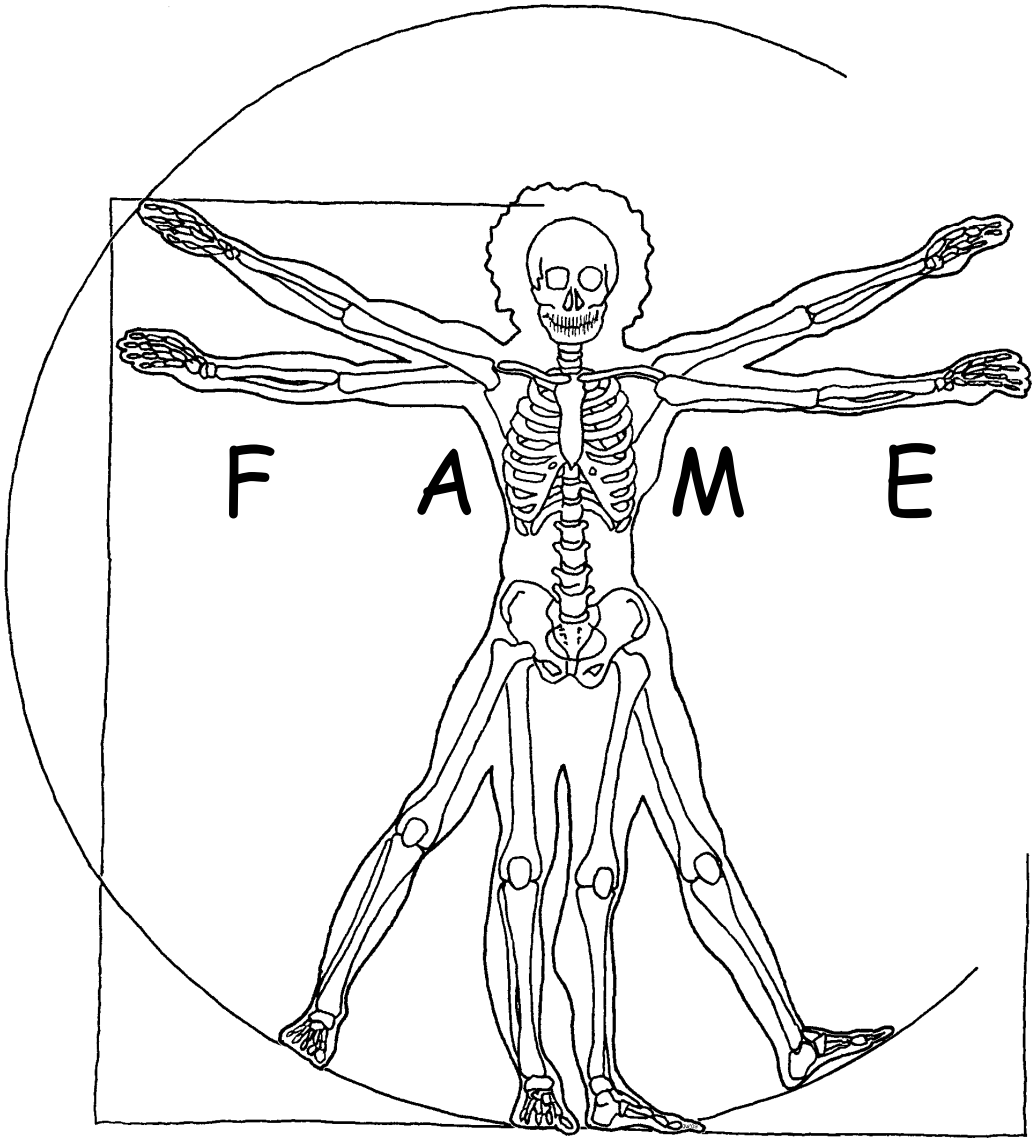
Fysisch-Anthropologische Mededelingen



Newsletter of the Dutch Association of Physical Anthropologists

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Contents

From the editor

This new FAME begins with an obituary of Prof. dr R. Luyken, our first honorary member, who died late last year.

Contrary to “tradition”, you will not find any Autumn Symposium abstracts in this issue for the simple reason that no abstracts were received.

But eleven of our members contributed abstracts, poster presentations and an article, thus making another interesting and up-to-date issue of Fame possible. Thank you all!

Obituary

Professor dr R Luyken (1918-2011)

Late last year one of the Dutch pioneers in the field of human nutrition died.
Already during his medical studies (1935-1942), Rijk Luyken was interested in the subject, at that time hardly an issue of scientific attention. As early as 1943 he defended his PhD thesis on lactoflavine deficiency.

