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ABSTRACT FORM

Reduced viability of *Taenia solium* cysticerci following antigenic challenge in pigs.

Carlton Evans*, Armando Gonzalez, Robert Gilman, Manuela Verastegui, Hugo Garcia, Alfonso Chavera, & The Cysticercosis Working Group in Peru.
*Department of Medicine, Addenbrooke's Hospital, Cambridge, CB2 2QQ, UK.

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ambulatory peritoneal dialysis (CAPD) related peritonitis and may lead to intra-abdominal abscess formation. In a retrospective study we reviewed the rate of abdominal complications, presence of bacteraemia and metastatic bacterial seeding during 68 episodes of *Staphylococcus aureus* CAPD-related peritonitis in 36 patients occurring between 1990 and 1995 at the Oxford Renal Unit. Blood cultures were taken on the day of presentation in 31 (46%) episodes, all of which were negative. There were no clinical cases of metastatic bacterial seeding. Intra-abdominal abscess formation was documented in two cases and a further patient died from septic shock within 24 hours of presentation, but all three had negative blood cultures. The apparent inability of *Staphylococcus aureus* to gain access to the bloodstream in this setting may provide important clues towards an understanding of the pathogenesis of metastatic infection.

P9.2

Reduced viability of *Taenia solium* cysticerci following antigenic challenge in pigs. C. Evans[1], A. Gonzalez, R. Gilman, M. Verastegui, H. Garcia, A. Chavera and The Cysticercosis Working Group in Peru. [1]Department of Medicine, Addenbrooke's Hospital, Cambridge CB2 2QQ, U.K.

Taenia solium cysticercosis is a common cause of human neurological disease in developing countries. Porcine cysticercosis contributes to economic hardship and is an essential stage in the parasite life-cycle. A treatment for infected pigs may be an effective way of controlling the parasite and preventing human disease. Our blinded randomized placebo-controlled study assessed the efficacy and safety of immunotherapy in 28 naturally infected pigs. Four weight-matched groups were inoculated with purified cysticercal antigen, crude cysticercal antigen with Freund's adjuvant, adjuvant alone or saline alone. Immunotherapy was well tolerated but had no effect upon the macroscopic appearance or histology of cysticerci. Most of the pigs given crude antigen plus adjuvant developed new antibody bands on electro-immuno transfer blot and the crude antigen caused a significant increase (from 10% to 34%, $P<0.04$) in the proportion of cysticerci that failed to evaginate and were therefore not viable for causing human infection.

P10.1

Randomised prospective study comparing teicoplanin plus aztreonam with cefuroxime by the intraperitoneal route in the treatment of CAPD peritonitis. R.G. Finch, I. Harding, A.P. Holliday, C.J. Wale, A. Innes, R.P. Burden and A.G. Morgan. Dept Microbial Diseases and Renal Medicine, The City Hospital and University of Nottingham NG5 1PB, U.K. and Thackelay's Research Consultancy, Devizes SN10 3NB, U.K.

Teicoplanin (T, 20 mg/l) plus aztreonam (A, 250 mg/l) were compared prospectively with cefuroxime (C, 125 mg/l) intraperitoneally for the empirical treatment of CAPD peritonitis. Drugs were given in every bag exchange for 10 days. A total of 79 patients (35 T+A, 44 C) who had 98 episodes of peritonitis were enrolled in the study. Median time on CAPD was 12 months in both groups, and the mean number of episodes of peritonitis per year was 0.8 (T+A) and 0.7 (C).

