

- 347 EVALUATION OF ALTERNATIVE STRATEGIES IN THE DIAGNOSIS OF PLEURAL TUBERCULOSIS. Villegas MV*, Labrada A, Weigle K, and Saravia NG. CIDEIM, Cali, Colombia; Department of Epidemiology, University of North Carolina, Chapel Hill, NC.

The diagnosis of pleural tuberculosis using conventional clinical and laboratory methods is inefficient. We evaluated the sensitivity, specificity and predictive values of PCR alone and in combination with Adenosine Deaminase (ADA), PPD, culture and pleural biopsy in 140 patients who consulted the Social Security Institute in Cali-Colombia for a primary etiologic diagnosis of pleural effusion. Four clinical categories were defined: 40 (30%) patients with confirmed pleural TB (by biopsy or culture), 19 (13.6%) probable TB (based on clinical suspicion and response to antituberculous drugs); 70 (50%) confirmed other etiology and 9 (6.4%) idiopathic. ADA was the single most sensitive (87%) and specific (86%) method. PCR was the second most specific method (90%) after culture (100%), which only detected 33% of pleural TB cases compared to 61% detected by PCR and 62% by biopsy. Sensitivity of ADA was increased from 87 to 92% when combined with PPD and yielded a negative predictive value (NPV) of 89%. The combination of ADA and PCR increased the sensitivity achieved with either method alone to 90%. Hence, the combination of ADA with PCR or PPD proved more efficient than the gold standards, biopsy and culture. The use of these combined methods could reduce the need to perform pleural biopsy while providing high diagnostic certainty within 24 to 72 hours.

- 348 Abalos FV*, Aguiar J, Guedenon A, Meyers WM, and Portaels F. Armed Forces Institute of Pathology (AFIP), Washington, D.C.; Institute of Tropical Medicine (ITM), Antwerp, Belgium; Lazaret-Akpakpa, Cotonou, Zangnanado, Benin; and Centre Sanitaire et Nutritionnel, Gbemoten, Zangnanado, Benin.

Mycobacterium ulcerans (MU) infection or Buruli ulcer (BU), after tuberculosis and leprosy is the third most common mycobacterial disease of immunocompetent inhabitants of the intertropics. BU afflicts primarily children in rural, riparian, agrarian environments, often with disabling physical sequelae involving skin and bone with a resulting serious socioeconomic impact. Recent epidemiologic data seem to qualify BU for "reemerging disease" status, particularly in West Africa. Radical surgery is often necessary for treatment. The specimens and clinical histories we studied were from 322 patients accessioned at the AFIP between 1962 and mid-1997 and came from Angola, Benin, Bolivia, Cameroon, Congo (Zaire), Congo-Brazzaville, Cote d'Ivoire, Ghana, Liberia, Nigeria, Papua New Guinea, Peru, Surinam, Togo, and Uganda. The largest number of patients (117) were from Benin. Aims were to: 1) describe histopathologic features; 2) obtain epidemiologic data; 3) formulate clinicopathologic correlations, and 4) improve early diagnostic capability. Primary histopathologic changes fell into 3 stages - necrosis, organizing granulomatous reaction, and healing and fibrosis. Diagnostic histopathologic features were contiguous coagulation necrosis of subcutis, vasculitis, mineralization, and acid-fast bacilli. There was good correlation between histopathologic diagnosis and rapid identification of MU by culture, PCR and oligonucleotide-specific capture plate hybridization techniques, in exudates or tissues sent to a central laboratory (ITM) in special transport media. Extensive deforming MU osteomyelitis developed in 5 patients. Muscle was rarely involved. Specific trauma related lesions were observed. Approximately 2/3 of the patients were under 15 years old. Only 2 patients presented with early preulcerative lesions. Our findings highlight: 1) a need for education in early recognition of BU at the village level by local medical and paramedical workers to avoid severe, sometimes life-threatening sequelae, and 2) development of more effective and less destructive methods of treatment.

Jean-Philippe

- 349 TOLERANCE AND EFFICACY OF A HIGHLY PURIFIED F(ab')₂ ANTIVENOM INJECTED THROUGH THE DIRECT INTRAVENOUS ROUTE: RESULT OF A TRIAL IN NORTH CAMEROON. Chippaux JP*, Amadi-Eddine S, Fagot P, Le Mener V, Lang J. Centre de Recherche sur les méningites et les schistosomiases, Niamey, Niger; Institut Pasteur du Cameroun, Coopération Française, Garoua, Cameroon; and Pasteur Mérieux Connaught, Lyon, France.

The objective of this trial, performed in two centers in North Cameroon, was to measure the tolerance and the efficacy of a highly purified and pasteurized F(ab')₂ antivenom administered through direct intravenous (IV) route. In addition, two treatment criteria were evaluated: spontaneous bleedings far from the site of the bite and the coagulation time in a dry tube. Forty-six patients were included (mean age, 21.2 years) bitten mostly by *Echis ocellatus*. They received 20 mL (two vials of 10 mL) of F(ab')₂ antivenom (manufactured by PMC) through the direct IV route in less than 5 minutes; the treatment was repeated two hours later in case of persistent bleeding. An additional dose was recommended 6 hours after the first administration if bleeding persisted or if the dry tube coagulation time was longer than 30 minutes. Thereafter, antivenom was administered daily until recovery. The hospital stay required by the protocol was fixed at at least 5 days, and patients were re-examined 3 weeks after the initial admission to evaluate delayed tolerance. During the trial a total of 86 doses (20 mL) were administered. The mean volume administered per subject was 37.4±3.9 mL. A haemorrhagic syndrome was observed at admission in 76% of the patients. Four patients presented with an early adverse event of mild or moderate intensity, for which a