Since then - assisted by his beloved wife - he conducted somatometric investigations on the nutritional status of children and adults in the most diverse locations. During 1945-1949 they worked in the former Dutch East Indies, where at first the nutritional status and physiology of ex-prisoners of Japanese POW camps were measured. During 1953-1955 they were active in former Dutch New Guinea. For a long time, his results formed the only specific information available on these areas. In Surinam, pre-school children from four different ethnic groups were measured, and research was also carried out on the Dutch Antilles, including the Windward Islands, as well as in for instance Kenya.
His numerous publications deal with Third World malnutrition. In children this may induce stunted growth, since growth and somatic development reflect the interaction between genetic potential and the environment. In the Netherlands, among others, the nutritional status of Marines before and after their first military training was measured, as was the nutritional status of immigrants. His research included in addition to information on food consumption also clinical and biochemical parameters. The detailed somatometry was in accordance with the physical anthropological approach of those days.

In 1954 he joined the Central Institute of Nutrition Research TNO in Zeist. During 1964-1970 he was head of the department Nutritional Status of the Dutch Population. In 1973 he was appointed professor of nutrition and food supply at the University of Amsterdam. He had various additional duties, such as for instance editor of the journal Voeding (Nutrition).

For many years, he tried to convince his colleagues, cardiologists, endocrinologists, of the relevance of attention to and understanding of the nutritional status of their patients. In 1979 in recognition of all their work in the tropics, Rijk Luyken and his wife, mrs F.W.M. Luyken-Koning, were awarded the Eijkman medal.

Luyken's work is certainly also relevant for physical anthropologists. Not only his contributions to the field of growth and development, but also his studies on the ecological adaptation of humans in relation to the availability of essential nutrients can be considered as a study of evolutionary processes.

When Rijk heard of the struggle of a small group of interested people to save the field of human anthropology, when due to a severe recession the only existing Institute of Human Biology in Utrecht was threatened with closure in 1983, he strongly supported the actions to realize the foundation of the Dutch Association of Physical Anthropologists and became one of its first members. In appreciation of his support and in recognition of his work, he was made an honorary member. Our older members will remember with respect this kind, modest, and friendly man.

Machteld Roede
Maastricht

✦

Abstracts of articles and books

SAMENVATTING VAN EEN ARCHEOLOGISCH HUMAAN DNA ONDERZOEK DAT ALS DEELONDERZOEK GEPUBLICEERD IS

Altena, Eveline
Forensisch Laboratorium voor DNA-Onderzoek, Leids Universitair Medisch Centrum, Leiden.

In: Lauwerier, R.C.G.M., A. Müller, D.E. Smal 2011: Merovingers in een villa; Romeinse villa en Merovingisch grafveld Borgharen – Pasestraat. Onderzoek 2008-2009. Rapportage Archeologische Monumentenzorg 189, Rijksdienst voor het Cultureel Erfgoed.
Deze publicatie is gratis te downloaden op:
http://www.cultureelerfgoed.nl/archeologie/archeologie/publicaties

Voor dit project is DNA onderzoek uitgevoerd op vijf individuen uit drie Merovingische graven (DNA monsters zijn onder forensische omstandigheden verzameld en onderzocht). De graven bevonden zich op een voormalig Romeins villa terrein in Borgharen. Tijdens verschillende opgraafcampagnes zijn 23 graven geïdentificeerd. De graven zijn gedateerd tussen de tweede helft van de 6e eeuw en het eerste kwart van de 7e eeuw.
In één van de graven was een volwassen vrouw bijgezet waarvan de resten nog min of meer in anatomisch verband lagen. Aan haar voeteneind was een bundeltje bijgezet met de resten van twee jonge kinderen, niet in anatomisch verband. Het graf bevatte verder weinig bijgiften en kan als relatief eenvoudig worden omschreven. Van één van de kinderen kon vastgesteld worden dat het een jongetje was en op basis van autosomale Short Tandem Repeats (STRs) kon ook vastgesteld worden dat het hoogst waarschijnlijk de zoon van de volwassen vrouw was. Helaas kon dit niet bevestigd worden met het mitochondriale DNA. Dit kon niet getypeerd worden voor het jongetje. Van het tweede kind was te weinig informatie beschikbaar om het geslacht met zekerheid te bepalen en een genetische relatie met de volwassen vrouw aan te tonen of uit te sluiten.
De andere twee onderzochte individuen betroffen een meisje van ongeveer 11 jaar (geslachtsbepaling op basis van aanwezige bijgiften) en een volwassen man. Zij waren beiden in een apart graf begraven, maar er waren sterke overeenkomsten, zoals het graftype (houten container) en de relatief grote rijkdom van de bijgiften.

Het geslacht van het meisje werd bevestigd door DNA onderzoek en op basis van autosomale STRs is het zeer waarschijnlijk dat het hier vader en dochter betreft.

