Arthur O. Anderson MD
Annotated Bibliography 2012 – 1972

Chapter: Scientific and Ethical Importance of Animal Models in Biodefense Research
James R Swearengen, Arthur O Anderson
Biodefense Research Methodology and Animal Models, Second Edition, CRC Press. Taylor & Francis Group, Boca Raton, FL 01/2012: pages 27-43; , ISBN: 978-1-4398-3632-3

Journal Article: Ultrastructural localization of extracellular matrix proteins of the lymph node cortex: evidence supporting the reticular network as a pathway for lymphocyte migration.
Gregg P Sobocinski, Katherine Toy, Walter F Bobrowski, Stephen Shaw, Arthur O Anderson, Eric P Kaldjian
BMC immunology. 01/2010; 11:42. · 2.53 Impact Factor
ABSTRACT: The lymph node (LN) is a crossroads of blood and lymphatic vessels allowing circulating lymphocytes to efficiently recognize foreign molecules displayed on antigen presenting cells. Increasing evidence indicates that after crossing high endothelial venules, lymphocytes migrate within the node along the reticular network (RN), a scaffold of fibers enwrapped by fibroblastic reticular cells (FRC). Light microscopy has shown that the RN contains specific extracellular matrix (ECM) proteins, which are putative molecular "footholds" for migration, and are known ligands for lymphocyte integrin adhesion receptors. To investigate whether ECM proteins of the RN are present on the outer surface of the FRC and are thus accessible to migrating lymphocytes, ultrastructural immunohistochemical staining of cynomolgus monkey LN was performed using antibodies to human ECM proteins that were successfully employed at the light microscopic level. The fibrillar collagens I and III were observed primarily within the reticular network fibers themselves. In contrast, the matrix proteins laminin, fibronectin, collagen IV, and tenascin were observed within the reticular fibers and also on the outer membrane surface of the FRC. These findings suggest a molecular basis for how the RN functions as a pathway for lymphocyte migration within the lymph node.

Journal Article: Reduced levels of protein tyrosine phosphatase CD45 protect mice from the lethal effects of Ebola virus infection.
Rekha G Panchal, Steven B Bradfute, Brian D Peyser, Kelly L Warfield, Gordon Ruthel, Douglas Lane, Tara A Kenny, Arthur O Anderson, William C Raschke, Sina Bavari
Cell host & microbe. 09/2009; 6(2):162-73. · 13.02 Impact Factor
ABSTRACT: Ebola virus (EBOV) infection of humans is a lethal but accidental dead-end event. Understanding resistance to EBOV in other species may help establish the basis of susceptibility differences among its hosts. Although rodents are resistant to EBOV, a murine-adapted variant is lethal when injected intraperitoneally into mice. We find that mice expressing reduced levels of the tyrosine phosphatase CD45 are protected against EBOV, whereas wild-type, CD45-deficient, or enzymatically inactive CD45-expressing mice succumbed to infection. Protection was dependent on CD8(+) T cells and interferon gamma. Reduced CD45-expressing mice retained greater control of gene expression and immune cell proliferation following EBOV infection, which contributed to reduced apoptosis, enhanced viral clearance, and increased protection against the virus. Together, these findings suggest that host susceptibility to EBOV is dependent on the delicate balance of immune homeostasis, which, as demonstrated here, can be determined by the levels of a single regulator.

Journal Article: Fibroblastic reticular cells and their role in viral hemorrhagic fevers.
Keith E Steele, Arthur O Anderson, Mansour Mohamadzadeh

Expert review of anti-infective therapy. 06/2009; 7(4):423-35. · 3.28 Impact Factor

ABSTRACT: Viral hemorrhagic fevers (VHFs) caused by Ebola, Marburg and Lassa viruses often manifest as multiple organ dysfunction and hemorrhagic shock with high mortality. These viruses target numerous cell types, including monocytes and dendritic cells, which are primary early targets that mediate critical pathogenetic processes. This review focuses on fibroblastic reticular cells (FRCs), another prevalent infected cell type that is known as a key regulator of circulatory and immune functions. Viral infection of FRCs could have debilitating effects in secondary lymphoid organs and various other tissues. FRCs may also contribute to the spread of these deadly viruses throughout the body. Here, we review the salient features of these VHFs and the biology of FRCs, emphasizing the potential role of these cells in VHFs and the rapid deterioration of immune and hemovascular sytems that are characteristic of such acute infections.

Journal Article: Reduced expression of CD45 protein-tyrosine phosphatase provides protection against anthrax pathogenesis.

Rekha G Panchal, Ricky L Ulrich, Steven B Bradfute, Douglas Lane, Gordon Ruthel, Tara A Kenny, Patrick L Iversen, Arthur O Anderson, Rick Gussio, William C Raschke, Sina Bavari

The Journal of biological chemistry. 04/2009; 284(19):12874-85. · 4.77 Impact Factor

ABSTRACT: The modulation of cellular processes by small molecule inhibitors, gene inactivation, or targeted knockdown strategies combined with phenotypic screens are powerful approaches to delineate complex cellular pathways and to identify key players involved in disease pathogenesis. Using chemical genetic screening, we tested a library of known phosphatase inhibitors and identified several compounds that protected Bacillus anthracis infected macrophages from cell death. The most potent compound was assayed against a panel of sixteen different phosphatases of which CD45 was found to be most sensitive to inhibition. Testing of a known CD45 inhibitor and antisense phosphorodiamidate morpholino oligomers targeting CD45 also protected B. anthracis-infected macrophages from cell death. However, reduced CD45 expression did not protect anthrax lethal toxin (LT) treated macrophages, suggesting that the pathogen and independently added LT may signal through distinct pathways. Subsequent, in vivo studies with both gene-targeted knockdown of CD45 and genetically engineered mice expressing reduced levels of CD45 resulted in protection of mice after infection with the virulent Ames B. anthracis. Intermediate levels of CD45 expression were critical for the protection, as mice expressing normal levels of CD45 or disrupted CD45 phosphatase activity or no CD45 all succumbed to this pathogen. Mechanism-based studies suggest that the protection provided by reduced CD45 levels results from regulated immune cell homeostasis that may diminish the impact of apoptosis during the infection. To date, this is the first report demonstrating that reduced levels of host phosphatase CD45 modulate anthrax pathogenesis.

Journal Article: Fibroblastic reticular cell infection by hemorrhagic fever viruses.

Keith E Steele, Arthur O Anderson, Mansour Mohamadzadeh

Immunotherapy. 03/2009; 1(2):187-97. · 1.85 Impact Factor

ABSTRACT: Viral hemorrhagic fevers (VHFs) often cause high mortality with high infectivity, multiorgan failure, shock and hemorrhagic diathesis. Fibroblastic reticular cells (FRCs) within secondary lymphoid organs provide a supporting scaffold to T-lymphocyte areas. These cells regulate the movement of various immune cells and soluble molecules that promote T-lymphocyte homeostasis. We previously reported Ebola virus infection of FRCs, but ascribed little significance to this finding. Here, we studied infection of FRCs by Ebola, Marburg and Lassa viruses. We demonstrate that FRCs, or the extracellular 'conduit' of the fibroblastic reticulum of nonhuman primates, are targets of Ebola, Marburg and Lassa viruses. Furthermore, we observed that FRC damage correlates temporally and spatially with lymphocyte damage and that FRCs serve as nidi of fibrin deposition. In addition, we show that nonhuman primate FRCs express p75 NGF receptor and tissue transglutaminase. Our data suggest that viral infection of FRCs may be crucial to the immunological dysfunction and coagulopathy characteristic of VHFs. We further propose that p75 NGF receptor and tissue transglutaminase may be involved in FRC-associated dysfunction during the course of infection.

Chapter: Ethical and Legal Dilemmas in Biodefense Research
Jeffrey E Stephenson, Arthur O Anderson
01/2007: pages 559-577; , ISBN: 978-0-16-079731-6

Journal Article: Designing a biocontainment unit to care for patients with serious communicable diseases: a consensus statement.
Philip W Smith, Arthur O Anderson, George W Christopher, Theodore J Cieslak, G J Devreede, Glen A Fosdick, Carl B Greiner, John M Hauser, Steven H Hinrichs, Kermit D Huebner, [.....], Chuck Rogge, Leo A Daly, Gary A Roselle, Mark E Rupp, Anthony R Sambol, Joann E Schaefer, John Sibley, Andrew J Streifel, Susanna G Von Essen, Kelly L Warfield
Biosecurity and bioterrorism : biodefense strategy, practice, and science.
02/2006; 4(4):351-65. · 1.94 Impact Factor
ABSTRACT: In spite of great advances in medicine, serious communicable diseases are a significant threat. Hospitals must be prepared to deal with patients who are infected with pathogens introduced by a bioterrorist act (e.g., smallpox), by a global emerging infectious disease (e.g., avian influenza, viral hemorrhagic fevers), or by a laboratory accident. One approach to hazardous infectious diseases in the hospital setting is a biocontainment patient care unit (BPCU). This article represents the consensus recommendations from a conference of civilian and military professionals involved in the various aspects of BPCUs. The role of these units in overall U.S. preparedness efforts is discussed. Technical issues, including medical care issues (e.g., diagnostic services, unit access); infection control issues (e.g., disinfection, personal protective equipment); facility design, structure, and construction features; and psychosocial and ethical issues, are summarized and addressed in detail in an appendix. The consensus recommendations are presented to standardize the planning, design, construction, and operation of BPCUs as one element of the U.S. preparedness effort.

