ABSTRACTS

TI: Etiology of immune stromal (interstitial) keratitis.
AU: Schwartz-GS; Harrison-AR; Holland-EJ
So : Cornea,1998 May: 17 (3): 278-81

AB:We compared the etiologies of immune stromal keratitis (ISK), also known as interstitial keratitis (IK), in a recent group of patients with active and inactive ISK. METHODS: We reviewed the charts of 97 patients seen in the cornea clinic at the University of Minnesota from 1985 through 1994. Fifty-five patients were classified as having active ISK, defined by stromal inflammation without ulceration within 1 year of presentation. Forty-two patients were identified as having inactive ISK, defined by evidence of past stromal inflammation including stromal scarring, stromal thinning, ghost vessels, and reduplication of Descemet's membrane without active inflammation for the 1 year before presentation. We determined the etiology of the ISK by careful review of the patient's ocular examination, as well as medical and laboratory workup. Patients were labeled with the diagnosis of idiopathic ISK if no identifiable etiology was found. RESULTS: Herpes simplex virus (HSV) accounted for 71.4% of unilateral active ISK. Idiopathic accounted for 14.3%, and varicella-zoster virus accounted for 8.6% in this group. HSV was the etiologic factor of 50.0% of inactive unilateral cases, whereas 33.3% were idiopathic. Sixty percent of cases of bilateral, active ISK were from idiopathic causes. Syphilis was the cause of 48.5% of bilateral inactive cases. In this group, 33.3% were from idiopathic causes. CONCLUSION: Although syphilis has been recognized for many years as the cause of 90% of cases of ISK, this is no longer true. We demonstrated that active ISK is most commonly caused by HSV or is idiopathic and that, although syphilis is the leading cause of inactive, bilateral ISK, it is responsible for only 18.6% of total cases.

TI: A new recombinant antigen latex agglutination test (Syphilis Fast) for the rapid serological diagnosis of syphilis.
AU: Young-H; Moyes-A; de-Ste-Croix-I; McMillan-A
SO: Int-J-STD-AIDS. 1998 Apr; 9(4): 196-200

AB: We report an assessment of Syphilis Fast, a new latex test that uses a pool of 3 recombinant Treponema pallidum antigens (TpN15, TpN17, and TpN47) for the serodiagnosis of syphilis. Specificity was evaluated by screening 1518 unselected blood specimens in parallel with Syphilis Fast, the Captia SelectSyph-G EIA and the Venereal Disease Research Laboratory (VDRL) cardiolipin antigen test while sensitivity was tested using a panel of 99 treponemal sera (treated and untreated) representing various stages of infection and 15 treponemal sera detected on screening. The specificity of Syphilis Fast on initial testing (99.8%) was significantly higher (P<0.02) than that of Captia SelectSyph-G (99.2%) and the VDRL (99.1%): the specificity of Syphilis Fast remained significantly higher (P<0.02) after repeat testing (respective values 99.9%, 99.5% and 99.4%). There was no difference in the sensitivity of Syphilis Fast and Captia SelectSyph-G on initial (93% vs 92.1%) or repeat (95.6% vs 94.7%) testing: both were significantly more sensitive (P<0.001) than the VDRL (46.5% on initial and 43.9% on repeat testing). The sensitivities of the Treponema pallidum haemagglutination test (TPHA) and FTA-abs were 98.2% and 95.6% respectively. Negative reactions in Syphilis Fast and SelectSyph-G were associated with treated infections and correlated with low TPHA titres (< or = 80). We conclude that Syphilis Fast is a highly specific, simple and fast screening test with a sensitivity comparable to native antigen treponemal tests and that it merits consideration as a front-line screening test.

TI: Illuminating the agent of syphilis: the Treponema pallidum genome project.
AU: Norris-SJ; Fraser-CM; Weinstock-GM
SO: Electrophoresis. 1998 Apr; 19(4): 551-3
AB: As the causative agent of the common sexually transmitted disease syphilis and a fastidious, microaerophilic obligate parasite of humans, Treponema pallidum subsp. pallidum is one of the few prominent infectious agents that has not been cultured continuously in vitro. T pallidum therefore represents an attractive candidate for genomic sequencing. Preliminary sequence results from the 1.13 million base pair genome are consistent with the expected limited metabolic capabilities of this spirochete, but indicate that the bacterium may express toxins and surface proteins that have not been identified previously.