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DETECTION OF THE TURKISH INVERSION-DELETION $(\delta\beta)^O$ THALASSEMIA IN A FAMILY SEEKING PRENATAL DIAGNOSIS AND PREVENTION

Bilgen, Turker[1], Marion Phylipsen[3], Yunus ARIKAN[1], M. Akif Yesilipek[2], Cornelis L. Harteveld[3], and Ibrahim Keser[1]

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Beta-thalassemia (β-thal) is hereditary blood disorder caused by anomalies in the beta chain synthesis of hemoglobin. β-thal is generally caused by point mutations. On the other hand, at least 60 different beta globin gene related deletions have been described so far. We report here a family with Turkish type Inversion-Deletion $(\delta\beta)^o$ Thalassemia seeking prenatal diagnosis and prevention. The couple with thalassemia minor clinical and hematological findings was screened for beta globin gene mutations by direct sequencing. The mother was found to be carrier for -30 (T→A), while sequence analysis was failed in father. Genetic analyses in the father were expanded to detect the possible deletion with taking into account the elevated HbF level. Detailed molecular analyses of β globin locus in father by MLPA have revealed heterozygosity for deletion of the complete δ and β globin genes, confirmed by Gap-PCR. Screening of the other family members have shown that his mother and sister were also carrier for the Turkish type of inv/del $(\delta\beta)^o$ thalassemia mutation. During the prenatal diagnostic testing based on mutation analyses for maternal mutation and SNP based haplotyping, we were able to conclude that out of four fetuses, one was carrier for maternal mutation and the other one was normal while remaining two had both of maternal and paternal mutations. Because the presence of deletion in father was not known during prenatal diagnosis attempts, we were able to test the fetal samples for deletion later on. The deletion has been shown with later MLPA studies in two fetuses showing homozygosity of maternal mutation -30 (T→A) and -30 (T→A) mutation related SNP set with sequencing analyses.

Even though β-thal is usually caused by point mutations, deletional type mutations complicating the diagnosis and genetic counseling have to be considered especially when the mutation screening by routine methods has failed.

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UNIPARENTAL DISOMY AND PROGRESSIVE CLONAL SELECTION: A COMMON MECHANISM CAUSING LATE ONSET β-THALASSEMIA MAJOR?

Harteveld, C.L.[1], Rifaldi, C.[2], Giambona, A.[3], Ruivenkamp, C.[1], Hoffer, M.[1], Borgnia-Pignatti, C.[4], Maggio, A.[3], Cappellini, M.[2] and Giordano, P.C.[1]

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Background We present three cases of "severe late onset β-thalassemia" in three independent subjects, all presenting with the mild phenotype of beta thalassemia minor up to adult age and developing a severe transfusion dependent phenotype in the third and fourth decade of life when a presumed homozygosity for the β-thalassemia mutation is observed. Two subjects had a father carrier and a non-carrier mother and one male subject was married and had 3 children of which only one was carrier.
Method Direct sequencing of the β-globin genes. Multiplex Ligation dependent Probe Amplification (MLPA) analysis of the HBB (β-globin) gene cluster. The Affymetrix GeneChip Human Mapping 262K *NspI* array (Affymetrix, Santa Clara, CA, USA).
Results In all three cases molecular analysis shows sequences in which homozygosity for the beta-thalassemia mutation occurs in the presence of a small but consistent wildtype signal in DNA extracted from peripheral blood, from buccal mucose and from erythroid cultures. Loss of heterozygosity due to a deletion of one allele was excluded by MLPA analysis. Affymetrix SNP-array analysis reveals homozygosity for a large number of SNP's in a region on the short arm of chromosome 11 containing the beta-globin gene with a low background of wildtype

SNP's, indicating mosaicism for a partial uniparental isodisomy of chromosome 11p.

Conclusion We demonstrate that uniparental isodisomy of part of chromosome 11p15 accounts for the observed mosaicism in all three independent cases. Clonal selection for hematopoietic stem cells containing the uniparental isodisomy for the mutant beta-globin gene during life may account for the progressive development of the disease.

A similar observation for a single case was made by Chang et al. (Haematologica 2008, 93(6):913-916), who found this in a single patient with late-onset β-thalassemia Major. Our study demonstrates that uniparental isodisomy of chromosome 11p15 is apparently more frequently associated with late-onset transfusion dependent β-thalassemia in presumed carriers at birth, representing a novel mechanism leading to this special form of beta-thalassemia and in other late-onset genetic diseases.

