Pelger–Huet anomaly is an autosomal dominant hereditary disorder. It is caused by mutation of lamin B receptor (LBR) located on chromosome 1. This receptor (by helping cholesterol synthesis) becomes a structural base of the cell's membrane. Some syndromes caused by impairment of sterol biosynthesis have been reported. Among these, Greenberg dysplasia has LBR receptor mutations connected with Pelger anomaly. Although, in case of heterozygous individuals, the Pelger anomaly seems a harmless phenomenon, examination of animal and human homozygotes suggests that other genetic malformations and death may be associated with it. This reinforces the probability that modified forms of LBR, or its decreased expression, may cause an altered membrane function and embryonic developmental problems.

In our hospital we found a Pelger phenomenon in the full blood count of a child with Fryns syndrome. This is a new contribution to establish a possible aetiology of malformations with unclarified genetic background. Is Fryns syndrome related in some way to Greenberg dysplasia or even perhaps the same genetic mutation with different symptoms?

TP6.28

MATERNAL SERUM SCREENING FOR DOWN SYNDROME IN THAI PREGNANT WOMEN

S. Sangkitporn, S. Lamlertkittikul, S.K. Sangkitporn, V. Chandeying
National Institute of Health, Department of Medical Sciences, Nonthaburi, Thailand
Email: somchai@dmsc.moph.go.th

Down syndrome is one of the most important causes of mental retardation in the population. The main aim of this pilot study was to evaluate the sensitivity of maternal serum screening (triple test) to identify women at an increased risk for an affected pregnancy and to reduce the incidence of invasive amniocentesis procedures. Triple test involves combining the maternal age risk with the risks associated with the concentrations of maternal serum alpha-fetoprotein, unconjugated estriol, and human chorionic gonadotropin that are measured by a chemiluminescence immunoassay method.

The study consisted of 1000 pregnant women, attending antenatal care unit, Hat Yai Center Hospital. The gestational range for the study group was 14–19 weeks. 171 of these women were considered at increased risk for Down syndrome and 141 of them had an amniocentesis. Among 199 pregnant women over 35 years of age, 93 of them were triple test positive. The results of karyotyping show that there were 4 cases with trisomy 21, 1 case with 47 XXX and 1 case with chromosome translocation. All these chromosome abnormalities were detected in pregnant women over 35 years of age.

In conclusions, the use of triple test as a screening tool in our population could reduce the number of amniocenteses, while no cases of Down syndrome would be missed.

TP6.29

RAMAN SPECTROSCOPY AS A SCREENING METHOD FOR DRUGS OF ABUSE AND THEIR PRECURSORS

M.P.M. Marques, R. Calheiros, N. Milhazes, F. Borges
Research Unit "Molecular Physical-Chemistry"; Biochemistry Dep., Faculty Sciences and Technology, Univ. Coimbra, 3001-401 Coimbra, Portugal
Email: pmc@ci.uc.pt

Identification of illicit drugs, namely MDA (3,4-methylenedioxyamphetamine) and MDMA (3,4-methylenedioxymethamphetamine), is usually carried out using techniques such as colorimetric tests, GC-MS or NMR spectroscopy. However, these methods have proved to be poorly selective, expensive and often time-consuming when compared to vibrational spectroscopy (e.g. Raman), which provides unique fingerprint spectra for each different compound analysed.

The present work reports a Raman spectroscopic study, coupled to theoretical (ab initio) calculations, of several β-methyl-β-nitrostyrene derivatives, which are important intermediates in the synthesis of illicit amphetamine-like drugs.

The Raman spectra obtained showed characteristic features for each of the compounds studied. Moreover, it was verified that their vibrational pattern is strongly affected by the presence of a para substituent in the aromatic ring (either O-CH3 or S-CH3), as well as by an O $\rightarrow$ S substitution. Based on the complete ab initio conformational analysis performed for these systems, a thorough assignment of the experimental spectroscopic data was performed, leading to a ready and unequivocal differentiation and identification of this kind of synthetic precursors of illegally produced drugs of abuse – namely through the bands at 1300 cm^{-1} (NO2 stretching modes), as well as at 250 and 1440 cm^{-1} (typical of the CH3 group).

The described results indicate that Raman spectroscopy is a most promising tool for Forensic Sciences, as a screening method for determining the composition profiles of illicit substances, as well as for tracking clandestine laboratories. Thus, it will hopefully be possible, in the near future, to rely on a Raman database that will constitute an invaluable tool for both forensic control and toxicological studies.

TP6.30

NEW INSIGHTS ON COCAINE–OPIATES INTERACTIONS

M.P.M. Marques, J.M.P.J. Garrido, A.M.S. Silva, F. Borges, A.M.O. Brett
Research Unit "Molecular Physical-Chemistry"; Biochemistry Dep., Faculty Sciences and Technology, Univ. Coimbra, 3001-401 Coimbra, Portugal
Email: pmc@ci.uc.pt

The simultaneous self-administration of opiates and cocaine–"speedballing"–is relatively widespread among drug users, and is probably responsible for higher levels of euphoria compared to those produced by each drug separately. Although the underlying biological basis for abuse of cocaine and opiate combinations is still unclear, clinical studies can give some insight into the desire for this dual abuse.

Up to this date, the pharmacological reasons for cocaine use in opiate-dependent individuals are poorly understood, and little is known about the patterns of cocaine and heroin or morphine co-use. Thus, the present study was undertaken, using electrochemistry, Raman and NMR spectroscopy, in order to investigate the possible interactions between opiates and cocaine, at a molecular level.