TI: Immune stimulation by syphilis and malaria in HIV-2-infected and uninfected villagers in West Africa.
AU: N'Gom-PT; Jaffar-S; Ricard-D; Wilkins-A; Ariyoshi-K; Morgan-G; Da-Silva-AP; Whittle-HC
SO: Br-J-Biomed-Sci. 1997 Dec; 54(4): 251-5

The conclusions are that HIV-2 infection is associated with lower CD4% and higher neopterin and beta 2-microglobulin levels than controls, and co-infection with syphilis is associated with a further lowering of CD4%, suggesting a worse suppression of the immune system. Co-infection with malaria is associated with a modest immune disturbance.

TI: Identification of persistent infection in experimental syphilis by PCR.
AU: Wicher-K; Abbruscato-F; Wicher-V; Collins-DN; Auger-I; Horowitz-HW
SO: Infect-Immun. 1998 Jun; 66(6): 2509-13

AB: The studies described herein were designed to evaluate the usefulness of the PCR in detecting persistent syphilitic infection. Three groups of animals were used: a nonimmune group infected with Treponema pallidum (NI/TP), a nonimmune group injected with heat-killed treponemes (NI/HKTP), and an immune and reinfected group (I/TP). All animals were inoculated with similar numbers of organisms distributed at 10 sites on the clipped back and in both testes. The persistence of the treponemes was examined by PCR and the rabbit infectivity test (RIT). The kinetic studies and statistical analysis of their results demonstrated that the rate of bacterial clearance from the NI/TP group was very low and incomplete at 4 months after infection. It was significantly different from those of both the NI/HKTP (P < 0.001) and I/TP (P < 0.05) groups. No statistically significant differences in treponemal elimination were found between the NI/HKTP and I/TP groups. PCR can detect the DNA of dead

organisms, but the latter are eliminated by the host relatively quickly (15 to 30 days) as compared to elimination of live treponemes (>120 days). PCR results correlated well with RIT results. These data suggest that PCR-positive specimens obtained from an untreated patient(s) or collected weeks after treatment indicate persistent infection. They also show that the process of elimination of T. pallidum from primary sites of infection is prolonged and incomplete.

TI: Novel recombinant-antigen enzyme immunoassay for serological diagnosis of syphilis.
AU: Young-H; Moyes-A; Seagar-L; McMillan-A
SO: J-Clin-Microbiol. 1998 Apr; 36(4): 913-7

AB: Enzyme immunoassay (EIA) is an ideal method for screening large numbers of patients for syphilis. We evaluated a novel immunecapture EIA (ICE Syphilis; Murex Diagnostics) that uses three recombinant Treponema pallidum antigens (TpN15, TpN17, and TpN47) and compared the results with those obtained by the native T. pallidum antigen EIA (Captia SelectSyph-G; Centocor) that we currently use for the serodiagnosis of syphilis. Specificity was evaluated by screening 1,184 unselected serum specimens in parallel by the ICE Syphilis and SelectSyph-G assays, while sensitivity was tested with a panel of 101 serum specimens containing antitreponemal antibodies (treated and untreated) from patients with various stages of infection. The specificity of the ICE Syphilis EIA (99.8%) on screening was significantly higher ($P < 0.02$) than that of the SelectSyph-G EIA (99.2%). The sensitivity of the ICE Syphilis EIA was significantly higher ($P < 0.01$) than that of the SelectSyph-G EIA on both initial (99 versus 91.4%) and repeat (100 versus 92.4%) testing. The ICE Syphilis EIA was also significantly more sensitive ($P < 0.01$) than the fluorescent treponemal antibody-abs (92.4%) but not the T. pallidum hemagglutination assay (97.1%). Sera containing antitreponemal antibodies gave a much higher antibody index (absorbance of test serum/kit cutoff) by the ICE Syphilis EIA than by the SelectSyph-G EIA. This combined with the overall high sensitivity makes the ICE Syphilis EIA an ideal test for excluding or detecting treponemal infection in human immunodeficiency virus (HIV)-infected patients. The ICE Syphilis EIA was positive with sera from all 15 HIV-infected patients in the study, whereas sera from 3 HIV-infected patients were negative by the SelectSyph-G EIA. We conclude that the high sensitivity and specificity of the ICE Syphilis EIA and its suitability for automation make it an ideal screening test.