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SEGMENTAL DUPLICATIONS INVOLVING THE α-GLOBIN GENE CLUSTER AS A MODULATING FACTOR IN β-THALASSEMIA INTERMEDIA

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Recently we have described two cases of heterozygosity for the common β°-thalassemia mutation β39 (C→T) presenting with a thalassemia intermedia phenotype (1). Multiplex Ligation dependent Probe Amplification (MLPA) analysis of the α-globin gene cluster revealed two new rearrangements, consisting of a full duplication of the α-globin genes locus including the upstream regulatory elements. Here, we present two other case; one, a family of mixed Sephardic Ashkenazi

Jewish origin living in Canada, in which the propositus (a 2 yrs old girl) presented with a pronounced microcytic hypochromic anemia, a borderline HbA2 and heterozygous for a β polyA mutation. Only one parent showed mild microcytic hypochromic anemia due to heterozygosity for the β-mutation. The second case, a 6 yrs old girl of middle-eastern origin living in the U.K., has severe anemia and splenomegaly, while the mother from whom she has inherited the β^0-thalassemia mutation is clinically asymptomatic. MLPA analysis of the α-globin gene cluster revealed two new rearrangements, consisting of a full duplication of the α-globin gene cluster and the upstream regulatory elements. The first is a duplication of approximately 435 kb between position 75563-510533 from the telomere (UCSC Genome Browser, May 2004) and the second, approximately 107 kb between positions 90548-198161.
We report the clinical and hematological data and the molecular characterization. We conclude that α-globin gene duplication is more common than previously thought and should be investigated as a contributing cause in all unexplained unusually severe heterogeneous β thalassemia.

(1) Harteveld et al. Blood Cells Mol Dis. 2008 May-Jun;40(3):312-6.

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MOLECULAR SPECTRUM OF β-THALASSEMIA IN EAST JAVA, INDONESIA

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[3] Hematology Laboratory, Child Health Department, Dr. Soetomo Hospital, Surabaya, Indonesia.

Defining the spectrum of specific thalassemia mutations is an important issue when planning prevention programs in large multi ethnic countries such as Indonesia. In a first attempt to define the prevalence of the common mutations in East Java we selected a cohort of 17 transfusion- dependent patients attending the Dr. Soetomo Hospital, Surabaya, Indonesia. After basic diagnostics we performed direct DNA sequencing for all β-globin genes. The results obtained on 34 independent chromosomes revealed the following prevalence rates: c.79 G>A p. Glu27Lys (Hb

E) 47.0%; c.92+5G>C (IVS-I-5 G>C) 20.6%; c.109_110 delC p.Pro37Leu fs X7 [codon 35 (–C)] 17.6%; c.46del T p.Trp16Gly fsX4 [codon 15 (–T)] 5.9%; c.126_129delCTTT p. Phe42Leu fs X19 (codons 41/42) 2.9%; c.316-197 C>T [IVS-II-654 (C>T)] 2.9%; c*112 A>G (PolyA) 2.9%. Our preliminary results show that the distribution of the prevalent mutations in our cohort is quite homogeneous but with different forms than previously reported. This indicates that more studies on a larger scale and in different geographical areas are needed to refine our provisional results and to characterize the molecular background of the disease in the whole country.

SPATIAL VARIATIONS IN BIOAVAILABLE Sr IN THE NETHERLANDS AS A POTENTIAL PROVENANCE INDICATOR IN DUTCH ARCHAEOLOGY

Kootker, Lisette M.[1], Gareth Davies[2] and Henk Kars[1]

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Nederlands Aardwetenschappelijk Congres 11 (NAC11), 29-30 maart 2012, Veldhoven, Nederland

Strontium isotope ratios ($^{87}Sr/^{86}Sr$) are a powerful tool to investigate the provenance of archaeological material. Due to the high variability of geological lithologies in both chemical composition and age, $^{87}Sr/^{86}Sr$ ratios can be used as indicators of geological regions. The isotopic strontium signature of geological materials is taken up in our food chain by erosion of bedrock and through soils, vegetation and livestock and is eventually taken up in the human skeleton where it substitutes for calcium in hydroxyapatite in shell, bone, dentine and tooth enamel. In order to interpret the provenance of an individual based on Sr isotope ratios, a map of the bioavailable $^{87}Sr/^{86}Sr$ is required. However, due to landscape evolution and changes in agricultural practice, bioavailable

Sr in may have changed over time requiring maps to be evaluated for individual time periods.

This PhD project aims to evaluate the spatial distribution of bioavailable $^{87}Sr/^{86}Sr$ per archaeological period to assess the applicability of strontium isotopes as a proxy for interregional mobility within the Netherlands. Sampling will concentrate on archaeological animal and human remains and modern rodents. Initial results are presented here, demonstrating a considerable spatial variability in bioavailable Sr in The Netherlands.

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THE MAN FROM AKKAZ

Maat, G.J.R.

In: Tell Akkaz in Kuwait (J.Gachet-Bizollon ed.). Travaux de la Maison de l'Orient et de la Méditerranée 57(TMO), Lyon 57: 307-317, 2011.