Treatment was successful in 41/43 (95.3%) evaluable episodes in patients receiving T+A, compared with 40/48 (83.3%) receiving C (95% CI 24.3%, +0.3%). A total of 19 episodes (where patients had developed a further infection) were subsequently re-randomized for treatment, of which 13 received T+A. Each of these 13 episodes responded successfully, but 3 of the 6 episodes receiving C failed. Pathogens, mostly Gram-positive (including 47 coagulase-negative staphylococci and 7 *Staphylococcus aureus*), were isolated in 80 episodes (81.6%). The bacteriological response rate (6-week follow-up) was 29/34 (85.3%) for T+A, compared with 28/41 (68.3%) for C (95% CI 35.6%, +1.6%). Five pathogens persisted in the C arm, compared with none in the T+A arm. The remaining unsuccessful responses were recurrences of the causative organism. Mean dialysate levels of T were 4.5–6.1 mg/l during the dosing period, and the C_{max} in serum was 9.0 mg/l on day 10. Total clearance was estimated at 0.0033 l/h/kg at steady state. Six adverse events were reported in 5 patients (3 T+A, 2 C). Only one event (diarrhoea) was considered possibly related to the study drugs (T+A). Minor elevations in liver function tests were more frequent in patients receiving T+A.

It is concluded from this study that both regimens are effective and well tolerated in treating CAPD peritonitis. Teicoplanin dosage at 20 mg/l/exchange for 10 days gives adequate dialysate concentrations while maintaining serum concentrations at an acceptably low level.

P10.2

Assessment of the *in-vitro* activity of meropenem against clinical isolates in 70 U.K. laboratories. J.M. Greenhalgh and P.J. Turner. Antibiotic Development Group, Infection Therapeutic Research Department, Zeneca Pharmaceuticals, Mereside, Alderley Park, Macclesfield SK10 4TG, U.K.

Data on the antibacterial activity of meropenem (MEM) against 13,000 clinical isolates collected at 70 laboratories throughout the U.K. between January and June 1995 have been compiled into a computer database for analysis.

The commonest method used was disc-diffusion, the strains tested were recent clinical isolates which had been speciated fully. Comparators (55 in total) were those used routinely in each participating laboratory. MEM was the only agent tested against all strains, others were limited in spectrum of activity.

The results demonstrate the effectiveness of MEM as a broad spectrum agent with significant activity against Gram-positive and -negative aerobes and anaerobes. This is exemplified by the fact that 99.7% of methicillin-susceptible *Staphylococcus aureus* were susceptible to MEM compared to 98.8% to both ceftazidime (CAZ) and gentamicin (GM) and 87.1% to ciprofloxacin (CIP). Comparable percentages for Enterobacteriaceae were MEM: 99.1, CAZ: 85.6, GM: 95 and CIP: 94.6; for *Pseudomonas aeruginosa* 93.1, 88, 82 and 75.4. Against *Bacteroides fragilis* 98.8% of strains were susceptible to MEM compared to 98.4 to metronidazole and 84.6 to clindamycin.

P10.3

Rifampin resistance in *Neisseria meningitidis* due to alteration in membrane permeability. F.J.R. Abadi, P.E. Carter and T.H. Pennington. Dept Medical Microbiology, Aberdeen University Medical School, Aberdeen AB9 2ZD, U.K.

Rifampin-resistant (rifr) *Neisseria meningitidis* strains are known to have single point mutations in the central conserved regions of the rpoB gene. We have demonstrated two distinct resistance phenotypes in strains with identical mutations in this region, an intermediate level of resistance in rifr clinical isolates, and a high level in mutants selected *in vitro*. The possible role of membrane permeability in the latter was investigated by measuring minimum inhibitory concentrations in the presence of Tween 80; values for high level resistant mutants were reduced to intermediate levels, whereas those of intermediate level resistance strains were unaffected. High level resistant mutants were also found to have increased resistance to Triton X-100 and gentian violet. Sequencing of the meningococcal mtrR gene and its promoter region (which determine resistance to hydrophobic agents in *Neisseria gonorrhoeae*) from sensitive or intermediate level resistant strains and high level resistant mutants generated from them showed no mutation within this region. 2-D gel electrophoresis of two parent and rifr mutant strains showed an identical shift in pI of one protein indicating that differences between parent and high rifr mutant are not confined to the rpoB gene. These results indicate that both permeability and rpoB mutations play a role in determining the resistance of *N. meningitidis* to rifampin.