TI: STD vaccines—an overview.
AU: Barbosa-Cesnik-CT; Gerbase-A; Heymann-D
SO: Genitourin-Med. 1997 Oct; 73(5): 336-42

AB: OBJECTIVES: To describe the role and current status of vaccine research against sexually transmitted diseases (STDs). METHODS: The available literature was reviewed with particular emphasis on bacterial STDs. RESULTS: Strategic approaches to possible implementation of STD vaccine programmes were analysed. The status of vaccines against bacterial STDs (syphilis, chancroid, gonorrhoea, and chlamydia) is described in detail. CONCLUSIONS: The development of safe and effective STD vaccines offers a potent tool for the control of STDs, including direct and indirect prevention of HIV infection. Future priorities should be in the development of vaccines against gonorrhoea, chlamydia, and syphilis. When such vaccines become available, caution should be exercised to ensure that they do not interfere with the effectiveness of other prevention programmes.

TI: Serologic testing of cornea donors.
AU: Glasser-DB
SO: Cornea. 1998 Mar; 17(2): 123-8

AB: PURPOSE: To review the current requirements and rationale for serologic testing of cornea donors and to provide guidelines for dealing with results of nonrequired tests. METHODS: Eye Bank Association of America (EBAA) and Food and Drug Administration (FDA) regulations are examined with respect to current knowledge of the risk of donor-to-host transmission of systemic infectious diseases via corneal transplantation. RESULTS: Negative screening tests are required for human immunodeficiency virus (HIV) 1 and 2, hepatitis B surface antigen (HBsAg), and hepatitis C virus (HCV) before release of tissue for transplantation. Other tests reported by organ-procurement organizations commonly include hepatitis B core antibody (anti-HBc), syphilis, cytomegalovirus (CMV), and human T-lymphotropic virus (HTLV) I and II. No systemic infectious-disease transmission from donor corneas supplied by EBAA-member eye banks has occurred in the last 12 years, a period during which >400,000 corneas were provided for transplantation. CONCLUSION: EBAA donor-screening requirements, including serologic testing, have resulted in an excellent safety record. Requirements for serologic testing should continue to be regularly reviewed as new information becomes available.

TI: Evaluation of a new competitive immunoassay (BioElisa Syphilis) for screening for Treponema pallidum antibodies at various stages of syphilis.
AU: Ebel-A; Bachelart-L; Alonso-JM
SO: J-Clin-Microbiol. 1998 Feb; 36(2): 358-61

AB: The BioElisa Syphilis, a new competitive enzyme immunoassay (EIA) for Treponema pallidum whole antigen that uses specific human immunoglobulin G (IgG) antibodies as the competitor, was evaluated for potential use in screening for syphilis at various stages. The results obtained by this competitive EIA were compared with those obtained by the fluorescent treponemal antibody absorption (FTA-abs) test and the T. pallidum hemagglutination assay (TPHA). Serum samples from 434 patients with positive TPHA and FTA-abs test results, including patients with primary, latent, secondary, and tertiary syphilis and neurosyphilis, were investigated. Two samples tested negative by competitive EIA but were weakly reactive by the TPHA and the FTA-abs test. Sixteen serum samples from patients with clinically documented active syphilis, including several patients infected with human immunodeficiency virus, tested positive by the competitive EIA. There was a direct inverse correlation between EIA indices and titers in the TPHA and the FTA-abs test for all samples that tested positive. Specificity was assessed by testing 358 serum samples which tested negative for syphilis by TPHA and the FTA-

abs test, including 100 serum samples from patients with documented infectious or autoimmune diseases. Only two serum samples gave a weakly positive EIA result. Thus, competitive EIA had a sensitivity of 99.5% and a specificity of 99.4% relative to the results of the FTA-abs test and TPHA. Our evaluation shows that BioElisa Syphilis is a sensitive, specific, and simple assay for screening for syphilis.