In 1993, during the archaeological excavations of the site of Akkaz, Kuwait, human skeletal remains were found more or less in their anatomical context within a tomb of 0.6 x 1.9 m made of small and medium size erected stones: this poorly preserved tomb was situated in the southern nave of a contemporary church (5/6th-8th c.). The skeleton lay extended, with the head to the west and the face facing to the north. After reconstruction and analysis it appeared that they had belonged to a 34 to 50-year-old male. The serious degree of molar attrition for age corresponded well with that seen in other populations living on a diet containing abundant amounts of abrasives, but lacking dates as a major foodstuff, in the desert of the Arabian Peninsula. The most prominent disease features noticed on this skeleton were connective tissue and cartilage ossifications due to Diffuse Idiopathic Skeletal Hyperostosis. In the literature this disease is frequently associated with rich diets, obesity and a monastic way of life. Additional mild changes from osteoarthritis noticed on the joints of the spine and phalanxes were not usual for a male of this age.

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DNA ONDERZOEK OP DE MIDDELEEUWSE GRAFKELDER VAN DE VAN DOERNE FAMILIE

Smeding, Risha, Eveline Altena en Peter de Knijff

Forensisch Laboratorium voor DNA Onderzoek, Leids Universitair Medisch Centrum

In: SOJA bundel 2011, in press

Begin jaren zestig werd tijdens een restauratie van de St. Willibrorduskerk in Deurne een grafkelder herontdekt. De grafkelder is vermoedelijk in gebruik geweest van 1462 tot 1526. De skeletresten zijn in 2004 opgegraven, waarna er fysisch antropologisch onderzoek is verricht. Op het FLDO is in 2009 en 2010 DNA onderzoek gedaan op zeven individuen. Op de grafzerk aan de toegang van het graf stond het volgende geschreven:

> *Henrick van Doerne (gestorven 1508) bij zijn vader Everden van Doerne, zijn ooms, zijn broers, zijn kinderen, zijn zus en zijn neven en Cristina van Hemert (gestorven 1499).*

Het graf zou dus van Henrick van Doerne en zijn familie moeten zijn. Door de resultaten van het fysisch antropologische onderzoek (leeftijdsbepaling, geslachtsbepaling, MNI) en het DNA onderzoek (geslachtsbepaling, ySTR, auSTR, HVR1 mtDNA haplotypen) te vergelijken met de beschikbare genealogie hebben we getracht uit te zoeken of het graf daadwerkelijk tot de familie van Doerne zou kunnen behoren.
De jongste individuen die in de kelder zijn aangetroffen betreffen een baby en een kindje van ongeveer zes jaar. Het jongste individu vermeld in de genealogie is Johannes van Doerne, het ten minste tien jaar oude neefje van Henrick. Echter, van niet alle leden van de familie die vermeld zijn in de genealogie is de leeftijd bij overlijden bekend. Het minimum aantal aangetroffen individuen (20) is in overeenstemming met het aantal individuen dat volgens de genealogie begraven zou kunnen zijn (max. 28). Het aantal aangetroffen mitochondriale haplotypen (4) past eveneens binnen de genealogie (max. 6). Een aangetroffen vader-zoon relatie binnen de zeven onderzochte individuen, waarvan een van beide individuen een leeftijd had van ongeveer 30 jaar, valt ook in te passen binnen de genealogie. De enige

duidelijke inconsistentie die we hebben kunnen aantreffen was het aantal ySTR profielen. We hebben in totaal drie verschillende ySTR profielen aangetroffen bij vier van de onderzochte mannen. Echter, volgens de genealogie zouden alle mannen die begraven zijn in de grafkelder moeten afstammen van Gevardus van Doerne, de grootvader van Henrick en dus zouden zij allen een identiek ySTR profiel moeten hebben. De DNA resultaten en de beschikbare genealogie zijn betreft verwantschap in de mannelijke lijn dus inconsistent met elkaar. Of er (ook) andere individuen dan de op de grafsteen vermelde leden van de van Doerne familie in de kelder hebben gelegen, de genealogie misschien incorrect is, of dat er sprake is van ten minste twee valse vaderschappen, blijft vooralsnog gissen.

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A CARNIVOROUS NICHE FOR JAVA MAN?
A preliminary consideration of the abundance of fossils in Middle Pleistocene Java

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In: C.R. Palevol (2011), doi:10.1016/j.crpv.2011.04.002

Considering anatomical and archaeological aspects of *Homo erectus*, it is likely that meat of vertebrates was an important part in its diet. Unfortunately, no or hardly any information is available for Java Man (*Homo erectus*). Therefore, in this paper, the Number of Identified Specimens (NISP) of five Middle Pleistocene Javanese sites are examined, and the Minimum Number of Individuals (MNI) from two of them are calculated, to acquire information about the possible ecological role of Javanese *Homo erectus*. Although one has to be extremely careful with the interpretation of fossil bone assemblages, in order to try to gain some insight about the abundance of species in palaeocommunities, it is argued that both the NISP and the MNI indicate that the bone accumulations reflect at least two trophic levels in the ecological pyramid, that of primary and secondary consumers. The occurrences of the remains of *Homo erectus* are comparable with the quantity of secondary consumers, i.e. large carnivores. This could suggest that this species had, as an omnivore, a carnivorous niche, in Java.