P10.4

Comparative activities of ceftriaxone with other antimicrobial agents against meningococci. D.E. Yakubu, F.J.R. Abadi and T.H. Pennington. Dept Medical Microbiology, Aberdeen University Medical School, Aberdeen AB9 2ZD, U.K.

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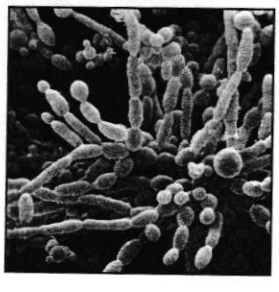

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TITLE & AUTHORS: ***Toxoplasma gondii* encephalitis in *Nramp 1* congenic mice**

Carlton Evans, Craig Roberts, James Alexander, Jenefer Blackwell

JH Xuereb
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ABSTRACT

The *Ity/Lsh/Bcg* Natural resistance associated macrophage protein gene (*Nramp 1*) regulates macrophage priming and activation for antimicrobial activity, influencing susceptibility to infection with intracellular pathogens. Previous experiments have shown route of administration and parasite virulence dependent effects of *Nramp 1* on susceptibility to *T. gondii* infection.[1,2] In vertebrates, *Nramp 1* expression is restricted to cells of the macrophage/monocyte lineage, but the *Drosophila* homologue (*malvolio*) of *Nramp 1* is expressed in both macrophages and sensory neurones, suggesting that *Nramp 1* may influence events in the brain. We therefore studied the effects of *Nramp 1* on early *T. gondii* infection in male and female B10.L-Lsh^r (N20) resistant and B10 susceptible congenic mice. Eight month old mice were infected with 20 RRA *T. gondii* cysts by gavage and tissues collected on alternate days. The time to 50% mortality was 4 days in male susceptible mice but 9-10 days for all other groups. By day 5, mortality had reached 55% for male susceptible mice, 25% for male resistant mice and <10% for resistant/susceptible female mice. Male sex and the susceptible *Nramp 1* allele were therefore both associated with earlier mortality. There was 100% mortality by day 10 in all groups. Frozen sections of the brain revealed meningo-encephalitis by day 4 and immunohistochemical staining with polyclonal rabbit anti-*T. gondii* antibodies demonstrated early cyst formation by day 10. Immunohistochemistry for inducible nitric oxide synthase (iNOS) and the macrophage markers F4/80 and M1/70, and semi-quantitative RT-PCR for iNOS, IL-12, and *Nramp 1* mRNA will be presented to show the kinetics of the early immune response to infection in the brain.

1. McLeod R et al. *J. Immunol.* 1989; 143: 3031-3034.
2. Blackwell JM et al. *Clin. Exp. Immunol.* 1994; 97: 107-112.

? Early cyst formation

Posters

Sindbis Virus, *Escherichia coli*, and Baculovirus Recombinants Expressing *Toxoplasma gondii* SAG-1. Xiong Cheng, Pam Hair, Shirley Hunter, Marielle Gold, Lisa Ashbaugh, and Michael Milhausen, HESKA Corp., Fort Collins, CO, USA.

SAG-1 is a primary surface molecule found on tachyzoites from all *T. gondii* strains. We have constructed and analyzed several recombinant versions of this gene in Sindbis virus, *E. coli* and baculovirus. Twelve different Sindbis based recombinants were designed and tested *in vitro*. These included various regions of the SAG-1 gene fused to other sequences representing tissue plasminogen activator signal sequence, glutathionine-S-transferase gene, and sequences specifying factor Xa cleavage site. Additionally , the SAG-1 gene was cloned in baculovirus, with and without the sequences specifying the glycerolphosphatidyl inisitol attachment site on the C terminus. The latter construct successfully secreted SAG-1 protein into the medium following infection of SF9 cells. Protein was purified from SF9 cultures as well as from several recombinants cloned into *E. coli*. Studies were conducted in mice assessing serological responses of different constructs of the SAG-1 gene following infection with viable Sindbis recombinant constructs and following injection of protein isolated from *E. coli* and baculovirus. All of the protein formulated in several adjuvants produced demonstrable titers to the SAG-1 gene product. Only three of the twelve Sindbis based recombinants stimulated antibody production to SAG-1 protein. Initial mouse challenge studies, using oral delivery of brain derived tissue cysts, did not demonstrate protection from lethal challenge.