TI: T lymphocytes are required for protection of the vaginal mucosae and sensory ganglia of immune mice against reinfection with herpes simplex virus type 2.
AU: Milligan-GN; Bernstein-DI; Bourne-N
SO: J-Immunol. 1998 Jun 15; 160(12): 6093-100

AB: Intravaginal inoculation of mice with an attenuated strain of herpes simplex virus type 2 (HSV-2) resulted in vigorous HSV-specific immune responses that protected against subsequent challenge with fully virulent HSV-2 strains. Even in the presence of high titers of HSV-specific Ab, T cell-dependent mechanisms were required for protection of the vaginal mucosae of HSV-immune mice and could be detected by 24 h after intravaginal reinoculation. Depletion of specific T cell subsets from HSV-immune mice before HSV-2 reinoculation demonstrated that CD4+ T cells were primarily responsible for this protection. Similarly, optimal protection of the sensory ganglia against reinfection with HSV-2 was dependent on the presence of T cells. Infectious HSV-2 was not detected in the sensory ganglia or spinal cord of HSV-immune mice depleted of only CD4+ or CD8+ T cells, suggesting that the T cell-mediated protection could be provided by either subset. Similarly, neutralization of IFN-gamma during challenge of HSV-immune mice resulted in diminished protection of the vaginal mucosa, but not of the sensory ganglia. These results suggest that the ability to induce vigorous HSV-specific T cell responses is an important consideration in the design of vaccines to protect both the vaginal mucosa and sensory ganglia against HSV-2.

TI: A comparison of PCR with virus isolation and direct antigen detection for diagnosis and typing of genital herpes.
AU: Slomka-MJ; Emery-L; Munday-PE; Moulsdale-M; Brown-DW
SO: J-Med-Virol. 1998 Jun; 55(2): 177-83

AB: Patients attending the genitourinary medicine clinic at Watford General Hospital, UK, were examined for clinical signs of genital herpes infection. Genital swabs were taken from 194 patients (126 female, 68 male) who presented with genital ulceration or symptoms which were suggestive of genital herpes infection. Swabs from these patients were tested by three methods: (i) Detection of herpes simplex virus (HSV) antigen by direct HSV enzyme immunoassay (EIA), (ii) HSV isolation in Vero cell culture and (iii) HSV polymerase chain reaction (PCR). HSV was detected in 76 patients (39%) by EIA, in 93 (48%) by isolation in cell culture, and in 115 (59%) by PCR. Isolation by cell culture has been considered as the "gold standard" for the detection of HSV in genital lesions, but in this study HSV PCR was significantly more sensitive. Comparison of the three methods was as follows: Cell culture vs. PCR: Sensitivity 93/115 (80.9%), Specificity 79/79 (100%). HSV EIA vs. PCR: Sensitivity 75/115 (65.2%), Specificity 78/79 (98.7%). HSV EIA vs. Cell culture: Sensitivity 75/93 (80.7%), Specificity 100/101 (99%). EIA was less effective in detecting HSV among recurrent than among first episode infections, in comparison to culture or HSV PCR. This is the first comparison of HSV PCR with two other routine diagnostic methods for confirming genital herpes infection in a symptomatic population. The infecting HSV type was identified by restriction digestion of 108 HSV amplicons: HSV-1:37/108 (34%), HSV-2:71/108 (66%). In this population HSV-1 causes a significant proportion of genital herpes cases, and HSV-1 genital infection was detected in significantly more first episode infections (40.3%) than among recurrent infections (22.2%).