Chapter: Scientific and Ethical Importance of Animal Models in Biodefense Research
Arthur O Anderson, James R Swearengen
Biodefense: Research Methodology and Animal Models, (Edited by) J.R. Swearengen, CRC Press, Boca Ratan, FL. 01/2006: pages 25-40; , ISBN: 978-0-8493-2836-7

Journal Article: Dendritic cells endocytose Bacillus anthracis spores: implications for anthrax pathogenesis.
Katherine C Brittingham, Gordon Ruthel, Rekha G Panchal, Claudette L Fuller, Wilson J Ribot, Timothy A Hoover, Howard A Young, Arthur O Anderson, Sina Bavari
Journal of immunology (Baltimore, Md. : 1950). 06/2005; 174(9):5545-52. · 5.79 Impact Factor
ABSTRACT: Phagocytosis of inhaled Bacillus anthracis spores and subsequent trafficking to lymph nodes are decisive events in the progression of inhalational anthrax because they initiate germination and dissemination of spores. Found in high frequency throughout the respiratory track, dendritic cells (DCs) routinely take up foreign particles and migrate to lymph nodes. However, the participation of DCs in phagocytosis and dissemination of spores has not been investigated previously. We found that human DCs readily engulfed fully pathogenic Ames and attenuated B. anthracis spores predominately by coiling phagocytosis. Spores provoked a loss of tissue-retaining chemokine receptors (CCR2, CCR5) with a concurrent increase in lymph node homing receptors (CCR7, CD11c) on the membrane of DCs. After spore infection, immature DCs displayed a mature phenotype (CD83(bright), HLA-DR(bright), CD80(bright), CD86(bright), CD40(bright)) and enhanced costimulatory activity. Surprisingly, spores

activated the MAPK cascade (ERK, p38) within 30 min and stimulated expression of several inflammatory response genes by 2 h. MAPK signaling was extinguished by 6 h infection, and there was a dramatic reduction of secreted TNF-alpha, IL-6, and IL-8 in the absence of DC death. This corresponded temporally with enzymatic cleavage of proximal MAPK signaling proteins (MEK-1, MEK-3, and MAP kinase kinase-4) and may indicate activity of anthrax lethal toxin. Taken together, these results suggest that B. anthracis may exploit DCs to facilitate infection.

Journal Article: Conduit for privileged communications in the lymph node.
Arthur O Anderson, Stephen Shaw
Immunity. 02/2005; 22(1):3-5. · 21.64 Impact Factor
ABSTRACT: A study by Sixt et al. in this issue of Immunity identifies conduit-associated dendritic cells whose privileged access to antigen arriving by the conduit enables uptake and processing of antigen within 90 min of antigen inoculation, long before the arrival of dendritic cells from skin.

Journal Article: Risk of occupationally acquired illnesses from biological threat agents in unvaccinated laboratory workers.
Janice M Rusnak, Mark G Kortepeter, Robert J Hawley, Arthur O Anderson, Ellen Boudreau, Edward Eitzen
Biosecurity and bioterrorism : biodefense strategy, practice, and science. 02/2004; 2(4):281-93. · 1.94 Impact Factor
ABSTRACT: Many vaccines for bioterrorism agents are investigational and therefore not available (outside of research protocol use) to all at-risk laboratory workers who have begun working with these agents as a result of increased interest in biodefense research. Illness surveillance data archived from the U.S. offensive biological warfare program (from 1943 to 1969) were reviewed to assess the impact of safety measures on disease prevention (including biosafety cabinets [BSCs]) before and after vaccine availability. Most laboratory-acquired infections from agents with higher infective doses (e.g., anthrax, glanders, and plague) were prevented with personal protective measures and safety training alone. Safety measures (including BSCs) without vaccination failed to sufficiently prevent illness from agents with lower infective doses in this high-risk research setting. Infections continued with tularemia (average 15/year), Venezuelan equine encephalitis (1.9/year), and Q fever (3.4/year) but decreased dramatically once vaccinations became available (average of 1, 0.6, and 0 infections per year, respectively). While laboratory-acquired infections are not expected to occur frequently in the current lower-risk biodefense research setting because of further improvements in biosafety equipment and changes in biosafety policies, the data help to define the inherent risks of working with the specific agents of bioterrorism. The data support the idea that research with these agents should be restricted to laboratories with experience in handling highly hazardous agents and where appropriate safety training and precautions can be implemented.

Journal Article: Redundancy in tumor necrosis factor (TNF) and lymphotoxin (LT) signaling in vivo: mice with inactivation of the entire TNF/LT locus versus single-knockout mice.
Dmitry V Kuprash, Marat B Alimzhanov, Alexei V Tumanov, Sergei I Grivennikov, Alexander N Shakhov, Ludmila N Drutskaya, Michael W Marino, Regina L Turetskaya, Arthur O Anderson, Klaus Rajewsky, Klaus Pfeffer, Sergei A Nedospasov
Molecular and cellular biology. 01/2003; 22(24):8626-34. · 5.53 Impact Factor
ABSTRACT: Homologous genes and gene products often have redundant physiological functions. Members of the tumor necrosis factor (TNF) family of cytokines can signal activation, proliferation, differentiation, costimulation, inhibition, or cell death, depending on the type and status of the target cell. TNF, lymphotoxin alpha (LTalpha), and LTbeta form a subfamily of a larger family of TNF-related ligands with their genes being linked within a compact 12-kb cluster inside the major histocompatibility complex locus. Singly TNF-, LTalpha-, and LTbeta-deficient mice share several phenotypic features, suggesting that TNF/LT signaling pathways may regulate overlapping sets of target genes. In order to directly

address the issue of redundancy of TNF/LT signaling, we used the Cre-loxP recombination system to create mice with a deletion of the entire TNF/LT locus. Mice with a triple LTbeta/TNF/LTalpha deficiency essentially manifest a combination of LT and TNF single-knockout phenotypes, except for microarchitecture of the spleen, where the disorder of lymphoid cell positioning and functional T- and B-cell compartmentalization is severer than that found in TNF or LT single-knockout mice. Thus, our data support the notion that TNF and LT have largely nonredundant functions in vivo.

Journal Article: Spatial and molecular organization of lymph node T cell cortex: a labyrinthine cavity bounded by an epithelium-like monolayer of fibroblastic reticular cells anchored to basement membrane-like extracellular matrix.
E P Kaldjian, J E Gretz, A O Anderson, Y Shi, S Shaw
International immunology. 11/2001; 13(10):1243-53. · 3.42 Impact Factor
ABSTRACT: Naive T cells encounter antigen-presenting cells within the cortex of lymph nodes to initiate primary immune responses. Within this T cell cortex is the reticular network (RN)--a system of collagen fibers and extracellular matrix (ECM) wrapped by fibroblastic reticular cells (FRC). We have investigated the distribution of various molecules, including ECM proteins and proteoglycans, in the T cell cortex of both human and rodent lymph node. We confirm and extend reports of matrix elements in the RN. In addition, we find that staining for the laminin-alpha3 chain and for tenascin reveals a 'hollow' reticular pattern, consistent with localization to the basement membrane-like covering of reticular fibers. In contrast, keratan sulfate is observed in a fine linear pattern within the RN, suggesting it is localized to the core of the fibers. Staining with the marker ER-TR7 indicates that FRC cover all identifiable ECM surfaces of the T cell cortex. Based on these findings and previous reports, we conclude that cortical lymphocytes migrate within a 'labyrinthine cavity' free of fibrillar ECM, distinguishing the T cell cortex from other loose connective tissues, and that the FRC lining of the cavity constitutes an epithelium-like boundary. We propose that this spatial organization facilitates ameboid leukocyte crawling along preformed paths of least resistance and that the basement membrane-like ECM of the FRC may facilitate fluid transport within the RN by limiting leakage from the fiber.

Journal Article: Generation of heterogeneous rabbit anti-DNP antibodies by gene conversion and hypermutation of rearranged VL and VH genes during clonal expansion of B cells in splenic germinal centers.
D Sehgal, E Schiaffella, A O Anderson, R G Mage
European journal of immunology. 01/2001; 30(12):3634-44. · 5.10 Impact Factor
ABSTRACT: The mechanisms described here account for development of the heterogeneous high-affinity anti-DNP antibodies that rabbits can produce. Rearranged immunoglobulin light and heavy chain genes from single DNP-specific splenic germinal center B cells were amplified by PCR. We found that in clonal lineages, rearranged V[kappa] and V[H] are further diversified by gene conversion and somatic hypermutation. The positive and negative selection of amino acids in complementarity-determining regions observed allows emergence of a variety of different combining site structures. A by-product of the germinal center reaction may be cells with sequences altered by gene conversion that no longer react with the immunizing antigen but are a source of new repertoire. The splenic germinal center would thus play an additional role in adults similar to that of the appendix and other gut-associated lymphoid tissues of young rabbits.

Journal Article: Lymph-borne chemokines and other low molecular weight molecules reach high endothelial venules via specialized conduits while a functional barrier limits access to the lymphocyte microenvironments in lymph node cortex.
J E Gretz, C C Norbury, A O Anderson, A E Proudfoot, S Shaw
The Journal of experimental medicine. 12/2000; 192(10):1425-40. · 13.85 Impact Factor
ABSTRACT: Lymph-borne, soluble factors (e.g., chemokines and others) influence lymphocyte

recirculation and endothelial phenotype at high endothelial venules (HEVs) in lymph node cortex. Yet the route lymph-borne soluble molecules travel from the subcapsular sinus to the HEVs is unclear. Therefore, we injected subcutaneously into mice and rats a wide variety of fluorophore-labeled, soluble molecules and examined their distribution in the draining lymph nodes. Rather than percolating throughout the draining lymph node, all molecules, including microbial lipopolysaccharide, were very visible in the subcapsular and medullary sinuses but were largely excluded from the cortical lymphocyte microenvironments. Exclusion prevailed even during the acute lymph node enlargement accompanying viral infection. However, low molecular mass (MW) molecules, including chemokines, did gain entry into the cortex, but in a very defined manner. Low MW, fluorophore-labeled molecules highlighted the subcapsular sinus, the reticular fibers, and the abluminal and luminal surfaces of the associated HEVs. These low MW molecules were in the fibers of the reticular network, a meshwork of collagen fibers ensheathed by fibroblastic reticular cells that connects the subcapsular sinus floor and the HEVs by intertwining with their basement membranes. Thus, low MW, lymph-borne molecules, including chemokines, traveled rapidly from the subcapsular sinus to the HEVs using the reticular network as a conduit.

