Uploaded to VFC Website

March 2013

This Document has been provided to you courtesy of Veterans-For-Change!

Feel free to pass to any veteran who might be able to use this information!

For thousands more files like this and hundreds of links to useful information, and hundreds of "Frequently Asked Questions, please go to:

Veterans-For-Change

Veterans-For-Change is a 501(c)(3) Non-Profit Corporation
Tax ID #27-3820181

If Veteran's don't help Veteran's, who will?

We appreciate all donations to continue to provide information and services to Veterans and their families.

https://www.paypal.com/cgi-bin/webscr?cmd=_s-xclick&hosted_button_id=WGT2M5UTB9A78

Note: VFC is not liable for source information in this document, it is merely provided as a courtesy to our members.

Porphyria cutanea tarda preceding AIDS

SIR—In porphyria cutanea tarda IgG is deposited in and around blood vessels in the skin and at the dermoepidermal junction,[1] possibly as a result of vascular damage by porphyrin-light reaction. Porphyria cutanea tarda has been reported in patients with known HIV infection or in patients who subsequently developed AIDS.[3] We report a case of porphyria cutanea tarda which preceded AIDS.

A 53-year-old man, not known to be HIV-infected, had blisters on the dorsum of his hands with erosions and milia for four weeks' duration (figure, top). Erythema of the face and temporal hypertrichosis were noted. The patient did not consume alcohol. Histopathological examination revealed typical features of porphyria cutanea tarda. Direct immunofluorescence study showed intense IgA deposits at the dermoepidermal junction and the dermal vasculature (figure, bottom). Serum protein electrophoresis detected polyclonal gammopathy: IgA 9·6 g/L, IgG 24·7 g/L, IgM 3·72 g/L. Urine uroporphyrin was 543 nmol/day. Liver function tests were normal except for AST of 65 U/L. Hepatitis B surface antigen and anti-HAV and anti-HCV antibodies were not detected. Serum anti-HIV antibody was positive by western blot. CD4 count was 29/μL. Six weeks after the onset of skin blisters and two weeks after the diagnosis of porphyria cutanea tarda, the patient was admitted to hospital with pulmonary insufficiency and neurological abnormalities. He was found to have pneumocystes pneumonia, immunoblastic CNS lymphoma, and AIDS.

