated by corticosteroids (26), further increasing the effects of stress on the immune system. A hypothesis was recently proposed suggesting that the effects of maternal stress on the fetus's immune system are important for the development of atopy and asthma (27).

Similarly, early life stress, possibly the result of increased parental stress during the perinatal period, affects the development and the development of atopy and asthma, which may carry over into adulthood. Increased parenting difficulties such as perinatal maternal depression, parents' marital adjustment problems and parenting problems, are associated with increased rates of asthma before 3 years of age (28). In genetically predisposed infants caregivers' stress during the first few months of life was associated with an increased risk of wheezing up to 14 mo of age (29), which was independent of other factors that could be influenced by caregiver's stress.

**Mechanism of Stress-Asthma Interactions**

The exact pathways mediating the effects of stress on asthma are not clear. There are various possibilities, including altered symptom perception during asthma attacks (30), direct effects of stress on bronchoconstriction (31-34) and deterioration of self-management strategies. However, evidence from other inflammatory diseases indicates that the effects of stress on airway inflammation are likely important determinants of stress-induced asthma exacerbations.

An increasing body of evidence shows that mediators of the stress response such as corticosteroids and catecholamines drive the Th1/Th2 balance toward a Th2 phenotype, which might accelerate the onset of infectious diseases and allergic disorders (35-37). Indeed, restraint stress in mice causes a shift in Th1/Th2 balance toward Th2-dominant immunity (38), and academic stress in humans also polarizes the immune response towards a Th2 phenotype (39).

The role of stress in asthma has been proposed as an important area for further study (40). Much of what we know regarding the effects of stress on inflammation comes from studies on gastrointestinal disorders and arthritis.

**Stress and Inflammation**

While there is mounting evidence from studies in animal models of a role for stress in the initiation and/or exacerbation of arthritis and inflammatory disorders of the gut (41-44), only recently has data become available on stress-induced modulation of allergic inflammation and function in the airways (45,46). Contrasting results have been obtained using a variety of experimental approaches to induce psychological stress in animal models of inflammatory disease. These differences are related not only to the inflammatory model used but also to certain characteristics of the stressful event that modulate its impact on inflammation (9,41,47-53).

Duration of exposure to stress appears to be one important variable and stress has markedly different effects on the immune system depending on whether it is acute or chronic. Acute stress exacerbates while chronic stress attenuates delayed-type hypersensitivity reactions in rats and mice (48,54,55), and repeated but not acute stress suppresses inflammatory plasma extravasation (51). However, in general, exacerbation of inflammatory disease has been correlated to chronic or repeated exposure to a stressor, rather than short term or acute stress (41-44,53,56). Chronic stress has been shown to suppress different immune parameters including delayed type hypersensitivity, (57,58) antibody production, (59,60) NK activity, (61-63) leukocyte proliferation, (64) skin homograft rejection, (65) and virus-specific T cell and NK cell activity (66). In a murine model of asthma, short-term stress decreases airway inflammation while long-term exposure to the stressor results in a marked increase in inflammatory cell numbers in the airways (45). This suggests that in the airway, as in other compartments of the body, as duration of stress exposure increases different physiological mechanisms are engaged and exert qualitatively distinct effects on the inflammatory response. The degree to which stress impacts on the immune system may be significantly affected by the relative concentrations of epinephrine, norepinephrine and corticosterone. Such interplay of the SNS and HPA in the lung may influence the airways' immune response and differences in concentrations and ratios of stress mediators may explain distinct inflammatory responses to stress of varied duration.

Chronic or repeated long-term exposure to stress leads to adaptation of the HPA axis response including down-regulation of glucocorticoid receptor expression, consequent loss of negative feedback on hypothalamic and pituitary secretion of CRF and adrenocorticotropic hormone (ACTH) respectively (67) and blunting of the corticosteroid response (55,67). An impaired HPA axis response has been associated with an enhanced inflammatory response following stress in
continued from page 7

a rat model of colitis (56). In some cases of stress-induced exacerbation of inflammatory diseases there is also evidence that the HPA axis is hypo-responsive to stress (68). A decrease in glucocorticoid response consequent to chronic stress may not only lead to a loss of the associated immunosuppressive effects but may also unmask pro-inflammatory actions of other stress induced mediators such as CRF and catecholamines (69-73). The pro-inflammatory effects of CRF are mediated, at least in part, through mast cell activation (72,73).