Detection of 60 kD tachyzoite antigen of *Toxoplasma gondii* by a murine CD4+ T cell clone. Gaby Reichman and Hans-Georg Fischer, Institute for Medical Microbiology and Virology, Heinrich-Heine-University, Dusseldorf, Germany.

Infection with *Toxoplasma gondii* is controlled by a T cell mediated immune response. To identify parasite antigens which are recognized by protective T lymphocytes, a panel of murine CD4+ T cell clones were raised against crude *Toxoplasma* lysate (TLA). Among them, clone 3Tx9 belongs to the TH1 subtype secreting high titres of interleukin-2, interferon-γ and tumor necrosis factor without producing IL4 and IL10.
The expression pattern of the antigen recognized was determined in T cell proliferation assays. Clone 3Tx9 was stimulated by all 3 *T.gondii* sub groups comprising mouse-virulent and avirulent strains. Tested for reactivity with different parasite stages 3Tx9 cells were stimulated by tachyzoites as a source of antigen whereas bradyzoites did not exhibit antigen activity. Identify of stages was confirmed by immunofluorescence staining using tachyzoite and bradyzoite-specific monoclonal antibodies. So far, 2 tachyzoite-specific antigens are described: SAG1/p30 and SAG2/p22. Following SDS-PAGE of TLA and electroelution of separated proteins, combined T cell blot analysis and ELISA revealed that clone 3Tx9 reacts with an antigen of about 60 kD which co-migrates with a family of rhoptry proteins. We, therefore, conclude that clone 3Tx9 defines a new tachyzoite-specific antigen which might be a rhoptry protein.
Since tachyzoites are rapidly multiplicating and spreading through the host , a T cell response directed against this parasite stage could restrict parasite growth during the early phase of infection.

***Toxoplasma gondii* encephalitis in Nramp 1 congenic mice.** Carlton Evans, Craig Roberts*, James Alexander*, Jenefer Blackwell, Department of Medicine, Addenbrooke's Hospital, Cambridge, England and *Department of Immunology, University of Strathclyde, 31 Taylor Street, Glasgow , Scotland.

The Ity/Lsh/Bcg Natural resistance associated macrophage protein gene (Nramp 1) regulates macrophage priming and activation for antimicrobial activity, influencing susceptibility to infection with intracellular pathogens. Previous experiments have shown route of administration and parasite virulence dependent effects of Nramp 1 on susceptibility to *T.gondii* infection. In vertebrates, Nramp 1 expression is restricted to cells of the macrophage/monocyte lineage, but the *Drosophila* homologue (Malvolio) of Nramp 1 is expressed in both macrophages and sensory neurones, suggesting that Nramp 1 may influence events in the brain. We, therefore, studied the effects of Nramp 1 on early *T. gondii* infection in male and female B10.L-Lshr (N20) resistant and B10 susceptible congenic mice. Eight month old mice were infected with 20 RRA *T. gondii* cysts by gavage and tissues collected on alternate days. The time to 50% mortality was 4 days in male susceptible mice but 9-10 days for all other groups. By day 5, mortality had reached 55% for male susceptible mice, 25% for male resistant mice and <10% for resistant/susceptible female mice. Male sex and the susceptible Nramp 1 allele were therefore both associated with earlier mortality. There was 100% mortality by day 10 in all groups. Frozen sections of the brain revealed meningoencephalitis by day 4 and immunohistochemical staining with polyclonal rabbit anti-*T.gondii* antibodies demonstrated early cyst formation by day 10. Immunohistochemistry for inducible nitric oxide synthase (iNOS) and the macrophage markers F4/80 and M1/70, and semi-quantitative RT- PCR for iNOS, IL-12, and Nramp 1 mRNA will be presented to show the kinetics of early immune response to infection in the brain.