Journal Article: A morphological and immunohistological study of the human and rabbit appendix for comparison with the avian bursa

Joseph F. Dasso, Harold Obiakor, Hanh Bach, Arthur O. Anderson, Rose G. Mage

Developmental & Comparative Immunology. 01/2000;

ABSTRACT: Diversification of the primary antibody repertoire occurs in young rabbit appendix. As a prelude to molecular investigation of whether human appendix has a similar role, we compared the lymphoid morphology and distribution of common B- and T-cell subsets in frozen and/or paraffin-embedded normal appendix specimens at various ages. IgA, IgM and IgG staining patterns were similar in frozen human and rabbit appendices. The elongated follicles of the young human and rabbit appendices regressed with age to resemble Peyer's patches. Although similar in morphology to the bursa, human and rabbit appendix follicles differ in that they do not involute completely with age and contain significant numbers of germinal center (GC) T cells although the number is low early in life. If the human appendix functions as a primary lymphoid organ, it may occur during the first few months of age when the GC T-cell density is low.

Journal Article: TNF and lymphotoxin beta cooperate in the maintenance of secondary lymphoid tissue microarchitecture but not in the development of lymph nodes.

D V Kuprash, M B Alimzhanov, A V Tumanov, A O Anderson, K Pfeffer, S A Nedospasov

Journal of immunology (Baltimore, Md. : 1950). 01/2000; 163(12):6575-80. · 5.79 Impact Factor

ABSTRACT: Inactivation of genes encoding members of TNF and TNF receptor families reveal their divergent roles in the formation and function of secondary lymphoid organs. Most lymphotoxin alpha (ltalpha)- and all lymphotoxin beta receptor (ltbetar)-deficient mice are completely devoid of lymph nodes (LNs); however, most lymphotoxin beta (ltbeta)-deficient mice develop mesenteric LNs. Tnf- and tnfrp55-deficient mice develop a complete set of LNs, while ltbeta/tnfrp55 double-deficient mice lack all LNs, demonstrating cooperation between LTbeta and TNFRp55 in LN development. Now we report that ltbeta/tnf double-deficient mice develop the same set of mucosal LNs as do ltbeta-deficient mice, suggesting that ligands other than TNF signal through TNFRp55 during LN development. These LNs retain distinct T and B cells areas; however, they lack follicular dendritic cell networks. Structures resembling germinal centers can be found in the LNs from immunized ltbeta-deficient mice but not in ltbeta/tnf double-deficient mice. Additionally, stromal components of the spleen and LNs appear to be more severely disturbed in ltbeta/tnf double-deficient mice as compared with ltbeta-deficient mice. We conclude that LTbeta and TNF cooperate in the establishment of the correct microarchitecture of lymphoid organs.

Journal Article: Gene conversion and hypermutation during diversification of VH sequences in developing splenic germinal centers of immunized rabbits.

E Schiaffella, D Sehgal, A O Anderson, R G Mage

Journal of immunology (Baltimore, Md. : 1950). 05/1999; 162(7):3984-95. · 5.79 Impact Factor

ABSTRACT: The young rabbit appendix and the chicken bursa of Fabricius are primary lymphoid organs where the B cell Ab repertoire develops in germinal centers (GCs) mainly by a gene conversion-like process. In human and mouse, V-gene diversification by somatic hypermutation in GCs of secondary lymphoid organs leads to affinity maturation. We asked whether gene conversion, somatic hypermutation, or both occur in rabbit splenic GCs during responses to the hapten DNP. We determined DNA sequences of rearranged heavy and light chain V region gene segments in single cells from developing DNP-specific GCs after immunization with DNP-bovine gamma-globulin and conclude that the changes at the DNA level that may lead to affinity maturation occur by both gene conversion and hypermutation. Selection was suggested by finding some recurrent amino acid replacements that may contribute increased affinity for antigen in the complementarity-determining region sequences of independently evolved clones, and a narrower range of complementarity-determining region 3 lengths at day 15. Some of the alterations of sequence may also lead to new members of the B cell repertoire in adult rabbits comparable with those produced in gut associated lymphoid tissues of young rabbits.

Journal Article: Gene-conversion in rabbit B-cell ontogeny and during immune responses in splenic germinal centers

Rose G Mage, Devinder Sehgal, Enrico Schiaffella, Arthur O Anderson

Veterinary Immunology and Immunopathology. 01/1999; · 2.08 Impact Factor

ABSTRACT: Combinatorial diversity is limited in rabbits because only a few VH genes rearrange. Most diversification of the primary repertoire is generated by somatic hypermutation and gene conversion-like changes of rearranged VH in B cells that migrate to appendix and other gut associated lymphoid tissues (GALT) of young rabbits. The changes are referred to as gene conversion-like because the non-reciprocal nature of the alterations introduced has not yet been demonstrated. There are many similarities between rabbits and chickens in how their B cells develop and diversify their repertoires. However, although the majority of rabbit B cells may have rearranged and diversified their V genes early in life, some B cells in adult rabbits have rearranged VH sequences that are identical or nearly identical to germline sequences. We found these cells in splenic germinal centers (GC) on days 7 and 10 after immunization of normal adult rabbits with DNP-BGG. By day 15, all rearranged VH sequences were diversified. We find an overall pattern of splenic precursor cells whose germline or near germline sequences change both by gene conversion and point mutations during early divisions and mainly by point mutations during later divisions. These events, in parallel with diversification of light chain sequences, may produce the diverse combining sites that serve as substrates for further affinity maturation by selection either within GC or later among emigrant cells in sites such as bone marrow. Some of the sequences altered by gene conversion in splenic germinal centers may also produce new members of the B-cell repertoire in adult rabbits comparable to those produced in GALT of neonatal rabbits.

Journal Article: Analyses of single B cells by polymerase chain reaction reveal rearranged VH with germline sequences in spleens of immunized adult rabbits: implications for B cell repertoire maintenance and renewal.

D Sehgal, E Schiaffella, A O Anderson, R G Mage

Journal of immunology (Baltimore, Md. : 1950). 12/1998; 161(10):5347-56. · 5.79 Impact Factor

ABSTRACT: We used PCR to amplify rearranged VHDJH genes in single cells collected by micromanipulation from splenic germinal centers of immunized adult rabbits. In the course of the study, the objective of which was to analyze diversification of rearranged VHDJH sequences, we were surprised to find cells 7 and 10 days after immunization with rearranged VH1a2 as well as a-negative (y33 and x32) sequences that were identical or close to germline (10 or fewer changes). About 58% (82/140) of the

sequences had unique CDR3 regions and were unrelated. In seven different germinal centers, we found one to four different clones with two to seven members. Clonally related cells underwent diversification by hypermutation and gene conversion. We found that contrary to published reports, adult rabbits indeed have newly diversifying B cell receptors in splenic germinal centers. The attractive idea that the rabbit, like the chicken, develops its B cell repertoire early in life and depends upon self-renewing cells in the periphery to maintain its B lymphocyte pool throughout life, is challenged by the current finding. Although a major population of B lymphocytes may be generated early in life, diversified extensively, and maintained by self-renewal in the periphery, some sources of cells with sequences close to germline do exist in adult rabbits and appear in the developing germinal centers. Although considerable repertoire diversity is generated in young rabbits, mechanisms for continued generation of B cell receptor diversity are retained in adult life, where they may confer survival advantage.

Journal Article: HIV-induced decline in blood CD4/CD8 ratios: viral killing or altered lymphocyte trafficking?
Yvonne J. Rosenberg, Arthur O. Anderson, Reinhard Pabst
Immunology Today. 01/1998;
ABSTRACT: During HIV infection, CD4+-cell numbers and CD4/CD8 ratios decline in the blood. This is usually attributed to direct viral killing or to other indirect mechanisms. However, current models generally assume that such changes in the blood are representative of changes in total CD4+-cell numbers throughout the body. This article discusses the importance of alterations in CD4+- and CD8+-cell migration in regulating blood lymphocyte levels and questions the extent of virus-mediated CD4+-cell destruction.

Chapter: Mucosal Vaccines For the Military
M.T. Dertzbaugh, M.K. Hart, M.L.M. Pitt, M. Kende, A.O. Anderson
Handbook of Mucosal Immunology, 2nd Ed. P.L. Ogra et al eds, Academic Press, San Diego, CA Pp. 839-849;

Journal Article: Pathology of experimental Ebola virus infection in African green monkeys. Involvement of fibroblastic reticular cells.
K J Davis, A O Anderson, T W Geisbert, K E Steele, J B Geisbert, P Vogel, B M Connolly, J W Huggins, P B Jahrling, N K Jaax
Archives of pathology & laboratory medicine. 09/1997; 121(8):805-19. · 2.58 Impact Factor
ABSTRACT: Ebola virus has been responsible for explosive lethal outbreaks of hemorrhagic fever in both humans and nonhuman primates. Previous studies showed a predilection of Ebola virus for cells of the mononuclear phagocyte system and endothelial cells. To examine the distribution of lesions and Ebola virus antigen in the tissues of six adult male African green monkeys (Cercopithecus aethiops) that died 6 to 7 days after intraperitoneal inoculation of Ebola-Zaire (Mayinga) virus. Tissues were examined histologically, immunohistochemically, and ultrastructurally. A major novel finding of this study was that fibroblastic reticular cells were immunohistochemically and ultrastructurally identified as targets of Ebola virus infection. The role of Ebola virus-infected fibroblastic reticular cells in the pathogenesis of Ebola hemorrhagic fever warrants further investigation. This is especially important because of recent observations indicating that fibroblastic reticular cells, along with the reticular fibers they produce, maximize the efficiency of the immune response.