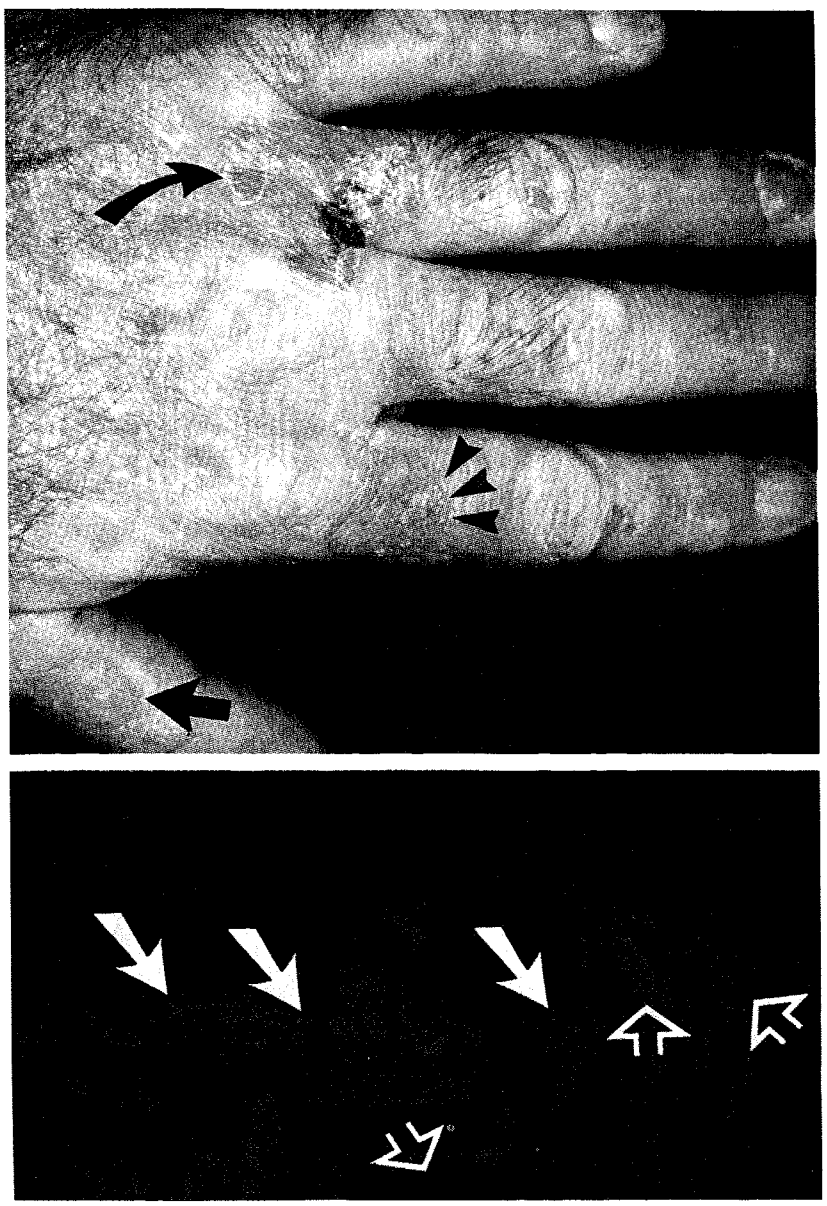

Figure: **Skin eruption on hand (top) and immunofluorescence in dermoepidermal junction (bottom)**

The relation between porphyria cutanea tarda and AIDS is unclear. Liver damage by hepatitis or by alcohol consumption cannot account for the development of porphyria in all cases,[2] including ours. HIV infection predisposes patients to photosensitivity,[3] and this may play a pathogenic role. HIV infection may interfere with porphyrin metabolism. Our case and others[2] should alert clinicians to the possibility for HIV infection when encountering patients with porphyria cutanea tarda.

In this patient, the disproportionate increase of serum IgA may account, at least in part, for the IgA deposition in his skin. Interleukin-4 and interleukin-5 are the two T-cell helper subset 2 secreted cytokines responsible for stimulating IgA production by B cells. The massive increase in serum IgA in this patient infers an occurrence of T helper 1 to 2 immune switching, which has been linked to the progression from HIV seroconversion to AIDS[4] as observed in this patient.

*Susan Ash, David T Woodley, *Lawrence S Chan*
Department of Dermatology, Northwestern University, Chicago IL 60611-3010, USA

1 Epstein JH, Tuffanelli DL, Epstein WL. Cutaneous changes in the porphyrias. *Arch Dermatol* 1973; **107:** 689–98.
2 Conlan MG, Hoots WK. Porphyria cutanea tarda in association with human immunodeficiency virus infection in a hemophiliac. *J Am Acad Dermatol* 1992; **26:** 857–59.
3 Toback AC, Longley J, Cardullo AC, et al. Severe chronic photosensitivity in association with acquired immunodeficiency syndrome. *J Am Acad Dermatol* 1986; **15:** 1056–57.
4 Clerici M, Shearer GM. A T_H1–T_H2 switch is a critical step in the etiology of HIV infection. *Immunol Today* 1993; **14:** 107–11.

HIV transmission by donor semen

SIR—In September, 1985, in *The Lancet*, Sydney researchers claimed "convincing evidence for transmission of HTLV-III [HIV]" to four women after in-vitro fertilisation with semen donated by a bisexual man.[1] This report still remains the only evidence for HIV transmission by such means and is also considered one of the most important pieces of evidence proving the infectivity of semen. The evidence for transmission of HIV was based on western blot testing where each individual had the following bands: donor p24/gp41; first woman gp41; second woman p24/gp41; third woman p24/gp41; fourth woman p24. However, the present Australian criteria for a positive western blot are "reactivity to at least one glycoprotein (gp41–5, gp110–120, or gp160) and three other viral proteins of *gag* (p12, p18, p24, p40, p55) or *pol* (p34, p53, p68) origin. A negative western blot had to show no reactivity to viral proteins; reactivity to viral proteins that did not fulfil positive or negative criteria was considered indeterminate".[2] Thus, by the present criteria for a positive western blot in Australia none of the four women or even the donor would be considered HIV positive. Neither would any be positive under the criteria set by the FDA and the American Red Cross. In fact, two of the women would not be positive by any criteria anywhere in the world.[3]

According to Fauci, "the least likely explanation for an indeterminate western blot is that the individual is infected with HIV", and "The most likely explanation is that the patient being tested has antibodies that crossreact with one of the proteins of HIV. The most common patterns of reactivity are antibodies that react with p24 and/or p55".[4] The above data pose these questions: have these five individuals been retested and if so, have they all been found positive and by what criteria; if some or all were not found positive have the authors modified or retracted their claims; if not retested, why not and are they still considered to be

infected with HIV; have any of these individuals been treated for HIV/AIDS and if so, with what drugs and on the basis of what tests?