The immunomodulatory response to stress involves several independent pathways. In a rat model of colitis the antagonist of the HPA axis response, α-helical corticotropin-releasing factor cannot block enhancement of inflammation induced by repeated restraint stress (41) indicating the involvement of a pathway independent of the HPA axis. Similarly the restraint stress induced increase in BAL cytokine levels following allergen challenge (45) and decrease in IL-1β in airways of influenza infected rats (74) are unaffected by treatment with a corticosteroid receptor antagonist. Dobbs et al demonstrated that both corticosterone and catecholamine-mediated mechanisms were involved in the stress-induced suppression of anti-viral cellular immunity (75). Further studies suggested that coordinated interactions between these two physiological response mechanisms are required to optimize development of a restraint stress induced immune response to experimental influenza infection (76).

Conclusions
Current clinical studies aim to define the role of stress on asthma symptoms and severity. As we develop a greater understanding of the intricate interactions between the nervous and the immune system the effects of stress on inflammatory diseases will become clearer. However, little is known about the effects of stress on airway inflammation, mucus production, mucociliary clearance and local mucosal defenses. More mechanistic studies are needed to define how the stress response exerts its immunomodulatory effects in the airways and to identify pathways amenable to therapeutic intervention. One problem contributing to the dearth of information regarding the effects of stress on the airways is the lack of relevant animal models.

Research in these areas could provide further insight into how an individual’s state of mind may influence airway inflammation and mucosal defenses in the airway. Such information may prove valuable not only in understanding the effects of stress in asthma but also the influence of emotions in other inflammatory airway and lung diseases.

References
2003 President’s Report

Dear Colleagues:

This first year of my stewardship of the Society has been one of great activity and, I believe, of considerable accomplishment. As we entered this year we had before us an agenda developed from strategic planning sessions held at, and voiced membership concerns heard at, the 2002 International Congress in Orlando. This included the need to improve communication among the members, the need to re-establish a reliable and exciting Mucosal Immunity Update (MIU), and the need to hold more frequent and more high profile meetings relating to mucosal immunity on a yearly basis. In addition, the leadership of the Society took note of the strong desire of non-US members to become a more integral part of the Society.

I am happy to say that we have made significant progress on all of these fronts and I would like to take a moment to outline the details of our activities.

To address the issue of membership interaction, and ultimately membership retention and recruitment, I appointed an eight-member international Membership Committee chaired by Dr. Cathryn Nagler-Anderson. This Committee has met via telephone on several occasions, both to map effective communication strategies and to plan and then to perfect a most important vehicle for membership communication – a new SMI Web site. Working with a new Website designer and Webmaster, the Committee has created an attractive and user-friendly Website that will serve as a major source of information for all mucosal immunologists, especially SMI members who have access to a Members-Only section.

Among the departments of the Website are sections containing the latest information about international and regional meetings, and, in the Members-Only section, a section containing information on how to communicate with colleagues with similar research interests. As we move into 2004 I am confident that we can add additional features to the Members-Only section that will help our members’ professional careers, such as job postings and funding sources. In addition, we plan to make teaching slides relating to mucosal immunity available in this space. Clearly, access to this area of the Website will become a major membership benefit. You can visit the Website at www.socmucimm.org.

Regarding the second charge, to create a Mucosal Immunology Update (MIU) that is published on a regular basis and that contains up-to-date, highly relevant mini-reviews of general interest to mucosal immunologists, I appointed an eight-member international Publications Committee headed by Dr. Jo Viney. The membership of this committee also serves as the MIU Editorial Board and will take turns in editing individual issues of MIU. This group has already mapped out the focus of MIU issues for the next few years and will be using several different approaches to create Updates that whet the interest of SMI members. With this current issue of MIU, I am pleased to report that under Jo’s leadership we have successfully published four issues this year, all within 2003. In addition, we are on track for 2004, since the early issues of this upcoming year are already in advanced planning. The Editorial Board welcomes ideas for future issues of MIU and will entertain the possibility of guest editorships; this might be an excellent opportunity for young investigators to bring new research to the attention of the SMI community.

For the third concern, the need to sponsor annual meetings between International Congresses, we decided to maximize our relationship with the Federation of Clinical Immunology Societies (FOCIS) of which SMI is a member along with other Societies with an immunological focus. This organization provides an opportunity to its member societies to sponsor satellite meetings before the main meeting.

Corresponding Author: Harissios Vliagoftis

E-mail: hari@ualberta.ca

continued on page 10
Thus, in May 2003, we sponsored a satellite meeting to the annual FOCIS Meeting in Paris, France, with Dr. Nils Lycke of Sweden as the program chair. Dr. Lycke gathered together an exceptional faculty, and subsequently ran an excellent forum highlighted by work conducted by our European colleagues. The 2004 annual meeting will be held in Montreal, Canada, again as a satellite meeting, in this case immediately preceding the International Congress of Immunology, which is being jointly co-organized by FOCIS. Dr. Brian Kelsall has agreed to be the program chair of this meeting and has gathered together another excellent faculty. All in all, we expect these annual meetings, held in conjunction with another larger meeting, will become major events on the mucosal immunologists calendars.