Journal Article: Cords, channels, corridors and conduits: critical architectural elements facilitating cell interactions in the lymph node cortex
J. Elizabeth Gretz, Arthur O. Anderson, Stephen Shaw
Immunological Reviews. 03/1997; 156(1):11 - 24. · 11.15 Impact Factor
ABSTRACT: The lymph node cortex is a critical site for encounter between recirculating T cells and their specific antigens. Due to its extreme plasticity, little is understood of the underlying functional unit of the

lymph node cortex, the paracortical cord. The idealized paracortical cord (approximately 100 nm by 1000 µm) stretches from a medullary cord to the base of a B-cell follicle. In cross-section, a cord can be visualized as a set of nested cylinders consisting of spaces bounded by cells. The spaces are: i) the lumen of the high endothelial venule (HEV), ii) perivenular channels - narrow potential spaces (0.1 µm) tightly encircling the HEV, iii) corridors – broad spaces (10–15 µm) constituting the majority of the parenchyma, and iv) the cortical sinus. In addition to these spaces for cell traffic, the conduit (fifth space) is a special delivery system for the transit of soluble factors to the HEV and emigrating lymphocytes. The cellular barriers between these spaces are high endothelium, tibroblastic reticular cells, or sinus-lining cells. This review describes the spaces of the paracortical cord and their cellular boundaries, outlines the movement of cells and fluids through these spaces, and discusses how this anatomy affects the efficiency of surveillance by T cells.

Chapter: New Technologies for Producing Systemic and Mucosal Immunity by Oral Immunizatioin: Immunoprophylaxis in Meals, Ready-to-Eat

Arthur O Anderson

Emerging Technologies for Nutrition Research, National Academy Press, Washington D.C., 01/1997: pages 451-500;

Journal Article: Sophisticated strategies for information encounter in the lymph node: the reticular network as a conduit of soluble information and a highway for cell traffic.

J E Gretz, E P Kaldjian, A O Anderson, S Shaw

Journal of immunology (Baltimore, Md. : 1950). 08/1996; 157(2):495-9. · 5.79 Impact Factor

ABSTRACT: The lymph node is the crossroad in which soluble signals and cells carried by lymph meet lymphocytes emigrating from blood. Efficient interactions among these elements depend on the reticular network, which comprises reticular fibers, related extracellular matrix components, and associated fibroblastic reticular cells. This network provides a three-dimensional scaffold for attachment of APCs and pathways for the migration of T cells to these APCs. In addition, the network constitutes a miniature conduit system for bulk flow delivery of soluble molecules to distinct sites in the paracortex, particularly the high endothelial venule. The delivered mediators, such as chemokines, regulate the phenotype of the high endothelial venule, the recruitment of lymphocytes, and the behavior of the recruited lymphocytes. Thus, the reticular network is a multifunctional infrastructure that facilitates encounters of cells with other cells and factors necessary for effective and efficient immune surveillance.

Journal Article: Orchestrated information transfer underlying leukocyte endothelial interactions.

K Ebnet, E P Kaldjian, A O Anderson, S Shaw

Annual review of immunology. 02/1996; 14:155-77. · **52.76 Impact Factor**

ABSTRACT: The specificity and efficiency of leukocyte binding to endothelial cells (ECs) depends on coordinated information transfer from the underlying tissue to endothelium and from there to the leukocyte. We address three distinct information-transfer points in this system: 1, How does the leukocyte read information from the EC? This process is best accounted for by the paradigm of a multi-step adhesion cascade optimized for rapid information readout; it consists of primary adhesion (rolling/tethering), triggering, and strong adhesion. Recent studies with T cells, monocytes, and eosinophils confirm the generality of the paradigm. The concept of primary adhesion has been expanded to involve not only the selectins, but also certain integrins; furthermore, it depends on receptor concentration on leukocyte microvilli. 2. What information from the underlying tissue does the EC transform into signals for the leukocytes? And what rules govern that process? We illustrate the principles with chemokines, believed to participate in the triggering step. The endothelium displays chemokines either (a) directly by "posting" them from other cells or (b) by integrating a variety of tissue and environmental signals and "relaying" that information by producing its own chemokines and surface

adhesion molecules. The rules for this endothelial transduction include specificity coupled with redundancy, amplification, synergy, and coordinated induction of ensembles of molecules. Finally, 3. How does the relevant information reach the endothelium? Simple diffusion is sufficient to deliver signals from cells close to the vessel. However, longer range soluble mediator transport appears to be facilitated by fiber bundles, particularly those ensheathed by fibroblastic reticular cells in the lymph node.

Chapter: Lymphocyte Trafficking
Arthur O Anderson, Stephen Shaw
CLINICAL IMMUNOLOGY,Principals and Practice. R.R. Rich, T.A. Fleisher, B.D. Schwartz, W.T. Shearer, and W. Strober (eds.). MOSBY-Year Book, inc. St. Louis, MO, 01/1996: pages 39-49;

Journal Article: Normal human sweat contains interleukin-8.
A P Jones, L M Webb, A O Anderson, E J Leonard, A Rot
Journal of leukocyte biology. 04/1995; 57(3):434-7. · 4.99 Impact Factor
ABSTRACT: Sweating in humans is induced by physical or emotional stress, which raises the possibility that sweating may relate to host defense. We therefore asked whether human eccrine sweat attracts leukocytes and found that it is chemotactic for human neutrophils. This activity was due to several chemoattractants, one of which was interleukin-8 (IL-8). Using immunohistochemistry and in situ hybridization IL-8 and its mRNA have been detected in sweat gland epithelium, indicating that IL-8 is produced in situ. This establishes a pattern of physiological IL-8 secretion by exocrine glands and suggests that, in addition to its role as a major inflammatory mediator, IL-8 also has physiological homeostatic functions.

Journal Article: Morphologic and functional alterations of mucosal T cells by cholera toxin and its B subunit.
C O Elson, S P Holland, M T Dertzbaugh, C F Cuff, A O Anderson
Journal of immunology (Baltimore, Md. : 1950). 03/1995; 154(3):1032-40. · 5.79 Impact Factor
ABSTRACT: Despite the mucosal immunogenicity and adjuvanticity in vivo of cholera toxin (CT), both CT and CT B subunit are strong inhibitors of T cell activation in vitro. This study asked whether such T cell inhibition is relevant to the mucosal effects of CT in vivo. The activation of T cells pulsed in vitro for only 15 to 120 min with CT or CT B subunit, respectively, was inhibited, consistent with the expected short exposure times in vivo. Although both CD8+ and CD4+ T cells were inhibited in vitro, CD8+ T cells bound more toxin and were inhibited to a greater degree than were CD4+ T cells. Intestinal gavage of mice with 10 micrograms CT did not alter the overall composition of Peyer's Patch, mesenteric lymph node, or spleen but did cause a marked depletion of intraepithelial lymphocytes, mainly CD8+ T cells, and of lymphocytes in the dome epithelium over Peyer's Patch. To determine whether such inhibition of T cells was functionally relevant in vivo, T cells from mice fed keyhole limpet hemocyanin (KLH) were adoptively transferred into naive recipients, who were then parenterally immunized. T cells from mice fed KLH alone inhibited both the systemic IgG and secretory IgA anti-KLH response, but T cells from mice fed KLH plus CT did not, indicating that mucosally applied CT was able to abrogate the induction of this suppressor T cell. We conclude that one of the mechanisms of CT's mucosal effects in vivo is the inhibition of certain mucosal T cell functions and alteration of the regulatory T cell environment in gut-associated lymphoid tissue.

Journal Article: Rabbit IgH sequences in appendix germinal centers: VH diversification by gene conversion-like and hypermutation mechanisms.
P D Weinstein, A O Anderson, R G Mage
Immunity. 12/1994; 1(8):647-59. · **21.64 Impact Factor**
ABSTRACT: Although the rabbit IgH locus contains approximately 100 VH genes, the majority of B cells rearrange VH1. To produce a primary repertoire containing a sufficient number of protective antibodies,

rearranged VH1-DH-JH sequences may diversify within rabbit B cells in an organ that functions like a chicken bursa, sheep ileal Peyer's patch, or both. It was suggested many years ago that the rabbit appendix could be a bursal equivalent. To reexamine this possibility, we analyzed rearranged heavy chain variable region sequences in B cells from light and dark zones of appendix germinal centers from 6-week-old rabbits. Our findings indicate that antibody diversification occurs by gene conversion-like and somatic hypermutation mechanisms in appendix germinal centers of young rabbits.

Journal Article: Long-term lymphoid reconstitution of SCID mice suggests self-renewing B and T cell populations in peripheral and mucosal tissues.

D M Hilbert, A O Anderson, K L Holmes, S Rudikoff

Transplantation. 09/1994; 58(4):466-75. · 4.00 Impact Factor

ABSTRACT: Peyer's patch, peripheral lymph node, and mesenteric lymph node cells were transferred to immunodeficient SCID mice to assess the long-term (150-300 days) potential of these cells to repopulate the host's immune system. Results demonstrate that, irrespective of donor population, total serum Ig and isotype distribution appear normal within 4 weeks of reconstitution and remain at normal levels for up to one year following cell transfer. At the cellular level, each donor population reconstitutes splenic T and B cell compartments in a progressive and quantitatively indistinguishable manner. Immunohistological analyses of reconstituted mice indicate that, although some qualitative differences are evident, normal splenic composition and architecture are observed. In contrast, gut reconstitution varies significantly with donor population. Peyer's patch cells yield normal-appearing gut tissue with extensive infiltration of the lamina propria and intraepithelial compartments by T cells and IgA-secreting plasma cells. Peripheral lymph node cells give rise to T cells found almost exclusively in the lamina propria, while IgA secreting plasma cells are rarely detected. The course and extent of reconstitution further suggest that all donor populations contain long-lived T and B cells as well as self-renewing lymphocytes capable of extensive expansion. This latter observation has potentially important implications for both transplantation biology and gene therapy applications.

Journal Article: Serum levels of alpha and gamma interferons in hemorrhagic fever with renal syndrome.