Eleni Papadopulos-Eleopulos, Valendar F Turner, David S Causer, John M Papdimitriou

*Department of Medical Physics, Royal Perth Hospital, Perth 6001, Australia; Department of Emergency Medicine, Royal Perth Hospital, and Department of Pathology, University of Western Australia, Perth

1 Stewart GJ, Tyler JPP, Cunningham AL, et al. Transmission of human T-cell lymphotropic virus the III (HTLV-III) by artificial insemination by donor. *Lancet* 1985; ii: 581–85.
2 Healey DS, Maskill WJ, Howard TS, et al. HIV-1 western blot: development and assessment of testing to resolve indeterminate reactivity. *AIDS* 1992; **6:** 629–33.
3 Papadopulos-Eleopulos E, Turner VF, Papadimitriou JM. Is a positive western blot proof of HIV infection? *Biotechnology* 1993; **11:** 696–707.
4 Fauci AS, Lane HC. Human immunodeficiency virus (HIV) disease: AIDS and related disorders. In: Isselbacher KJ, Braunwald E, Wilson JD, Martin JB, Fauci AS, Kasper DL, eds. Harrison's Principles of internal medicine. 13th ed. New York: McGraw-Hill Inc, 1994: 1566–618.

This letter has been shown to Prof G J Stewart, who has declined the offer of a reply—ED L.

Fetal antigen 1 and growth hormone in pituitary somatotroph cells

SIR—Fetal antigen 1 (FA1), originally isolated from second trimester human amniotic fluid[1] has been characterised as a new circulating member of the epidermal growth factor circulating (EGF) superfamily.[2] FA1 is a 32–38 kDa glycoprotein containing six EGF-like motifs, and it has been suggested that FA1 is the enzymatic cleavage product of a larger transmembrane precursor molecule defined by the cDNAs referred to as "human adrenal-specific cDNA, pG2"[2,3] and "human delta-like cDNA, dlk".[2,4] Immunocytochemical analysis of the human embryo and fetus revealed the presence of FA1 in fetal hepatocytes, adrenal cortex, and all glandular cells of the pancreas anlage. In newborn babies and adults, however, FA1 expression seems to be restricted to the insulin producing β-cells in the islets of Langerhans in the pancreas and to the adrenals where the most pronounced staining reaction was seen in zona glomerulosa.[2,5] Moreover, FA1 has been demonstrated in small cell carcinomas and carcinoid tumours of the lung.[2]

Because of the suggested relation between FA1 expression and neuroendocrine structures we analysed the pituitary gland and found cellular colocalisation of FA1 and human growth hormone (hGH). The figure shows that the FA1 staining was seen as a dot-like pattern corresponding to the Golgi-zone, whereas hGH was more uniformly distributed within the cytoplasm of the somatotroph cells, but with weak staining in the FA1-positive area. The Golgi apparatus is the site of post-translatory modification of proteins before secretion, and these findings suggest that somatotroph cells of the pituitary gland contribute to the circulating pool of FA1. The colocalisation of FA1 and somatotroph cells was observed in all five different apparently normal adenopituitary tissues examined.