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ANALYSIS OF MICROTRACES IN INVASIVE TRAUMAS USING SEM/EDS

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in: Forensic Science International 214 (2012) 96-104

Scanning electron microscopy in combination with energy-dispersive X-ray spectrometry (SEM/EDS) is a proven forensic tool and has been used to analyze several kinds of trace evidence. A forensic application of SEM/EDS is the examination of morphological characteristics of tool marks that tools and instruments leave on bone. The microtraces that are left behind by these tools and instruments on the bone are, however, often ignored or not noticed at all.
In this paper we will describe the use of SEM/EDS for the analysis of microtraces in invasive sharp-force, blunt-force and bone-hacking traumas in bone. This research is part of a larger multi-disciplinary approach in which pathologists, forensic anthropologists, toolmark and microtrace experts work together to link observed injuries to a suspected weapon or, in case of an unknown weapon, to indicate a group of objects that could have been used as weapon.
Although there are a few difficulties one has to consider, the method itself is rather simple and straightforward to apply. A sample of dry and clean bone is placed into the SEM sample chamber and brightness and contrast are set such that bone appears grey, metal appears white and organic material appears black. The sample is then searched manually to find relevant features. Once features are found their elemental composition is measured by an energy dispersive X-ray spectrometer (EDS).
This method is illustrated using several cases. It is shown that SEM/EDS analysis of microtraces in bone are a valuable tool to get clues about an unknown weapon and can associate a specific weapon with injuries on the basis of appearance and elemental composition. In particular the separate results from the various disciplines are complementary and may be combined to reach a conclusion with a stronger probative value. This is not only useful in the courtroom but above all in criminal investigations when one has to know for what weapon or object to look.

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Poster presentations

MAXILLARY SINUSITIS IN THE SAINT PETER PARISH (12-18TH CENTURY) IN GHENT, BELGIUM

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Poster presented at GPLF (groupe de paléopathologistes de la langue Française) in Toulon on 11-12 March 2011

In Europe, it may now be healthier to live in an urban environment than in a rural one. However, this has been a recent development and would certainly not have been the case in the Medieval Period. The cemetery of the Saint Peter parish was in use from the 12th to 18th centuries and excavated in 2002-2003 before development of the site. Twenty-two of the 83 skeletons had at least one sinus present. From those 62.86% showed evidence of maxillary sinusitis and there was no significant difference between the sexes. It therefore appears that upper respiratory tract infections were common and this could be taken as an indirect indicator of the air quality.

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ISOTOPE GEOCHEMISTRY IN DUTCH ARCHAEOLOGY. THE APPLICATION OF STRONTIUM ISOTOPES AS A PROXY FOR MIGRATION

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Poster to be presented in Biomaterials and Bioarchaeology at the International Symposium on Archaeometry (ISA) 2012. 28th May – 1st June 2012, Leuven, Belgium

Migration has been subject to research and debate for many decades and has become a key component of archaeological thinking. The original concepts of waves of migration in archaeology were based upon the dispersal of cultural artefacts. This approach led to an active debate about the extent to which the archaeological record represents the actual movement of people or the diffusion of ideas. A new perspective on this debate is provided by the discipline of archaeological science. In addition to aDNA studies, the application of isotope ratios, in particular those of strontium, of mineralized tissue (bone, dentine (ivory) and enamel) is used to study migration, specifically at the individual level. Isotope research in archaeology has matured over the last three decades, proved its potential in numerous studies, and is nowadays one of the most innovative research fields in archaeological science.

Despite its international success and proven potential, isotope research has rarely been applied in Dutch archaeology. The major contributing cause is the absence of a bioavailable strontium isotope distribution map of The Netherlands, which is a fundamental component for data interpretation. This PhD project therefore focuses on the collection of data to create this isotope distribution map. Based on this map, the spatial variation in bioavailable $^{87}Sr/^{86}Sr$ in The Netherlands will be evaluated and the applicability of isotope geochemistry as a proxy for interregional mobility will be assessed. The data and the bioavailable strontium distribution map ultimately will lead to more insight into the cultural diversity of ancient populations throughout The Netherlands.

MOLECULAR SPECTRUM OF β-THALASSEMIA IN OMAN. GEOGRAPHICAL PREVALENCE, NEW AND RARE β-THALASSEMIA DETERMINANTS AND NEW OPTIONS FOR PREVENTION

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Purpose. To determine the molecular background of β-thalassemia in the different regions of Oman. To prepare for a country-wide service for molecular diagnostics and prevention, following premarital screening and information.