Two other SMI meeting held under SMI sponsorship or with major SMI financial help are worthy of note. First, we are planning to continue to mount our customary mucosal immunology seminar at the AAI annual meeting. In 2003, Dr. Ivan Fuss organized this seminar around mucosal trafficking, and in 2004, Dr. Richard Blumberg will organize this seminar around the function of epithelial cells in the mucosal immune response. Second, we provided a major grant to support a Mucosal Immunology Symposium conducted by the European Mucosal Immunology Group (EMIG) in 2003 in Wurtzberg, Germany. As funds allow, I expect that we will provide similar support for EMIG in coming years as well and, in doing so, to broaden the impact of SMI in the international area. Finally, I want to mention that we are well into plans for the next International Congress to be held in Boston in 2005. Already a venue has been selected and we are organizing the various groups of individuals who will take part in the planning of this major triennial effort.

Obviously, the ambitious program we have launched and expect to continue at an even greater level requires that SMI must maintain a strong financial basis. This will require first that we increase our current level of membership, so that existing membership financial support is adequate to support our various activities. As we see it, if we can provide valuable services to the mucosal immunology community we should be able to retain and expand our membership. I hope you will agree that we are moving in the right direction in this regard. A second consideration is that we increase our annual membership dues by a modest amount. Our current dues are $70 per annum, and they have not been increased for several years. Based on our current financial outlays and our current financial inflows, we anticipate a deficit this year that can only be met by dipping into our limited reserves. I will be discussing this option with the other members of the Board of Councilors at the end of December, and I will report to you in early January 2004 about our direction in this critical area.

In the meantime, please accept my best wishes for a Happy Holiday Season, and my hope that 2004 will bring you much professional and personal success.

Warren Strober, MD

SMI News

New SMI Web site a success
SMI’s new Web site at www.socmucimm.org has attracted attention since its launch in early November. For the first month of operation, there were almost 21,000 hits by visitors from over 20 countries. According to Joshua Garrett, president of Amorphous Consulting, Inc., the designer and Web master, “this is extremely good considering that we have not yet publicized the new site extensively using blast emails. One very positive statistic is the number of people reaching the site using search engines and key words like “mucosal immunity”, “mucosal” and “immunology.”

Dr. Cathryn Nagler-Anderson, chair of the Membership Committee that is working to bring the benefits of SMI membership to all mucosal immunologists worldwide and who was active in the design of the new Web site, said “We are pleased with the ease of navigation and quick response of the site, which is critical for bringing users back time and time again. The Members Only section will become extremely valuable for SMI members as it addresses the immediate needs of researchers in our field. In one place we can communicate with each other, find out the research interests of other members, consider new career opportunities, revisit past issues of MIU, and have immediate access to possible funding sources for our research.” In the public areas information about both SMI and other meetings are carried on the home page along with the latest news from SMI and full information on how to join the Society.

To make renewing your membership for 2004 more convenient, the Members Only section will have a secure and personalized invoice with your current membership data, so that you can update the information and pay dues using a credit card. Members will be notified by email in January when this is available. A regular mailing will also be sent in January. Eventually SMI hopes to communicate with its members only be email to reduce printing and postage costs.

Visit www.socmucimm.org and let us know, at smi@paimgmt.com, how the site can continue to be improved and become even more useful to you and all SMI members in the coming months.
SMI News Continued . . .

Dr. Brian Kelsall to chair the SMI 2004 Annual Meeting
The SMI 2004 Annual Meeting will be held on July 18, 2004, as a full-day satellite meeting preceding the 4th Annual FOCIS Meeting and the 12th International Congress of Immunology (ICI), July 18 –23, 2004, in Montreal, Quebec, Canada (Details www.immuno2004.org).

Brian Kelsall, MD, has gathered an outstanding faculty for a full discussion of Dendritic Cells in the Induction and Regulation of Mucosal Immunity. The venue will be the Palais des congres de Montreal. Registration for the meeting will be possible on-line at www.immuno2004.org or through the ICI/FOCIS congress office in early 2004. Contact information will be available at this SMI Web site in early 2004. In the meantime, please put this date in your calendar and plan on attending.