T Krakauer, J W Leduc, J C Morrill, A O Anderson, H Krakauer

Viral immunology. 02/1994; 7(2):97-101. · 1.97 Impact Factor

ABSTRACT: Hemorrhagic fever with renal syndrome is an acute viral disease caused by Hantavirus. On the basis of clinical observation, the illness is divided into five sequential stages: febrile, hypotensive, oliguric, diuretic, and convalescent. Because interferons can be induced by viruses, and because their stimulating effects on immune cells can alter the course of viral infections, we examined the presence of alpha interferon (IFN-alpha) and gamma interferon (IFN-gamma) in 276 serum samples collected from 110 patients during the Korean Conflict. We tested these sera for IFN-alpha by bioassay with bovine kidney MDBK cells, and for IFN-gamma by a sandwich ELISA with antibodies specific for human IFN-gamma. We found variable, but persistently elevated levels of IFN-gamma throughout the various phases of the disease, which suggested persistent immune activation through convalescence. Moderate levels of IFN-alpha were found in all stages of infection.

Journal Article: The appendix functions as a mammalian bursal equivalent in the developing rabbit.

P D Weinstein, R G Mage, A O Anderson

Advances in experimental medicine and biology. 02/1994; 355:249-53. · 1.09 Impact Factor

ABSTRACT: In this paper we present genomic DNA sequence and histological evidence that the appendix is a site of diversification of the rabbit's primary antibody repertoire. By 6 weeks after birth, the B cell follicular regions of the rabbit appendix and the distribution of the resident lymphoid cells bear a strong morphological resemblance to similar regions within two primary lymphoid tissues, the chicken bursa and the sheep ileal Peyer's patch. However, similarities between the rabbit appendix, chicken bursa and sheep ileal Peyer's patch end as these animals reach adulthood. The rabbit appendix undergoes

morphological and cellular distribution changes as it matures taking on the appearance of a secondary lymphoid tissue, while the sheep ileal Peyer's patch and the chicken bursa both involute. We determined DNA sequences of PCR amplified rearranged variable region genes from germinal center B cells of 6 week old rabbits isolated from several different appendix dark zones and light zones. There was a trend toward a higher degree of diversification from the germ-line VH gene DNA sequence in dark zones than light zones. It is likely that both gene conversion and somatic hypermutation are responsible for the nucleotide changes we observed. Our findings suggest that the rabbit appendix functions as a mammalian bursal equivalent early in development. As the rabbit matures, the appendix appears to evolve into a secondary lymphoid tissue resembling secondary GALT in appearance and possibly in function.

Journal Article: Long-term thymic reconstitution by peripheral CD4 and CD8 single-positive lymphocytes.

D M Hilbert, K L Holmes, A O Anderson, S Rudikoff

European journal of immunology. 11/1993; 23(10):2412-8. · 5.10 Impact Factor

ABSTRACT: Significant immigration of peripheral T cells into SCID thymus was observed following reconstitution with normal Peyer's patch, mesenteric lymph node or peripheral lymph node cells. Immunohistologic and flow cytometric analyses reveal that T cells from these tissues are found in the thymus for as long as 177 days and can account for up to 67% of intrathymic cells. The returning cells express the CD3/T cell receptor alpha/beta complex, indicative of mature cells, and are equally divided among helper (CD4+CD8-) and cytotoxic (CD4-/CD8+) phenotypes. The immigration of peripheral T cells is not accompanied by the appearance of immature, double-positive (CD4+CD8+) thymocytes as seen in similar reconstitutions using bone marrow. Taken together, these results suggest that peripheral T cells from a variety of lymphoid organs may regularly re-enter the thymus and, thus, possibly play a role in normal thymic development.

Journal Article: In vitro culture of primary plasmacytomas requires stromal cell feeder layers.

A Degrassi, D M Hilbert, S Rudikoff, A O Anderson, M Potter, H G Coon

Proceedings of the National Academy of Sciences of the United States of America. 04/1993; 90(5):2060-4. · 9.68 Impact Factor

ABSTRACT: Attempts to grow primary murine plasmacytomas in vitro have, to date, been largely unsuccessful. In this study, we demonstrate that long-term in vitro growth of primary plasmacytomas is accomplished by using feeder layers composed of stromal cells from the initial site of plasmacytomagenesis. The early neoplastic lines established in this manner are dependent on physical contact with the stromal layer, which is mediated in part by CD44, for growth and survival. The stromal cells provide at least two stimuli for the plasma cells, one being interleukin 6 and the second, of unknown nature, resulting from direct physical interaction that cannot be replaced by soluble factors. These plasma cell lines have been passaged for as long as 20 months yet still maintain characteristics associated with primary plasmacytomas as they will grow in vivo only in pristane-primed animals, indicating a continued dependence on the pristane-induced microenvironment characteristic of early-stage tumors. The ability to grow primary plasmacytomas in culture and maintain their "primary" properties provides a model system for detailed analysis of early events in plasma cell tumor progression involving neoplastic cells completely dependent on physical contact with a stromal feeder layer for survival and expansion.

Journal Article: T cell adhesion to endothelium: the FRC conduit system and other anatomic and molecular features which facilitate the adhesion cascade in lymph node

Arthur O. Anderson, Stephen Shaw

Seminars in Immunology. 01/1993; 5(4):271-282. · 6.39 Impact Factor

ABSTRACT: Since T cell surveillance depends on movement from blood into tissue and back again, rapid, efficient and selective T cell adhesion to vascular endothelium is essential. This adhesion involves

a multistep cascade clarified by a recent consensus model: (1) initial tethering by selectin-mediated interactions; (2) triggering of adhesive function of T cell integrins by ligands at or near the endothelial surface; and (3) strong adhesion mediated by T cell integrins. We recapitulate this model, particularly as it pertains to the lymph node, and explore additional molecular and anatomic elements which contribute to the effectiveness of the adhesion cascades at that site: (1) importance of cytokines/soluble mediators as triggering ligands; (2) role of glycocalyx and proteoglycans on high endothelial venule (HEV) endothelium in capturing and presenting triggering cytokines; (3) remarkable function of what we designate the 'fibroblastic reticular cell (FRC) conduit system' in rapidly transporting cytokines to the HEV; (4) importance of the unique anatomy of the flap-valve junctions between HEV endothelium in enabling intravasation of cytokines and transmigration of lymphocytes. Taken together, these molecular mechanisms and these three anatomic features of lymph node facilitate extremely efficient lymphocyte traffic to this site critical for T cell-mediated immune responses. Analogous mechanisms contribute to T cell interaction with endothelium at other sites.

Journal Article: Efficacy of a Rift Valley fever virus vaccine against an aerosol infection in rats.
G W Anderson, J O Lee, A O Anderson, N Powell, J A Mangiafico, G Meadors
Vaccine. 11/1991; 9(10):710-4. · 3.77 Impact Factor
ABSTRACT: The formalin-inactivated Rift Valley fever virus (RVFV) vaccine, TSI-GSD-200, was administered subcutaneously to highly susceptible adult Wistar-Furth rats (LD50-1 p.f.u., ZH501 strain). Vaccine was administered on days 0, 7 and 28, the same time course used for at-risk personnel. Six months postimmunization, when the serum plaque-reduction neutralization titre (PRNT)80 had declined to low or undetectable levels, rats were challenged with 4.4 log10 p.f.u. of the virulent ZH501 strain in a nose-only dynamic aerosol apparatus. Ninety-seven per cent (33/34) of the non-vaccinated control rats died. In contrast, only 32% (33/105) of the vaccinated animals died. In vaccinated rats that succumbed, there was a doubling of the mean time to death and the cause of death shifted from hepatitis to encephalitis. Rats with a PRNT80 of greater than or equal to 1:40 were protected from clinical disease and histological evidence of hepatic or encephalitic lesions. While the precise mechanisms of immunity against aerosol challenge remain unresolved, here the serum PRNT titre correlated with protection.

Chapter: Tissue-Specific Expression of e and a messenger ribonucleic acid in allergy-prone C3H mice
AO Anderson, MLM Pitt, JD Cooley, M Vahey
Lymphatic Tissues and In vivo Immune Responses, S. Ezine, S. Berrick-Aknin and B. Imhof (eds), Marcel Dekker, N.Y., 01/1991: pages 509-512;

Chapter: Antigen-binding Fragments of Antibodies, Antiimmunoglobulins and Immune Homeostasis
A. J. Kulberg, A. O. Anderson
PROBLEMS OF INFECTOLOGY, MEDICINE, Korrekthb Abtopob, Moscow 01/1991: pages 241-251;

Journal Article: Properties of monocyte chemotactic and activating factor (MCAF) purified from a human fibrosarcoma cell line.
C O Zachariae, A O Anderson, H L Thompson, E Appella, A Mantovani, J J Oppenheim, K Matsushima
The Journal of experimental medicine. 07/1990; 171(6):2177-82. · **13.85 Impact Factor**
ABSTRACT: A monocyte chemotactic and activating factor (MCAF) has been purified from TNF-stimulated 8387 human fibrosarcoma cell line-conditioned media. The purified MCAF showed microheterogeneity yielding two bands on SDS-PAGE analysis. Fibrosarcoma-derived MCAF specifically

competed with THP-1 (a human monocytic cell line)-derived 125I-labeled MCAF in binding to human PBMC, whereas a similar basic heparin-binding leukocyte chemoattractant, IL-8, did not. The purified MCAF stimulated superoxide anion and N-acetyl beta-D glucosaminidase-releasing activity in human monocytes, as well as monocyte cytostatic augmenting activity against tumor cells and chemotactic activity for monocytes. When injected subcutaneously into Lewis rat ears, the purified human MCAF also induced considerable in vivo local monocyte infiltration beginning at 3 h and becoming maximal at 18 h. In conclusion, the data presented in this paper indicate that MCAF is a potent activator of monocytes as well as a monocyte recruitment factor that acts through receptors that are specific for this novel molecule. This novel cytokine might have an important role in tumor growth control due to its ability to attract and activate monocytes.