Methods. 174 alleles from 87 unrelated patients affected with β-Thalassemia major. routine hematology, HPLC and CE based separation and measurement of Hb fractions. Molecular analyses by direct sequencing and Gap-PCR.

Results. We have observed 13 different molecular defects. The IVS-I-5 (G→C) was the most prevalent (60.4%). Unlike a previous study (Daar et al.) the cd 39 (C→T) mutation and the cd5 (-CT) were the second and third in prevalence (18 and 5.6%). Ten different mutations were following at low prevalence (3.3 to 0.8%). Seven mutations found in our cohort were not found in the previous study while 9 observed previously were absent in our patients. A new mutation, (-120 C→T) was found in a healthy Omani control with no anemia. Alpha+ Thalassemia was found in 52% of the patients (25% in homozygous form).

Conclusion. Considering both studies, at least 22 different β-Thalassemia determinants can be expected in Oman with different regional distribution. Commercial kits will not cover all cases and direct sequencing is needed. Alpha Thalassemia is bound to play an important modulating role in genotype / phenotype correlation. Ongoing counseling initiatives, updating of peripheral equipments and a specialized genetic laboratory, will provide couples at risk with the choice of prenatal diagnosis, in addition to the current alternative which would be not to marry that particular partner. Being selective abortion allowed in case of a severe condition diagnosed on ultrasounds, the same should be valid for a severe defect diagnosed at the molecular level.

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Article

"STATE-OF-THE-ART" HEMOGLOBINOPATHY DIAGNOSTICS. IMPLEMENTING DIAGNOSIS, PREVENTION AND RESEARCH IN THE NETHERLANDS

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The disease

Hemoglobinopathies (HbP) are the most common monogenic recessive trait in man. The disorders are caused by mutations on the globin genes that may change the structure of the gene products (abnormal hemoglobins) or that may impair the expression of the genes (thalassemias). Because the trait (carrier state) have protected many world populations during the last 10,000 years against death in infancy due to malaria tropica, at least 7% of the world population originating from the tropical and subtropical belt of the old world is today a (healthy) HbP carrier. Children of parents who are both healthy carriers have 25% chance of being severely affected with the most common severe forms i.e. Sickle Cell Disease (SCD) and β-Thalassemia Major (Cooley anemia) (1).

The proteins

Sickle Cell Disease and β-Thalassemia major are disorders involving a protein essential for life, the hemoglobin molecule. The HbA tetramer ($\alpha 2/\beta 2$) is the protein that transports oxygen through our body. HbA is the major component of the red cells in postnatal life and like the red cells has a lifespan of 120 days. During an average lifespan we need to make 300 kg of hemoglobin and for this we need several perfectly functioning globin genes.

Genetics

In human α- and β-like globins are coded by two gene clusters located on chromosomes 16 and 11 respectively. Embryonic genes (ζ_2 and ε) are only active during early embryonic life, producing Hb Gower-1, Gower-2 and Hb Portland. Two

α- genes per chromosome (two of maternal and two of paternal origin, 4 in total = αα/αα) are expressed throughout fetal life producing the α globin needed for the formation of fetal hemoglobin (HbF = γ2/α2) in combination with the γ chains coded by 4 γ-genes per chromosome (also two of maternal and two of paternal origin). Shortly after birth, the 4 γ genes lose their expression while 2 β genes (one of maternal and one of paternal origin) become active. The 4 α genes stay active in postnatal life coding for the same α globin chains, now needed for the formation of adult hemoglobin HbA (α2/β2). Equally, the 4 α genes, with a limited amount of δ chains expressed by the 2 δ genes, also contribute to the formation of the minor postnatal tetramer HbA_2 (α2/δ2). This Hb fraction has no pathological relevance but is of significant interest for the diagnosis of β-thalassemia carriers.
Keeping in mind that the number of genes involved at a specific stage of life is important for the interpretation of the laboratory results. Because of the pre- and post-natal expression, pathological genotypes involving the 4 α genes manifest both in pre- and postnatal life while pathological β-globin genes are only significantly expressed in post-natal life. Therefore, sickle cell disease and β-thalassemia major come to expression only in the after-birth stages of life, when non-affected fetal cells have disappeared (1).