2004 AAI Symposium Program announced
Richard S. Blumberg, M.D., chair of the SMI Guest Society Symposium at Experimental Biology 2004 and the American Association of Immunologists (AAI) annual meeting on Sunday, April 18, 12:30 – 2:30 p.m. in Washington, D.C., has announced that the theme will be Function of Epithelial Cells in Mucosal Host Defense and Immune Regulation. The faculty will be: Richard S. Blumberg, M.D. (Harvard Medical School); Martin Kagnoff, M.D. (University of California - San Diego); Lora Hooper, Ph.D. (University of Texas - Southwestern); Sean Colgan, Ph.D. (Harvard Medical School).

This session is organized by SMI and there is no registration fee. Registration information for the AAI meeting can be found at www.faseb.org/meetings/eb2004.

Mérieux Foundation invites you to France
With the theme of Plant-Derived Vaccines and Antibodies the Mérieux Foundation has scheduled its meeting for March 21-24, 2004 at Veyrier-du-Lac, near Annecy, France

The meeting will review the state of research and applications (in human and veterinary medicine) of antigens and antibodies produced in plants, evaluate the prospects and limitations of this approach, and propose steps forward. This meeting seeks to bring together researchers, clinicians, and representatives of industry and regulatory agencies from developed and developing countries.

For more information, go to www.foundation-merieux.org or contact Michèle Michaud at michele.michaud@foundation-merieux.org.

First ESPGHAN Capri Meeting to be held in Italy
Featuring the topic Gut Inflammation: Impact on Gastrointestinal and Systemic Diseases, this meeting will be held May 27-29, 2004, at the Grand Hotel Quisisana-Capri (Naples) Italy.

Two specific aspects of this issue will be addressed: 1) Systemic diseases resulting from deranged intestinal immune responses with special attention to autoimmune diseases; 2) The impact of mucosal inflammation on gastrointestinal neuromuscular function with emphasis given to relationships between inflammation and functional gastrointestinal disorders.

For additional information and registration go to www.messaggi-events.org/capri2004 or contact messaggi_srl@tin.it.

American Physiological Society offers conference on IBD in Colorado
A conference on Immunological and Pathophysiological Mechanisms in Inflammatory Bowel Disease will be presented by The American Physiological Society on September 8-11, 2004 at Snowmass Village, Colorado, USA.

This translational conference will present the latest state-of-the-art advances in both experimental and clinical IBD with the overall objective being to emphasize how these new data may prove useful in treatment of IBD patients in the near future. By bringing together established IBD researchers with young investigators, this conference aims to interface what has been learned from experimental IBD studies with clinical aspects of chronic gut inflammation. The Organizing Committee will select oral presentations and posters from submitted abstracts.

Faculty for the conference will be Dr. Matthew Grisham, Louisiana State University, Health Sciences Center and Dr. Fabio Cominelli, University of Virginia Health System

For more information go to www.the-aps.org or contact meetings@the-aps.org

Society for Mucosal Immunology – Application for Membership
Membership in the Society for Mucosal Immunology is open to all immunologists, physicians, dentists, veterinarians, biochemists, or other scientists who do research in or who have an active interest in mucosal immunology, and who have published at least one first-authored paper in a peer-reviewed journal. Society membership includes a subscription to Mucosal Immunology Update. Go to the online application form at www.scmucimm.org.
The SOCIETY FOR MUCOSAL IMMUNOLOGY

www.socmucimm.org

SMI
Announces the

12th INTERNATIONAL CONGRESS
OF MUCOSAL IMMUNOLOGY (ICMI)

June 25 - 30, 2005
Boston Marriott Copley Place
Boston, Massachusetts, USA

Hold these dates and plan on joining us in 2005 in Boston, the home of the American Revolution!

The 12th ICMI promises another great scientific experience plus an opportunity for families to enjoy one of the major historical cities of the USA. An excellent hotel has been selected, with both modern conference facilities and immediate access to restaurants, shopping, and the historical charms of old Boston. Special housing for students at local universities is being planned.

The scientific program will be chaired by Drs. Richard Blumberg and Lloyd Mayer. A call for abstracts will be released in September 2004.

More information will be sent to SMI members in due course, and the SMI Web site (www.socmucimm.org) will be updated over the coming months with the latest information.

For further information about SMI, including membership, visit the SMI Web site at www.socmucimm.org, or contact:

Society for Mucosal Immunology | 4350 East West Highway, Suite 401 | Bethesda, MD 20814
Tel: (301) 718-6516 | Fax: (301) 656-0989 | Email: smi@paimgmt.com

Society for Mucosal Immunology
4350 East West Highway
Suite 401
Bethesda, MD 20814-4411

ADDRESS SERVICE REQUESTED

FIRST CLASS