Journal Article: In vitro culture of a primary plasmacytoma that has retained its dependence on pristane conditioned microenvironment for growth.
A Degrassi, D M Hilbert, A O Anderson, M Potter, H G Coon
Current topics in microbiology and immunology. 02/1990; 166:71-4. · 4.93 Impact Factor

Journal Article: Proinflammatory cytokines interleukin 1 and tumor necrosis factor induce cytokines that are chemotactic for neutrophils, T cells and monocytes.
C Larsen, C Zachariae, N Mukaida, A Anderson, M Yamada, J Oppenheim, K Matsushima
Progress in clinical and biological research. 02/1990; 349:419-31.

Chapter: Structure and Organization of the Lymphatic System
Arthur O Anderson
Immunophysiology: The role of cells and cytokines in immunity and inflammation. Oppenheim, J. J. and E. Shevach (eds.), Oxford University Press, NY 01/1990: pages 14-45;

Chapter: Production of alpha heavy chain mRNA in mucosal and lymphoid tissue of various strains of mice
MLM Pitt, M Vahey, JD Cooley, AO Anderson
Advances in Mucosal Immunology. T. T. MacDonald and S. J. Challacombe (eds.), Kluwer Academic Publishers, Lancaster, England. 01/1990: pages 306-307;

Chapter: C3 H mouse model of genetic predisposition to vaccine induced allergy
AO Anderson, MLM Pitt, S Lavu, JD Cooley, M Vahey
Advances in Mucosal Immunology. T. T. MacDonald and S. J. Challacombe (eds.), Kluwer Academic Publishers, Lancaster, England. 01/1990: pages 390-393;

Chapter: The Potential Role of Monocyte Chemotactic and Activating Factor (MCAF) in Tumor Growth
C. O. C. Zachariae, H. L. Thompson, A. O. Anderson, A. Mantovani, J. J. Oppenheim, K. Matsushima
Molecular and Cellular Biology of Cytokines. Wiley-Liss, Inc., 01/1990: pages 369-374;

Chapter: An Interleuken-1/Tumor Necrosis Factor Inducible Inflammatory Cytokine, Interleukin-8

K. Matsushima, C.G. Larsen, A. K. Samanta, N. Mukaida, A.O. Anderson, J. J. Oppenheim
Tumor Necrosis Factor: Structure, Mechanism of Action, Role in Disease and Therapy. Bonavida, B. and G. Granger (eds.), Basel, Switzerland; 01/1990: pages 140-145;

Journal Article: Production of interleukin-8 by human dermal fibroblasts and keratinocytes in response to interleukin-1 or tumour necrosis factor.
C G Larsen, A O Anderson, J J Oppenheim, K Matsushima
Immunology. 10/1989; 68(1):31-6. · 3.32 Impact Factor
ABSTRACT: Cultured normal human fibroblasts were stimulated to produce neutrophil-activating protein/interleukin-8 (IL-8) in response to IL-1 alpha (0.1-1000 U/ml) or tumour necrosis factor (TNF) alpha (0.1-1000 U/ml). Induction of mRNA for IL-8 in fibroblasts was rapid (within 30 min) and maximal responses were obtained with either 100 U/ml IL-1 alpha or 100 U/ml TNF alpha. Expression of mRNA for IL-8 was accompanied by the production of high levels of neutrophil chemotactic activity. IL-1 alpha (1000 U/ml), but not TNF alpha, induced mRNA for IL-8 in cultured normal human keratinocytes. The relevance of production of IL-8 by these cell types was evaluated further by comparing the local inflammatory effects of IL-1 alpha, TNF alpha and IL-8. Intradermal injection of either recombinant IL-8, IL-1 alpha or TNF alpha lead to a similar in vivo effect, i.e. dose-dependent accumulation of lymphocytes and polymorphonuclear leucocytes at sites of injection. The in vivo attraction of neutrophils and lymphocytes to the site of injection by TNF or IL-1 (which is not chemotactic for neutrophils or lymphocytes in vitro), may be partly mediated by locally produced IL-8. Thus, IL-8 may be a vital participant in the cascade of interacting cytokines that is induced by tissue injury and immunologically induced inflammation.

Journal Article: The neutrophil-activating protein (NAP-1) is also chemotactic for T lymphocytes.
C G Larsen, A O Anderson, E Appella, J J Oppenheim, K Matsushima
Science (New York, N.Y.). 04/1989; 243(4897):1464-6. · **31.20 Impact Factor**
ABSTRACT: T lymphocyte chemotactic factor (TCF) was purified to homogeneity from the conditioned media of phytohemagglutinin-stimulated human blood mononuclear leukocytes by a sequence of chromatography procedures. The amino-terminal amino acid sequence of the purified TCF showed identity with neutrophil-activating protein (NAP-1). Both TCF and recombinant NAP-1 (rNAP-1) were chemotactic for neutrophils and T lymphocytes in vitro supporting the identity of TCF with NAP-1. Injection of rNAP-1 into lymphatic drainage areas of lymph nodes in Fisher rats caused accelerated emigration of only lymphocytes in high endothelial venules. Intradermal injection of rNAP-1 caused dose-dependent accumulation of neutrophils and lymphocytes.

Journal Article: Biological and biochemical properties of a chemotactic cytokine
J. J. Oppenheim, C. G. Larsen, A. K. Samanta, A. O. Anderson, K. Matsushima
Advances in Science and Technology. 01/1989; 26:43-51.

Journal Article: Direct transdiaphragmatic traffic of peritoneal macrophages to the lung.
M L Pitt, A O Anderson
Advances in experimental medicine and biology. 02/1988; 237:627-32. · 1.09 Impact Factor

Journal Article: Mucosal priming alters pathogenesis of Rift Valley fever.
A O Anderson, L F Snyder, M L Pitt, O L Wood
Advances in experimental medicine and biology. 02/1988; 237:717-23. · 1.09 Impact Factor

Journal Article: Endocytic stripping of ligands from migrant lymphocytes in high endothelial venules (HEV): implications for immunomodulation vs viral pathogenesis.
A O Anderson, J M Ward
Advances in experimental medicine and biology. 02/1988; 237:525-31. · 1.09 Impact Factor

Journal Article: Studies on anti-viral mucosal immunity with the lipoidal amine adjuvant avridine.
A O Anderson, O L Wood, A D King, E H Stephenson
Advances in experimental medicine and biology. 02/1987; 216B:1781-90. · 1.09 Impact Factor

Journal Article: Reovirus infection in adult mice: the virus hemagglutinin determines the site of intestinal disease.
D H Rubin, M A Eaton, A O Anderson
Microbial pathogenesis. 03/1986; 1(1):79-87. · 1.94 Impact Factor
ABSTRACT: Reovirus type 1, strain Lang, and type 3, strain Dearing, induced site-specific intestinal lesions in the adult mouse after intravenous inoculation. Reovirus type 1 caused inflammation and epithelial changes such as loss of nuclear polarity, villus blunting and crypt hyperplasia restricted to the ileum. In contrast, reovirus type 3 induced duodenitis, jejunitis, and ulcerative colitis. In the duodenum and jejunum, the epithelial cells appeared normal, but hemorrhage and inflammation in the lamina propria was present. In the colon, superficial ulceration, crypt abscesses, and intraluminal hemorrhage was observed. Segregation analysis using reassortant clones derived from reoviruses 1 and 3, suggested the viral hemagglutinin, encoded by genome segment S1, to be the major viral determinant of site specific intestinal disease following intravenous inoculation.

Journal Article: Inhibition of plasmacytoma development in BALB/c mice by indomethacin.
M Potter, J S Wax, A O Anderson, R P Nordan
The Journal of experimental medicine. 06/1985; 161(5):996-1012. · **13.85 Impact Factor**
ABSTRACT: Indomethacin given continuously in the drinking water (20 micrograms/ml) to BALB/cAn pi mice during the latent period of pristane-induced plasmacytoma development dramatically reduced the plasmacytoma incidence from 34.9 to 2.2%. Additionally, indomethacin given from day 0 to 120 or begun as late as 60 d after a single injection of 1.0 ml pristane was also highly effective in reducing the development of plasmacytomas. Indomethacin treatment did not prevent the formation of a peritoneal inflammatory exudate or peritoneal oil granulomatous tissue, although it had a mild inhibitory effect on the intensity of the cellular inflammation, particularly after extensive treatment of greater than 100 d. Indomethacin treatment reduced the incidence of arthritis by 50%. A major effect of indomethacin treatment was a reduction in the appearance of microscopic plasmacytomas that appear in the oil granuloma before plasmacytomas can be detected by routine sampling of the peritoneal exudate. Between days 116 and 181, 16 of 20 mice given 0.5 ml pristane were found to have foci of plasmacytoma cells, while only 2 of 20 indomethacin-treated mice had foci-containing plasmacytoma cells. The number of mice with microscopic foci in the pristane-treated group greatly exceeded the expected incidence of plasmacytomas (22%) at this dose of pristane. The growth of primary plasmacytomas in transplant that is dependent on the pristane-conditioned peritoneal environment was not inhibited by indomethacin treatment. The role of indomethacin in inhibiting plasmacytoma development was not established; two possibilities are that it inhibits production of mutagenic and tissue destructive oxidants by inflammatory cells, and it inhibits prostaglandin synthesis and intracellular production of oxidant biproducts.

Journal Article: Reovirus serotype 1 intestinal infection: a novel replicative cycle with ileal disease.
D H Rubin, M J Kornstein, A O Anderson
Journal of virology. 03/1985; 53(2):391-8. · 5.40 Impact Factor
ABSTRACT: After oral inoculation, reovirus serotype 1 strain Lang was shown to specifically infect the epithelial cells of the ileum, while sparing the epithelial cells in the duodenum, jejunum, and colon. The initial site of replication was localized in cells of the crypts of Lieberkühn adjacent to Peyer's patches. Virus was subsequently found by immunoperoxidase staining in cells migrating up the crypt-villus complex throughout the ileum. The severity of the pathological changes in the ileum was proportional to the concentration of the viral inoculum. This site-specific infection of the ileum by reovirus may provide a model for diseases that are restricted to specific sites in the intestine.