causal relationship to the antivenom was considered possible or probable. None of 36 patients who returned for the visit at week 3 presented any adverse reaction. All patients recovered without any significant envenomation sequel although one patient suffered necrosis of the inferior limb, necessitating an amputation. Finally the mean hospital stay was 6.6 ± 0.9 days, and the mean time to cure was 1.1 ± 0.3 days (according to investigators judgement). This trial showed that the injection of highly purified F(ab')₂ through the direct IV route was well tolerated and very efficacious. The two treatment criteria used in this trial allowed a reduction in the number of antivenom administration without a lessening of treatment efficacy. This procedure allows local clinicians to treat venomous snake bites effectively with a smaller dose (approximately 40% less) and by using practical treatment criteria.

- 350 INFORMED CONSENT IN DEVELOPING NATIONS: WRITTEN vs ORAL CONSENT, PERSONAL vs COMMUNAL DECISION-MAKING, EQUAL PARTICIPATION AND LIABILITY. Cisse B,* Doumbo O, Toure YT, Sakai RK, Kaslow DC, Plowe CV, and Krogstad DJ. Mali-Tulane Tropical Medicine Research Center and Faculty of Medicine, Pharmacy and Dentistry, University of Mali, Bamako, Mali; University of Maryland School of Medicine, Baltimore, MD; and Tulane School of Public Health and Tropical Medicine, New Orleans, LA.

Major elements of informed consent in countries such as the US include: 1] written documents which the participant (or their guardian) must read and sign, 2] an emphasis on the autonomy of the individual, 3] equal participation of males and females, and 4] carefully phrased legal language intended to limit the legal and financial liability of the sponsoring institution. In contrast, many tropical medicine studies in endemic areas involve subjects who cannot read or write, who do not speak English, French or Spanish, whose cultures are focused more on the community than the individual and are often patriarchal, and who often have major medical needs unrelated to the subject under study. We have addressed these issues by: 1] oral consent in the local language (because oral agreements are used to sell land or transfer property in traditional villages), 2] ongoing discussions with the mothers and fathers of participating children during longitudinal cohort studies, 3] development of a village women's council to review protocols before they are presented to individual parents, and 4] assuming responsibility for initial medical care, even when the problems are unrelated to the subject under study. We suggest that review boards in the US should pay closer attention to cultural differences between the US and developing nations, because simply replicating the US approach overseas is rarely appropriate.

- 351 RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL OF FLUCONAZOLE FOR TREATMENT OF CUTANEOUS LEISHMANIASIS IN SAUDI ARABIA. Alrahji A*, Khyrat M, Ebrahim A, Rajab M, and Maguire JH. Department of Tropical Public Health, Harvard School of Public Health, Boston, MA; and Ministry of Health, Riyadh, Saudi Arabia.

The oral azole antifungal agents ketoconazole and itraconazole shorten the time to healing of cutaneous lesions of several species of *Leishmania*, but there are few data on the efficacy of fluconazole. We compared fluconazole and placebo for the treatment of cutaneous leishmaniasis in a randomized, double-blind trial in four health centers in Saudi Arabia. There were 106 persons who received 200 mg daily of oral fluconazole for 6 weeks and 103 persons who took placebo for the same period of time. Results are available for 145 persons. There was no difference between the groups in regard to age, gender, and duration, size, number and appearance of lesions. Parasites isolated from lesions of a subset of patients were *L. major* (zymodeme MON 26). Healing of lesions was complete for 63 of 80 persons (78.8%) who received fluconazole and 22 of 65 (33.8%) persons who received placebo ($p < 0.0001$). Eleven (13.8%) recipients of fluconazole and 33 (50.8%) recipients of placebo were considered treatment failures. Six persons in the fluconazole group and 10 persons in the placebo group were lost to follow-up after completing treatment but before their lesions had healed. By Kaplan-Meier analysis, time to healing was shorter for persons who received fluconazole (median 8.5 weeks) than those who received placebo (median 11.2 weeks, $p = 0.0001$). The incidence of adverse effects was low in both groups. We conclude that oral fluconazole is an effective and well-tolerated treatment of cutaneous leishmaniasis due to *L. major* in Saudi Arabia.

- 352 SINGLE-AGENT INJECTABLE AMINOSIDINE FOR 21 DAYS IS MORE EFFECTIVE THAN SODIUM STIBOGLUCONATE FOR THE TREATMENT OF VISCERAL LEISHMANIASIS. Jha TK, Olliaro P*, Thakur CPN, Kanyok TP, Singhanian BL, Singh IJ, Singh NK, Akhoury S, and Jha S. Kala-Azar Research Centre, Brahmapura, Muzaffarpur, Bihar, India; and UNDP/World Bank/WHO Special Programme in Tropical Diseases Research, Geneva, Switzerland.

Pentavalent antimonials have been the standard treatment for Visceral Leishmaniasis (VL) for over 40 years, but nowadays up to 25% unresponsiveness has been reported in India even with high dosage and prolonged administration of Sodium Stibogluconate (Sb), in the dose of 20 mg/kg daily for 20 to 40 days. In addition, Sb treatment is expensive and prolonged hospitalization add on the cost. Aminosidine (AM) is an aminoglycoside

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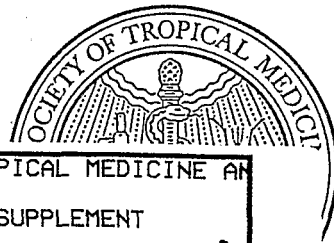
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