TI: Genital recurrent infection occurring 6 months after meningitis due to the same herpes simplex virus type 2 (HSV-2) strain evidence by restriction endonuclease analysis.
AU: Venot-C; Beby-A; Bourgoin-A; Giraudeau-G; Becq-Giraudon-B; Agius-G
SO: J-Infect. 1998 Mar; 36(2): 233-5
AB: Herpes simplex virus type 2 (HSV-2) is more often sexually transmitted and associated with genital recurrent infection. However, HSV-2 neurological manifestations such as meningitis were already reported. We describe a case of meningitis due to HSV-2, preceded by signs suggesting a common cystitis, in a woman with no history of primary or recurrent genital infection. Six months later genital herpetic lesions occurred. One HSV-2 strain was obtained from cerebrospinal fluid (CSF) and another from genital lesions. The molecular comparative analysis using restriction endonuclease digestion patterns showed the similarity of the two strains. Our report illustrates that HSV-2 infections are underdiagnosed and that molecular techniques can be of value in clarifying the physiopathology of HSV diseases.

TI: Long-term immunity and protection against herpes simplex virus type 2 in the murine female genital tract after mucosal but not systemic immunization.
AU: Gallichan-WS; Rosenthal-KL
SO: J-Infect-Dis. 1998 May; 177(5): 1155-61

AB: The degree and duration of immunity against herpes simplex virus type 2 (HSV-2) infection of the female genital tract were assessed after intranasal (i.nl.) or intraperitoneal (i.p.) immunization with a recombinant adenovirus vector expressing HSV glycoprotein B (AdgB8). After intravaginal HSV-2 challenge, control mice rapidly developed disease and displayed high virus titers in vaginal washes. In contrast, virus titers decreased significantly and at similar rates in i.nl. and i.p. immunized mice and by day 7 were undetectable in vaginal wash samples. Assessment of genital pathology and survival showed that only i.nl. immunization provided long-term protection. Examination of antibody-secreting cells (ASCs) during the decline in vaginal virus titers revealed that gB-specific IgA ASCs were only observed in the genital tissues of i.nl. immunized mice. These results indicate that mucosal immunization provides a high and long-lasting level of immunity from sexually transmitted viral infections of the female genital tract.

TI: Evaluation of a live attenuated recombinant virus RAV 9395 as a herpes simplex virus type 2 vaccine in guinea pigs.
AU: Spector-FC; Kern-ER; Palmer-J; Kaiwar-R; Cha-TA; Brown-P; Spaete-RR
SO: J-Infect-Dis. 1998 May; 177(5): 1143-54

AB: Recombinant virus RAV 9395 was constructed by deleting both copies of the gamma(1)34.5 gene, and the UL55 and UL56 open reading frames from herpes simplex virus type 2 (HSV-2) strain G. The potential use of RAV 9395 as an HSV-2 vaccine was investigated by evaluating the ability of RAV 9395 to protect guinea pigs from severe disease by HSV-2(G) challenge. RAV 9395 administered intramuscularly reduced both lesion development and severity in a dose-dependent manner in guinea pigs challenged with HSV-2(G). The frequency of reactivation of RAV 9395 from explanted dorsal root ganglia was low compared with that of HSV-2(G). Immunization with RAV 9395 at doses of 1 x 10(5) pfu and above generally precluded the establishment of latency by the challenge virus. The results presented in this report lend support for the development of genetically engineered live HSV vaccines.

TI: Detection and direct typing of herpes simplex virus in perianal ulcers of patients with AIDS by PCR.
AU: do-Nascimento-MC; Sumita-LM; de-Souza-VA; Pannuti-CS
SO: J-Clin-Microbiol. 1998 Mar; 36(3): 848-9

AB: The presence of herpes simplex virus type 1 (HSV-1) and HSV-2 in perianal ulcerations of 41 AIDS patients was assessed by virus culture and a type-specific PCR-based assay. HSV was isolated from the lesion site in 24 of 41 (58.5%) patients, and HSV DNA was detected by PCR in all 24 (100%) of these specimens. Additionally, PCR was used to detect HSV DNA in 12 of 17 (70.5%) HSV culture-negative samples. Thus, HSV genomic sequences could be demonstrated in 36 of 41 (87.8%) perianal ulcers in this series. Full agreement in HSV typing by either immunodot assay or PCR was seen in 24 samples that were positive by both virus culture and PCR. HSV-2 was demonstrated in 35 of 36 (97.2%) HSV-positive samples.