Journal Article: Effect of Avridine on enteric antigen uptake and mucosal immunity to reovirus (1/Lang).
A O Anderson, D H Rubin
Advances in experimental medicine and biology. 02/1985; 186:579-90. · 1.09 Impact Factor

Journal Article: The thymus in myasthenia gravis: an immunohistologic study.
M J Kornstein, J J Brooks, A O Anderson, A I Levinson, R P Lisak, B Zweiman
Advances in experimental medicine and biology. 02/1985; 186:929-36. · 1.09 Impact Factor

Journal Article: Differences in the peritoneal response to pristane in BALB/cAnPt and BALB/cJ mice.
A O Anderson, J S Wax, M Potter
Current topics in microbiology and immunology. 02/1985; 122:242-53. · 4.93 Impact Factor

Journal Article: Effect of Orally Administered Avridine on Enteric Antigen Uptake and Mucosal Immunity
AO Anderson, TT Macdonald, DH Rubin
Int. J. Immunotherapy. 01/1985; 1(2):107-115.

Journal Article: Multiple Effects of Immunological Adjuvants on Lymphatic Microenvironments. 1. Role of Immunologically-Relevant Angiogenesis in the Mechanisms of Action of CFA, MDP and Avridine
AO Anderson
Int. J. Immunotherapy. 01/1985; 1(3):185-195.

Journal Article: The immunohistology of the thymus in myasthenia gravis.
M J Kornstein, J J Brooks, A O Anderson, A I Levinson, R P Lisak, B Zweiman
The American journal of pathology. 12/1984; 117(2):184-94. · 4.89 Impact Factor
ABSTRACT: We have investigated cell subpopulations in frozen sections of thymus tissue obtained from myasthenic (MG) and control subjects. With the use of an avidin-biotin immunoperoxidase system with monoclonal antibodies, the following cell surface antigens were studied on frozen sections (12 MG and 3 control thymus); T11, T4, T6, T8, IgM, IgD, and Ia. The pattern of T cell phenotypes in MG thymus is similar to that of normal control thymus when examined by immunohistologic techniques. MG cortical

thymocytes are virtually all T11+, T4+, T8+, and T6+. In the medulla, at least 45% of thymocytes are T11+, with T4+ cells predominating over T8+ cells. Approximately 10% of medullary thymocytes are T6+. Scattered medullary cells expressing surface IgM and IgD are identified in both MG and normal thymuses. However, unlike the normal thymus, the MG thymus has numerous secondary follicles containing IgM- and IgD-bearing cells. This finding supports the hypothesis that the MG thymus microenvironment is aberrant. The Ia antigen is found in similar tissue section localization patterns in MG and control thymus. Ultramicroscopic studies show the Ia antigen predominantly on epithelial and interdigitating dendritic cells. By immunoperoxidase techniques, numerous keratin-positive cells are demonstrated in MG and control thymus. This suggests that thymic epithelial cells, like epithelial cells elsewhere, contain keratin. Because these data differ in degree from our previous findings in suspensions of MG thymocytes, this study emphasizes the importance of examining tissue sections as well as cell suspensions when one is studying lymphocyte surface markers.

Journal Article: POTENTIATION OF THE SECRETORY IgA RESPONSE BY ORAL AND ENTERIC ADMINISTRATION OF CP 20,961*
Donald H. Rubin, Arthur O. Anderson, Deborah Lucis
Annals of the New York Academy of Sciences. 12/1983; 409(1):866 - 870. · 3.16 Impact Factor

Journal Article: EFFECT OF ENTERIC PRIMING WITH REOVIRUS AND LIPOIDAL AMINE ADJUVANT ON MUCOSAL LYMPHATIC TISSUE AND ANTI- VIRAL IgA SECRETION*
Arthur O. Anderson, Alan Plotner, Donald H. Rubin
Annals of the New York Academy of Sciences. 12/1983; 409(1):769 - 775. · 3.16 Impact Factor

Journal Article: Correction of the Peripheral T-cell Functional and Microenvironmental Defects in BB Rats by Bone Marrow Transplantation
A Naji, WK Silvers, H Kimura, D Bellgrau, AO Anderson, CF Barker
Transplantation Proceedings. 03/1983; 15(1):1424. · 1.01 Impact Factor

Journal Article: Opsonization of alphaviruses in hamsters.
P B Jahrling, R A Hesse, A O Anderson, J D Gangemi
Journal of medical virology. 02/1983; 12(1):1-16. · 2.82 Impact Factor
ABSTRACT: Immune elimination of alphaviruses in immunized hamsters appears to involve formation of virus/antibody aggregates which are subsequently cleared from the circulation by cells of the reticuloendothelial system (RES). Virulent strains of Venezuelan (VEE) and Western equine encephalitis (WEE) viruses which were cleared slowly from the circulation of nonimmune hamsters, were cleared rapidly when inoculated into the blood of immunized hamsters. Likewise, when these viruses were mixed with specific hamster immune serum prior to inoculation, they were efficiently cleared from the circulation of nonimmune hamsters. Virus, mixed with specific immune serum, or inoculated into immunized hamsters, formed virus/antibody aggregates, as demonstrated by density gradient centrifugation, filtration through polycarbonate membranes, precipitation with Staphylococcus protein A, and electron microscopy. Cleared virus was concentrated primarily in liver and spleen, as confirmed by autoradiography. Immune clearance of virulent VEE was demonstrable within 5 to 6 days following immunization of hamsters with live attenuated VEE vaccine, strain TC-83. In these hamsters, a close association was established between formation of virus/antibody aggregates, rapid clearance, and survival of challenged hamsters. Adsorption of virus to hamster macrophages in culture was enhanced by immune serum in the presence of complement. These results are compatible with the hypothesis that immune clearance of virus in the intact hamster involves a complement-dependent interaction of virus/antibody complexes with cells which

possess Fc and complement receptors. The clearance of immune complexes by the RES serves to amplify the protective effect of neutralizing antibody alone.

Journal Article: Influence of islet and bone marrow transplantation on the diabetes and immunodeficiency of BB rats

Ali Naji, Willys K. Silvers, Hiromitsu Kimura, Arthur O. Anderson, Clyde F. Barker

Metabolism. 01/1983;

ABSTRACT: The results of islet transplantation in spontaneous autoimmune diabetes of BB rate were studied to determine whether this disease process might damage the transplanted islet tissue. Since BB rats are not genetically uniform, syngenetic grafts could not be used; therefore, allograft rejection was provented by rendering BB rats immunologically tolerant of WF transplantation antigens by neonatal inoculation with bone marrow cells. Despite the resultant tolerant stato, which permitted successful engraftment of WF skin allografts, the transplanted islets amellorated the spontaneous diabetes of BB rats only briafly before they were destroyed by immune insulitis. BB rats from the diabetic stock were found to suffer from abnormalities in T lymphocytes and their subsets as well as defective immune response patterns. When analyzed with monoclonal antibodies specific for rat lymphocyte markers, BB rats of the diabetic stock were found to be lymphocytopenic. There was a reduction in heiper T cells and a more severe deficit in the suppressor/cytotoxia subset. BB rats that were inoculated neonatally with bone marrow from normal donors were found to have a strikingly reduced incidence of diabetes. Moreover, the T cell functional, numerical, and microenvironmental defects that were present in noninoculated BB rats were restored in marrow-inoculated BB rats, findings possibly related to the decreased incidence of diabetes.

Journal Article: Review of : Cell Death in Biology and Pathology

A. O. Anderson

The Quarterly Review of Biology. 12/1982; 57:457-458. · **7.73 Impact Factor**

Journal Article: Transplantation of islets and bone marrow cells to animals with immune insulitis.

A Naji, D Bellgrau, A Anderson, W K Silvers, C F Barker

Diabetes. 09/1982; 31 Suppl 4:84-91. · **8.29 Impact Factor**

ABSTRACT: The results of islet transplantation in an animal model of spontaneous immune insulitis were studied to see whether this disease process might damage transplanted tissue. Since the insulitis occurs only in "BB" rats (which are not genetically uniform) syngeneic grafts could not be used, therefore allograft rejection was avoided by rendering "BB" rats tolerant of WF transplantation antigens by inoculating them neonatally with WF bone marrow cells. Despite the resultant tolerant state, which permitted successful engraftment of WF skin and islets transplanted to artificially diabetic "BB" rats, tolerant "BB" rats with spontaneous diabetes accepted transplanted WF islets only briefly before they were destroyed by immune insulitis. "BB" rats were found to have abnormalities in immune response (delayed skin graft rejection and decreased alloreactivity in mixed lymphocyte response). "BB" rats that were treated neonatally with WF bone marrow. Moreover, "BB" rats inoculated with WF bone marrow neonatally were found less likely to become diabetic than untreated "BB" controls. It is suggested that the chimeric state (persistence of WF bone marrow cells) may be responsible for the improved immune response and perhaps for the decreased susceptibility to diabetes.

Journal Article: Effect of immunological adjuvants on the appearance of monocyte and dendritic cell precursors in rat thoracic duct lymph.