The results obtained by any of the methods used reflect a chemical interaction between cocaine and morphine, but not between cocaine and heroin. This specific cocaine:morphine interaction was detected

in solution through electrochemical methods, and confirmed by both RMN and Raman spectroscopy coupled to theoretical methods. In fact, the structural data yielded by the ab initio calculations allowed the conclusion that the presence of the two terminal −O(C=O)CH3 groups in heroin seem to hamper the approximation of the cocaine molecule, while the approach to the morphine cavity was found to be much more favourable, as it does not involve any significant steric hindrance. Furthermore, only the protonated species of morphine, for which a slightly more open conformation was determined, leads to a detectable association with cocaine. The cocaine–morphine interplay is thus suggested to take place through the inner cavity of the morphine molecule, most probably through a (C=O)OH . . . O interaction.

TP6.31

CLUSTERIN IS DIFFERENTIALLY EXPRESSED IN MALIGNANT MELANOMAS AS COMPARED TO ACQUIRED MELANOCYTIC NEVI AND MODULATES UV-B-INDUCED APOPTOSIS IN VITRO

B. Shannan[1], M. Seifert[1], K. Leskov[2], D. Boothman[2], W. Tilgen[1], J. Reichrath[1]

[1]Department of Dermatology, The Saarland University Hospital, 66421 Homburg, Germany, [2]Department of Radiation Oncology, Case Western Reserve University, Cleveland, OH, USA

Email: bshannan@ureach.com

Aim: To establish a connection between clusterin (CLU) expression and malignant melanoma, and to see how this expression is regulated.

Methods: Paraffin sections of primary cutaneous malignant melanomas, metastases of malignant melanomas and acquired melanocytic nevi were analyzed immunohistochemically using antibodies that detect both isoforms of clusterin. The pro-apoptotic nCLU and the anti-apoptotic sCLU were detected in a proportion of malignant melanomas and metastases, but not in acquired melanocytic nevi. Additionally, expression of CLU in various melanoma cell lines (MeWo, SKMEl-28, SKMEL-5, SKMEL-25, and MelJuSo) was also analyzed.

Results: All melanoma cell lines revealed strong expression of CLU mRNA and protein. CLU mRNA and protein levels were regulated time-dependently by 1,25(OH)2 D3 treatment. Moreover, stable transfected and CLU over-expressing LNCaP CLU+ prostate carcinoma cells responded differentially as compared to untransfected LNCaP cells, analyzing cell cycle and apoptosis following UV- or 1,25(OH)2 D3-treatment. In contrast to benign acquired melanocytic nevi, CLU is expressed in malignant melanomas, metastases and melanoma cell lines. CLU expression is regulated time-dependently by 1,25(OH)2D3, indicating that antiproliferative effects of 1,25(OH)2D3 on melanoma cell lines may be at least in part mediated via regulation of CLU expression.

Conclusion: CLU may be of importance for the growth characteristics of melanoma cells, and CLU over expression protects against the cytotoxic effects mediated by 1,25(OH)2 D3 in prostate LNCaP cell lines. CLU seems to be important for the treatment of melanoma. However, its role must be further defined by more experiments.

TP6.32

BRITISH THORACIC SOCIETY GUIDELINES FOR BIOCHEMICAL ANALYSIS OF PLEURAL FLUID–A DISTRICT GENERAL HOSPITAL PERSPECTIVE

L.M. Cranfield, S. Ansari

Southend Hospital, Westcliff-on-sea, Essex SS0 0RY, UK

Email: Lesley.cranfield@southend.nhs.uk

In 2003 the British Thoracic Society published guidelines for the investigation of unilateral pleural effusions, aiming to establish a swift diagnosis while minimising unnecessary invasive investigations.

An algorithm was developed at Southend Hospital; the samples required on all patients were pleural fluid for protein and LDH, a blood gas syringe sample for pH and a paired serum sample for LDH and protein. Glucose measurement should only be requested on rheumatoid or connective tissue effusions and required paired pleural fluid and plasma glucose fluoride samples.

An audit covering six months was carried out to measure adherence to the sample requirements; assess whether Light's criteria discriminated between transudates and exudates better than pleural fluid protein alone; assess if pH measurement was clinically useful on all fluids.

Only 70% of requests had a paired serum sample and only 21% were accompanied by a suitable sample for pH. 42% requested glucose but only 18% had the correct samples collected.

The patients' case notes were reviewed to ascertain the clinical diagnosis. Clinically 71% of effusions were exudates and 25% transudates. Using pleural fluid protein alone the sensitivity for exudates was 51% which improved to 83% using Light's criteria.

Only 21% of patients had pH measured and in 18% (4 patients) indicated the need for aggressive treatment, two due to complicated parapneumonic effusions.

The samples recommended in the guidelines were not received in all patients; insufficient numbers of patients had pH measured, so conclusions cannot be drawn on the usefulness of pH in all patients. Excessive numbers of glucose requests were received.

TP6.33

SW AND WESSEX REGIONAL SURVEY OF CARDIAC MARKERS

J. Schroeder, R. Fisher

Department of Clinical Chemistry, Royal Cornwall Hospital, Truro, Cornwall TR1 3LJ, UK

Email: Jessica.Schroeder@rcht.cornwall.nhs.uk

The definition of myocardial infarction has been evolving over recent years. The new definition includes elevated troponin levels. Currently there are no published UK guidelines regarding the frequency and time intervals for troponin sampling. The choice of myocardial infarction (MI) and risk based thresholds for troponin measurements are still debatable. The aim of this survey was to review current practice in the SW and Wessex region laboratories.

In September 2004 a questionnaire was sent out to 21 laboratories, and 20 responses were received. All laboratories offered troponin, with 80% offering 'on demand' service, and 55% having a turn