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ACUTE TOXOPLASMIC ENCEPHALITIS IN *NRAMP 1* CONGENIC MICE.

Carlton Evans,[1] Craig Roberts,[2] James Alexander,[2] Jenefer Blackwell.[1] Dept of Medicine, Addenbrooke's Hospital, Cambridge, CB2 2QQ.[1] Dept Immunology, University of Strathclyde, Glasgow, G4 0NR.[2]

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TOXOPLASMA GONDII ENCEPHALITIS IN *NRAMP 1* CONGENIC MICE. Carlton Evans,[1] Craig Roberts,[2] James Alexander,[2] Jenefer Blackwell.[1] Dept of Medicine, Addenbrooke's Hospital, Cambridge, CB2 2QQ.[1] Dept Immunology, University of Strathclyde, Glasgow, G4 0NR.[2]

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Manchester, U.K., November 27–29, 1996

01

CERTAIN HLA-DQB AND TNF MICROSATELLITE ALLELES ARE ASSOCIATED WITH THE RATE OF HIV DISEASE PROGRESSION.

Khoo SH[1] Pepper L[2], Snowdon N[3], Wilkins EGL[1], Ollier WER[2], Mandal B K. Dept of Infectious Diseases[1], N Manchester General Hospital, ARC[2] and Dept of Immunology[3], Manchester University.

The rate of CD4 lymphocyte decline differs markedly between HIV-positive individuals, and may be influenced by cofactors, HIV phenotype and the host T- cell response. Host genetic differences may also account for some of these observed differences.

We examined HLA class I (B), class II (DRB1, DQA, DQB), TAP2 and TNF microsatellite allele frequencies in 33 HIV+ patients with slower disease progression (CD4 count > 400/mm3 at ≥ 7 years) and 23 with rapid progression (CD4 count < 200/mm3 within 5 years). HLA class I and II alleles were defined using sequence-specific oligotyping, TAP2 polymorphisms by ARMS-PCR and TNF microsatellites by fluorescence-based microsatellite mapping techniques. Allele frequencies were compared with a matched panel of HIV-negative controls (n = 68). All subjects and controls were Caucasian and resident in NW England. No relationship with TAP2 alleles was observed. No significant association with HLA-B8 or DR3 was seen but HLA-DQB1*0302 (26% *vs* 0%; p = 0.007) and DQB1*0303 (22% *vs* 0%; p = 0.03) were associated with faster progression. Possession of the TNF c2 allele in fast *vs* slow was 15% *vs* 61% (OR 8.8, 95% CI 1.7-53; p = 0.002). Our results suggest that HLA-DQB1*0302 and *0303, and the TNF c2 microsatellite are strongly associated with the rate of HIV disease progression.

02

STRUCTURE - FUNCTION RELATIONSHIPS OF *CLOSTRIDIUM DIFFICILE* TOXIN A **Craggs, J. and Borriello, S.P. Institute of Infection and Immunity, University Hospital, Nottingham NG7 2UH.**

***Clostridium difficile*, the aetiological agent of pseudomembranous colitis in humans, produces two known toxins, A and B. Both toxins are potent cytotoxins, whilst toxin A is also a tissue damaging enterotoxin that probably causes most of the gastrointestinal symptoms associated with *C. difficile* induced colitis.**

To study structure-function relationships of toxin A, seven overlapping DNA fragments representing the entire toxin A gene have been cloned 'in frame' with a maltose binding protein. One of these clones incorporates the entire repeat region of toxin A which is believed to be responsible for the binding of the toxin to its target cell. The protein products from these clones have been expressed in *E. coli* as maltose binding protein fusion complexes. Each peptide has been purified from *E. coli* and cleaved from the maltose binding protein fusion product. The purified toxin A peptides have been analysed in a variety of biological assays including non - specific binding to monoclonal antibodies, haemagglutination of rabbit erythrocytes and cytotoxicity to tissue culture cells.