A O Anderson, J T Warren

Advances in experimental medicine and biology. 02/1982; 149:791-9. · 1.09 Impact Factor

Chapter: Lymphocyte Locomotion, Lymphatic Tissues and Lymphocyte Circulation in the Rat
AO Anderson, ND Anderson, JD White
Animal Models of Immunological Processes, Hay, J. B. (ed.), Academic Press (London) 01/1982: pages 25-95;

Journal Article: Prevention of diabetes in rats by bone marrow transplantation.
Alinaji, W K Silvers, D Bellgrau, A O Anderson, S Plotkin, C F Barker
Annals of surgery. 10/1981; 194(3):328-38. · **7.49 Impact Factor**
ABSTRACT: Hyperglycemia, hypoinsulinemia and ketonemia often develop abruptly in previously normal young "BB" rats. The syndrome mimics human juvenile diabetes closely and is, thus, appropriate for assessing pancreatic transplantation. Transplantation of islet cells from closely histocompatible Wistar Furth (WF) donor resulted in permanent normoglycemia when immunosuppression with ALS was given. However, when islet cells from nondiabetic "BB" donors were transplanted to nonimmunosuppressed diabetic "BB" recipients, only transient normoglycemia followed. Transplantation of WF islets cells also failed in diabetic "BB" rats which were tolerant of WF antigens, again suggesting destruction of transplanted islet cells by the original disease process-possibly autoimmunity. Evidence for autoimmunity was strengthened by the finding that newly diabetic "BB" rats could be rendered normoglycemic by immunosuppression. Since genetic susceptibility to spontaneous autoimmune diabetes is unique to some members of the "BB" stock, an attempt was made to alter their vulnerability by modifying their cellular immune system. Accordingly, 50 million bone marrow cells from WF donors were inoculated into half the newborn members of "BB" litters, leaving the littermates as unmodified controls. Most bone marrow recipients were protected, only four of 37 (10.8%) ever becoming diabetic, while the incidence of diabetes in noninoculated littermates was 22 of 39 (56.4%). The ultimate goal in human diabetes, which also seems very likely to be an autoimmune disease, may not be replacement of destroyed islet cells but identification of potentially susceptible children and prevention of islet destruction by immunologic manipulation.

Journal Article: Presence of lymphoid dendritic cells in thoracic duct lymph from Lewis rats.
A O Anderson, J T Warren, D L Gasser
Transplantation proceedings. 07/1981; 13(2):1460-8. · 1.01 Impact Factor

Chapter: Structure and Function of Lymphatic Tissue
N.D. Anderson, A.O. Anderson
Spittel's Clinical Medicine, Harper-Row Publishers 01/1981: pages 1-47;

Chapter: Structure and Physiology of Lymphatic Tissues
Arthur O. Anderson MD, Norman D. Anderson MD
Cellular Functions in Immunity and Inflammation, Chapter 2, pp. Oppenheim, J. H. J., Rosenstreich, D. A., and Potter M. (eds.), Elsevier-North Holland Publishers, NY 01/1981: pages 29-76;

Journal Article: IMMUNE MODULATING EFFECTS OF POLY ICLC
Hilton B. Levy, E. Lvovsky, F. Riley, D. Harrington, A. Anderson, J. Moe, J. Hilfenhaus, E. Stephen
Annals of the New York Academy of Sciences. 12/1980; 350(1):33 - 41. · 3.16 Impact Factor

Adjuvant effects of the lipid amine CP-20,961.

A O Anderson, J A Reynolds
Journal of the Reticuloendothelial Society. 01/1980; 26(Suppl):667-80.

Chapter: Lymphocytes
N.D. Anderson, A.O. Anderson
Fundamentals of Clinical Hematology, Spivak (ed.), Harper-Row Publishers 01/1980: pages 155-197;

Journal Article: Basic mechanisms of lymphocyte recirculation in Lewis rats.
A O Anderson, N D Anderson, J D White
Advances in experimental medicine and biology. 02/1979; 114:73-83. · 1.09 Impact Factor
ABSTRACT: Lymphocyte locomotion in vivo depends upon an intact network of subplasmalemmal contractile microfilaments which are linked through the membrane to surface receptors, and the distribution and stabilization of recognition receptors may be controlled by microtubules and/or 10-nm filaments in the cytoplasm. The differential effects of cytochalasin-A and colchicine on lymphocyte homing and locomotion have proven useful in dissecting the subcellular events underlying the process of lymphocyte recirculation.

Journal Article: Heparin-induced coagulopathy.
W R Bell, N D Anderson, A O Anderson
The Journal of laboratory and clinical medicine. 05/1977; 89(4):741-50. · 2.62 Impact Factor
ABSTRACT: Intravenous heparin, at doses of 3.0 U./gm of body weight, produced an intravascular coagulopathy in rats which was manifested by intestinal tract hemorrhage, a reduction in plasma fibrinogen concentration, a rise in fibrinogen-fibrin degradation products, and the absence of a rise in platelet count noted in the control animals. This coagulopathy could not be produced by conventional anticoagulant doses of heparin or the injection of large doses of heparin in the presence of protamine sulfate. Specific studies excluded hypoxemia, metabolic acidosis, and endotoxemia as possible etiologic factors. The coagulation abnormalities observed in this study differ from those produced by injection of other polyanionic substances but their precise pathogenesis is still uncertain.

Chapter: Adjuvant Properties in Human Dialyzable Leukocyte Extracts (DLE) Containing Transfer Factor
A.O. Anderson, M.S. Ascher, L.A. Andron
Regulatory Mechanisms in Lymphocyte Culture Conference, Lucas, D. C. (ed.), Academic Press, New York 01/1977: pages 692-694;

Journal Article: Lymphocyte emigration from high endothelial venules in rat lymph nodes.
A O Anderson, N D Anderson
Immunology. 12/1976; 31(5):731-48. · 3.32 Impact Factor
ABSTRACT: Sequential events during lymphocyte emigration from high endothelial venuses (HEV) were studied by scanning and transmission electron microscopy combined with regional perfusion techniques. The results indicate that blood lymphocytes selectively adhere to HEV surfaces through microvilli which attach to shallow pits on the luminal surfaces of high endothelial cells. These intercellular contact points resist hydrodynamic and osmotic shearing forces, but can be disrupted by treatments which remove endothelial glycocalyx, hydrolyse lymphocyte surface glycoproteins, or chelate divalent cations. After this initial attachment phase, lymphocytes enter apical clefts between endothelial cells where they assume a motile configuration characterized by loss of microvilli and formation of irregular surface folds. Intramural lymphocytes adhere to adjacent endothelial cells through macular and villous contacts. Fibrillar electron-

dense material traverses the 15-20 nm gap at these points of adhesion. Microtubules and microfilaments are also seen around areas of cytoplasmic constriction in these motile lymphocytes. The migrating lymphocytes show cytoplasmic polarity which is oriented in the direction of movement as they pass through extracellular spaces in the venular wall and cross successive laminations in the perivascular sheath to enter the node. Since these lymphocytes enter channels between endothelial cells which are stained by intralymphatic injections with horseradish peroxidase, it is suggested that their entry into the node depends upon migration along a chemotactic gradient.

Journal Article: Specialized structure and metabolic activities of high endothelial venules in rat lymphatic tissues.

N D Anderson, A O Anderson, R G Wyllie

Immunology. 10/1976; 31(3):455-73. · 3.32 Impact Factor

ABSTRACT: Microscopic, histochemical and ultrastructural techniques were used to define characteristics of high endothelial venules (HEV) in rat lymphatic tissues. This endothelium contained acetyl esterase and acid hydrolase activities which were not altered by lymphocyte depletion. No immunoglobulins were detected on luminal surfaces of HEV by fluorescent antibody staining. Only minor structural differences were seen between HEV within lymph nodes and Peyer's patches. At both sites, high endothelial cells were linked together by macular junctional complexes and interlocking basal foot processes. Endothelial cell cytoplasm moulded about surfaces of lymphocytes migrating through the venular wall, and flocculant deposits of basement membrane formed over lymphocytes penetrating the basal lamina. The endothelium was ensheathed by three to five layers of overlapping reticular cell plates and connective tissue. Each plate was linked to the reticular meshwork of the node by collagen bundles and anchoring filaments which inserted into the plate's external limiting membrane. This permitted individual paltes to separate or approximate each other as tissue and intravascular pressure varied, and lymphocytes moved across the sheath by insinuating themselves into gaps between overlapping plates. This composite structure of the HEV wall appeared to facilitate lymphocyte entry into the node and minimized vascular leakage.

Journal Article: Microvascular changes in lymph nodes draining skin allografts.

N D Anderson, A O Anderson, R G Wyllie

The American journal of pathology. 11/1975; 81(1):131-60. · 4.89 Impact Factor

ABSTRACT: Histological, histochemical, ultrastructural, and radiolabeling characteristics of the microvasculature in regional nodes draining skin allograft sites are described. From 12 to 48 hours after grafting, these nodes show increased vascular permeability and altered lymphocyte traffic pattern. The rapid rise in lymphocyte migration indices and the apparent plugging of intermediate sinuses by lymphocytes suggest that both increased entry and decreased egress of recirculating cells contribute in "lymphocyte trapping." This is followed by redistribution of cortical capillary arcades as existing germinal centers dissolve and proliferating lymphocytes infiltrate the cortex. Normal microvascular patterns reappeared at 7 to 14 days as primary and secondary nodules form in the enlarged nodes. Increased length and arborization of high endothelial venules resulted from focal proliferation of endothelial cells in transition zones from high to low endothelium. In stimulated nodes, high endothelial cells exhibit increased cytoplasmic basophilia and acid hydrolase activities which correlate with the appearance of numerous polyribosomes, RER cisternae, and lysosomes in their cytoplasm. These "activated" endothelial cells phagocytose microthrombi within venular lumens.

Journal Article: Studies on the structure and permeability of the microvasculature in normal rat lymph nodes.

A O Anderson, N D Anderson

The American journal of pathology. 10/1975; 80(3):387-418. · 4.89 Impact Factor

ABSTRACT: The structure and permeability of the microvasculature in normal rat lymph nodes was studied by regional perfusion techniques. The results indicated that characteristic vascular units supplied each cortical lobule of lymphatic tissue. Numerous arteriovenous communications and venous sphincters innervated by unmyelinated nerve fibers were found in this vascular bed. These specialized vascular

structures permitted regional control of blood flow through high endothelial venules. Lymphocytes migrated across these venular walls by moving through intercellular spaces in the endothelium and between gaps in the laminated, reticular sheath. No direct anastomoses between blood vessels and lymphatics were seen, but tracer studies with horseradish peroxidase suggested that functional lymph node-venous communications were present in the walls of high endothelial venules.

Journal Article: Demonstration of candida in blood smears.
A O Anderson, J H Yardley
The New England journal of medicine. 02/1972; 286(2):108. · **53.30 Impact Factor**