TI: Evidence of latency and reactivation of both herpes simplex virus (HSV)-1 and HSV-2 in the genital region.
AU: Sucato-G; Wald-A; Wakabayashi-E; Vieira-J; Corey-L
SO: J-Infect-Dis. 1998 Apr; 177(4): 1069-72

AB: While superinfection with different herpes simplex virus (HSV) types has been demonstrated in animals, the ability of the two HSV types to colonize and reactivate in the same anatomic region in humans has not been well demonstrated. In 6 patients, both HSV-1 and HSV-2 was recovered from genital lesions. In 4 of them, who initially acquired genital HSV-1 infection, subsequent HSV-2 infection presented as a prolonged episode of genital lesions and a marked increase in the frequency of genital recurrences. While most of the subsequent clinical reactivations were HSV-2, in 2 patients the recurrence rate of genital HSV-1 increased after the acquisition of HSV-2. These data demonstrate the ability of a second HSV type to infect the same anatomic region and illustrate the difference in reactivation frequency of the two types in the same person. Typing of HSV isolates may be useful in persons with recent alteration in recurrence rates of genital HSV.

TI: Successful treatment of herpes simplex virus (HSV) recurrent genital infection with recombinant human (rh) granulocyte-macrophage colony stimulating factor (GM-CSF): a case report.
AU: Altamura-M; Geronimo-MG; Nappi-L; Ceci-O; Loizzi-P; Jirillo-E
SO: Immunopharmacol-Immunotoxicol. 1997 Nov; 19(4): 425-36

AB: In the present work, we describe the treatment with rhGM-CSF of a woman affected by HSV recurrent genital infection and not responsive to specific antiviral therapy. The therapeutic regimen consisted of a subcutaneous administration of 300 mg/day of rhGM-CSF for six days. Before treatment with rhGM-CSF, polymorphonuclear cell and monocyte functional capacities and the antibacterial activity exerted by T cells were profoundly depressed. After treatment, a normalization of immune functions and a progressive disappearance of clinical manifestations were observed.

TI: Haemophilus ducreyi infection causes basal keratinocyte cytotoxicity and elicits a unique cytokine induction pattern in an In vitro human skin model.
AU: Hobbs-MM; Paul-TR; Wyrick-PB; Kawula-TH
SO: Infect-Immun. 1998 Jun; 66(6): 2914-21

AB: Haemophilus ducreyi is the etiologic agent of the sexually transmitted genital ulcer disease chancroid. Predominantly a cutaneous pathogen, H. ducreyi is present in chancroid ulcers that are characterized by extensive neutrophil accumulation in intraepidermal lesions accompanied by a mononuclear infiltrate in the dermis. We used an in vitro human skin model composed of foreskin fibroblasts and keratinocytes to examine host skin cell interactions with H. ducreyi 35000. Bacteria replicated and persisted in artificial skin for at least 14 days. We observed H. ducreyi inside suprabasal keratinocytes using transmission electron microscopy. Although no bacteria were seen in the basal keratinocyte region, these cells were disrupted in infected cocultures. H. ducreyi infection stimulated increased secretion of interleukin-6 (IL-6) and IL-8 by skin cells. Conversely, tumor necrosis factor alpha and IL-1alpha levels were not elevated. IL-8 produced in response to H. ducreyi infection may be involved in recruiting polymorphonuclear leukocytes and other inflammatory cells, thereby contributing to the tissue necrosis and ulcer formation characteristic of chancroid.

TI: Polymerase chain reaction detection of Haemophilus ducreyi DNA.
AU: Roesel-DJ; Gwanzura-L; Mason-PR; Joffe-M; Katzenstein-DA
SO: Sex-Transm-Infect. 1998 Feb; 74(1): 63-5

AB: OBJECTIVES: To develop a polymerase chain reaction (PCR) method to detect Haemophilus ducreyi DNA in cultured isolates and clinical material. CONCLUSION: PCR amplification using primers from the 16s rRNA gene may be a useful alternative to culture for the detection of H ducreyi and the diagnosis of chancroid.