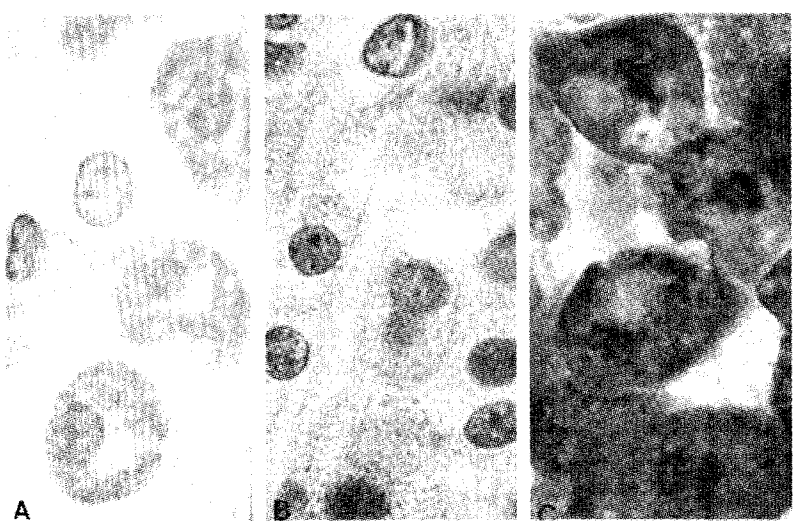

Figure: **Localisation of fetal antigen 1 and growth hormone**
Immunolabelling of A, hGH and B, FA1 in tissue from normal adenopituitary tissue with polyclonal rabbit anti-human hGH (DAKO A/S, Denmark) and monoclonal anti-human FA1, respectively (immunoperoxidase technique with 3-Amino-9-ethylcarbazole as chromogen). C, double-immunolabelling in the same tissue of hGH (alkaline phosphatase technique with fast red TR as chromogen) and FA1 (immunoperoxidase technique with 3,3'-diaminobenzidine tetrahydrochloride with nickel as chromogen) with the above mentioned antibodies. (Original micrographs×1250.)

J B Larsen, C H Jensen, H D Schrøder, B Teisner, P Bjerre, C Hagen

Department of Pathology, Odense University Hospital, 5000 Odense C, Denmark

1 Fay T, Jacobs I, Teisner B, et al. Two fetal antigens (FA1 and FA2) and endometrial proteins (PP12 and PP14) isolated from amniotic fluid. Preliminary observations in fetal and maternal tissues. *Eur J Obstet Gynecol Reprod Biol* 1988; **29:** 73–85.
2 Jensen CH, Krogh TN, et al. Protein structure of fetal antigen 1 (FA1). A novel circulating human epidermal-growth-factor-like protein expressed in neuroendocrine tumors and its relation to the gene products of dlk and pG2. *Eur J Biochem* 1994; **225:** 83–92.
3 Helman LJ, Sack N, Plon SE, Israel MA. The sequence of an adrenal specific human cDNA, pG2. *Nucleic Acid Res* 1990; **18:** 685.
4 Laborda J, Sausville EA, Hoffman T, Notario V. Dlk, a putative mammalian homeotic gene differentially expressed in small cell lung carcinoma and neuroendocrine tumor cell line. *J Biol Chem* 1993; **268:** 3817–20.
5 Jensen CH, Teisner B, Højrup P, et al. Studies on the isolation, structural analysis and tissue localization of fetal antigen 1 and its relation to human adrenal-specific cDNA, pG2. *Hum Reprod* 1993; **8:** 635–41.

Intermittent maple syrup disease

SIR—The case report by Asola (Nov 18, p 1338)[1] emphasises that patients with maple-syrup-urine disease, even mild variants, are at risk of encephalopathy when subjected to major metabolic stress. This disorder is widely regarded as very rare but this may not be so. Our experience suggests that the mild variants may be difficult to diagnose and therefore easy to overlook. During the episodes of decompensation, plasma aminoacid profiles are abnormal, but these often rapidly return to normal with treatment. Between attacks, plasma aminoacids are usually normal and the activity of the branched chain oxoacid (BCOA) decarboxylase complex in fibroblasts do not correlate well with the severity of the disease.[2] Whole-body leucine oxidation in vivo may provide better insight into the disorder.[3]

We studied two patients. One, a 15-year-old girl, presented at age 4 years with severe encephalopathy requiring intensive care (maximum plasma leucine 1600 μmol/L). Since then, on moderate protein restriction, she has been well with no episodes of decompensation and normal plasma aminoacid concentrations. The second, a boy aged 8 has had two episodes of encephalopathy with raised branched chain aminoacid concentrations but normal BCOA oxidation in cultured skin fibroblasts. Whole-body leucine oxidation was measured with a continuous infusion of 1-^{13}C-leucine[3] and was 5 μmol/kg per h and 11 μmol/kg per h, 31% and 68% of the reference values of children of similar age.[4] We conclude that measurement of the whole-body leucine oxidation establishes the diagnosis more reliably and