Two monoclonal antibodies (Mab's) have been raised to toxin A which appear to block the ability of the toxin to cause an enterotoxic effect. The first PCG-4, is believed to block binding of the toxin to its target cell, whereas the second 37B5, is believed to block an active site on toxin A responsible for enterotoxicity. Western blot analysis using these Mab's has revealed that of the seven toxin A fragments screened, only the repeat end binding region was recognised in both cases. This strongly suggests that both Mab's are blocking enterotoxicity by blocking binding of the toxin to its target cell.

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03

THE ROLE OF THE STAPHYLOCOCCUS AUREUS FIBRONECTIN-BINDING PROTEIN IN ADHESION TO INTACT HUMAN ENDOTHELIUM. Sharon Peacock[1], Tim Foster[2] and Anthony Berendt[1]. Adhesion and Infection Laboratory[1], Nuffield Department of Medicine, John Radcliffe Hospital, Oxford; and Moyne Institute[2], Trinity College, Dublin.

A well recognised complication of *Staphylococcus aureus* bacteraemia is seeding to distant sites. An essential first step in this process is interaction of the microorganism with vascular endothelium. A range of cell wall-associated adhesins which mediate adhesion to host plasma and matrix proteins have been identified, although their role in adhesion to intact human endothelial cells is unclear.

Using an *in vitro* assay, we have examined the adhesion of the following mutant strains to human umbilical vein endothelial cells: *Staphylococcus aureus* 8325-4 defective in fibronectin- and fibrinogen-binding proteins, protein A and coagulase; *Staphylococcus aureus* Phillips defective in collagen-binding protein; *Staphylococcus aureus* Newman defective in capsular polysaccharide.

Endothelial cell adhesion of *Staphylococcus aureus* 8325-4 deficient in fibronectin-binding protein was reduced to 25% of that demonstrated by the parent strain. Adhesion of this mutant was fully restored following complementation with a multicopy plasmid encoding fibronectin-binding protein. Adhesion of mutant strains defective in fibrinogen- and collagen-binding proteins, protein A, capsular polysaccharide and coagulase was not significantly different from that of the parent strain.

The fibronectin-binding protein appears to be important in adhesion of *Staphylococcus aureus* to intact human endothelial cells *in vitro*. Competitive adhesion inhibition assays using recombinant fibronectin-binding protein are in progress to evaluate this further.

04

QUANTITATIVE COMPARISON *IN VITRO* OF MUTATIONAL ANTIBIOTIC RESISTANCE OF *PROVIDENCIA STUARTII* USING A SPIRAL PLATER.

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The potential for spontaneous mutational antibiotic resistance of *Providencia stuartii* to gentamicin, tobramycin, amikacin, kanamycin, ampicillin and cefotaxime was determined quantitatively *in vitro* using a spiral plater. A gradient of drug was delivered across an isosensitest agar plate using the device and the agar plates were inoculated in radial streaks. The degree of resistance was estimated by dividing the antimicrobial concentration required to inhibit 90% of the colonies growing in the area beyond the MIC by the MIC itself. Strains repeatedly subcultured onto the antibiotic gradient plates became increasingly resistant to that antibiotic, the MIC's increasing up to 500-fold for some strain and antibiotic combinations. The degree of cross-resistance to other antimicrobials generated by this repeated subculture was also determined. The 13 strains tested consisted of two groups of strains; the first isolated since 1961, and the second isolated before 1944, prior to the introduction of aminoglycosides into medical use. No significant differences in the degree of resistance and degree of cross-resistance were observed between the groups.