Basic diagnostic tools for the hematology lab
The tools for basic diagnostics are still based on the basic hematological parameters and on the separation and estimation of the hemoglobin fractions. Dedicated HPLC and CE devices available on the market recognize all abnormal separations at a high degree of sensitivity. Frequent traits can be confirmed by simple or more complex additional analysis, however, although very sophisticated, HPLC and CE present, like any analytical method with inevitable limitations.
A normal individual after the age of 2 will present with about 96-97% HbA, ±3% HbA_2 and <1%HbF. Any change in this pattern will be anomalous and might indicate a hemoglobinopathy and will have to be investigated.
In the mixed Dutch population the prevalent HbP traits are HbS (the cause of sickle cell disease), β- and α-thalassemia.
HbS, very common in The Netherlands, will be easily detected as an anomalous fraction of about 40% or less in the healthy carrier and of about 80-90% in not yet transfused sickle cell patients. Equally, a new born with the trait or the disease will present with ±80% HbF and 10% HbA and 10% HbS or with ±20% HbS only, respectively.
Carriers of beta thalassemia will be diagnosed from the age of 1 by their microcytic hypochromic anemic state and by the elevated level of the HbA_2 fraction (>4%, N = 2.5- 3.5%). The child affected with beta Thalassemia major will be severely anemic

and not able to produce the normal HbA fraction. If not yet transfused, they will present with HbF and HbA_2 only.

$Alpha^+$ thalassemia is very common in the world population and can only be suspected at the hematological and biochemical level due to microcytic hypochromic parameters and eventually a reduced HbA_2 level. Confirmation of alpha thalassemia is done at the molecular level.

Molecular diagnostics

Molecular analysis is needed to confirm and for the prognosis of β-thalassemia and to offer prevention by early pregnancy molecular diagnostics. The main technologies involved are direct DNA sequencing for the many β-thalassemia and α-thalassemia point mutations and for SCD. Gap-PCR is the technology of choice for the common α-thalassemia deletions and MLPA is the ultimate solution for unknown deletion defects of either the β- or α-globin genes cluster.

The most established approach in DNA diagnostics to screen for the most common deletion defects causing alpha-thalassaemia or beta-thalassaemia is gap-PCR, because the method makes use of equipment already available in most diagnostic laboratories, is inexpensive and fast. For less common rearrangements in the alpha- and beta-globin gene clusters, Multiplex Ligation-dependent Probe Amplification (MLPA) has become a standard tool (3), besides Southern blotting and cytogenetic methods. Multiplex Ligation-dependent Probe Amplification is a technology based on ligation of probe-pairs hybridized to a region of interest to detect deletions or duplications by quantitative PCR and fragment analysis. Due to the implementation of MLPA for the detection of copy number variation in the alpha- and beta-globin gene clusters, more and more new types of deletions were detected. But also the discovery of duplications of the complete alpha-globin gene cluster including the Major Conserved Regions shed light on some unexpectedly severe cases of beta-thalassaemia Intermedia in beta-thalassaemia carriers.

However, by using MLPA the exact breakpoints of these novel deletions and duplications remain unknown. Knowledge of breakpoint sequences might give more insight in the molecular mechanisms giving rise to these rearrangements and may facilitate primer design for gap-PCR to screen for certain common population specific deletions(4). For this purpose a custom fine-tiling array for high resolution breakpoint determination was designed to perform array Comparative Genome Hybridization (aCGH). The oligonucleotides cover the complete alpha- and beta-globin gene clusters including the neighboring regions. Based on the results breakpoint primers were designed to perform gap-PCR and breakpoint sequencing.

References

1. Steinberg MH et al. Disorders of Hemoglobin. 2001 Cambridge University Press.
2. Giordano PC, Harteveld CL. Prevention of hereditary haemoglobinopathies in The Netherlands. Ned Tijdschr Geneeskd. 2006 Sep 30;150(39):2137-41.
3. Harteveld CL, Voskamp A, Phylipsen M, Akkermans N, den Dunnen JT, White SJ, et al. Nine unknown rearrangements in 16p13.3 and 11p15.4 causing alpha- and beta-thalassaemia characterised by high resolution multiplex ligation-dependent probe amplification. J Med Genet 2005 Dec;42(12):922-31.
4. Harteveld CL, Refaldi C, Cassinerio E, Cappellini MD, Giordano PC. Segmental duplications involving the alpha-globin gene cluster are causing beta-thalassemia intermedia phenotypes in beta-thalassemia heterozygous patients. Blood Cells Mol Dis. 2008 May-Jun;40(3):312-6. Epub 2008 Jan 14.

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Forthcoming events

February 17, 2012
34th Kroon-voordracht
From Tutankhamun to Ötzi: the use of modern scientific methods
in mummy research
Prof. dr Albert Zink (Institute for Mummies and the Iceman, Bolzano, Italy)
KNAW, Kloveniersburgwal 29, Amsterdam
www.snmap.nl

July 14, 2012 (probably)
Barge Forum – Speaker and title to be announced
LUMC, Leiden

August 27-29, 2012
Biennial European Meeting of the Paleopathology Association
Palais des Beaux Arts
Hosted by the Dept. of Anatomy of the Faculté de Médicine de Lille/Rijssel
www.paleopathology.org

September 3-6, 2012
18th Congress of the European Anthropological Association
"Human evolution and dispersals"
Ankara Turkey
email: info@eaa2012turkey.org