The spiral plater may prove to be a simple and efficient means of detecting spontaneous mutational resistance and the extent of cross resistance phenomena, thereby enabling identification of antimicrobial agents which induce fewer mutants and less cross-resistance, to aid successful treatment of infections due to *Prov. stuartii.*

05

ACUTE TOXOPLASMIC ENCEPHALITIS IN *NRAMP 1* CONGENIC MICE. Carlton Evans,[1] Craig Roberts,[2] James Alexander,[2] Jenefer Blackwell.[1] Dept of Medicine, Addenbrooke's Hospital, Cambridge, CB2 2QQ.[1] Dept Immunology, University of Strathclyde, Glasgow, G4 0NR.[2]

The *Ity/Lsh/Bcg* Natural resistance associated macrophage protein gene (*Nramp 1*) regulates macrophage antimicrobial activity. In mice, *Nramp 1* has resistant and susceptible alleles which influence susceptibility to *T. gondii* infection. The *Drosophila* homologue (*Malvolio*) of *Nramp 1* is expressed in both macrophages and sensory neurones. We therefore studied the effects of *Nramp 1* on early *T. gondii* infection in male and female B10.L-Lsh^r (N20) resistant and B10 susceptible congenic mice. Eight month old mice were infected with 20 *T. gondii* cysts of the RRA strain by gavage. Male sex and the susceptible *Nramp 1* allele were both associated with earlier mortality. Frozen brain sections 10 days post infection revealed mild meningo-encephalitis and immunohistochemical staining with polyclonal anti-*T. gondii* antibodies showed early cyst formation. Immunohistochemical staining with anti-Nramp 1 antibodies demonstrated neuronal localisation within cytoplasmic granules which increased after *T. gondii* infection. Semi-quantitative RT-PCR of brain tissue revealed increased mRNA for iNOS, IL-12, and KC following infection. Mice with the resistant *Nramp 1* allele showed a significantly greater increase in iNOS and IL-12 mRNA than susceptible animals which may partially explain the observed effects of *Nramp 1* on mortality.

06

HEPATITIS C AND G CO-INFECTION AND INTERFERON RESPONSE. CYW Tong[1], R Khan[1], H Williams[1], CH Toh[2], CA Hart[1], IT Gilmore[3]. Departments of Medical Microbiology[1], Haematology[2] and Gastroenterology[3], Royal Liverpool University Hospital and University of Liverpool, Liverpool, UK.

Objective: To study the effect of hepatitis C virus (HCV) and hepatitis G virus (HGV) co-infection on response to α-interferon (IFN) treatment.

Methods: 36 patients with chronic HCV infection were treated with 3 MU of IFN thrice weekly for at least 3 months. Virological response was monitored by PCR (Roche). HCV genotype was determined using a type specific PCR method. HGV RNA was sought using RT-PCR with primers directed at a conserved area of the HGV genome common to HGV and GB virus C.

Results: ( ) = HGV co-infection.

Response of HCV to IFN	No.	HCV genotype 1	HCV genotype 2	HCV genotype 3
Responders	20 56%	6(2) 32%(25%)	1(0) 50%	13(0) 87%
Non-responders	16 44%	13(6) 68%(75%)	1(0) 50%	2(1) 13%(7%)
Total	36	19(8)	2(0)	15(1)

Of the 9 patients with HGV co-infection, only one lost HGV RNA during treatment. This patient had HCV genotype 1 infection that did not respond to IFN.

Conclusions: HGV co-infection was commoner in IFN non-responders for HCV (7/16 vs 2/20). It is possible that this association is the result of frequent co-transmission of HGV with HCV genotype 1. HGV co-infected with HCV appears resistant to IFN treatment as most patients (8/9) remained HGV RNA positive despite IFN.

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