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513. Tuberculosis in pregnancy and childhood

P4969

A case-control study of the risk of adverse peri-natal outcomes due to tuberculosis during pregnancy

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Aim: The West Midlands, UK has seen a persistent rise in cases of tuberculosis (TB) in immigrants, and TB in pregnancy is more common amongst recent migrants to a country. Diagnosis is often delayed due to non-specific, late presentation, and this has been associated with prematurity and low birthweight (LBW). We aimed to determine the risk of adverse peri-natal outcomes in women with TB in pregnancy.
Methods: A case-control study was conducted at three hospitals in Birmingham, comparing pregnant women with TB (2004-6; n = 24) with healthy pregnant controls (n=72). Data concerning the course of pregnancy, birthweight and prematurity were collected from review of case notes. Healthy controls were matched for age and socio-economic status. Uivariate analyses of low birthweight and prematurity were undertaken, and a multivariate regression model constructed to explain differences by ethnicity and prematurity.
Results: Estimated incidence of TB was 62/100,000 pregnancies. 54.2% cases were pulmonary TB (41.7% extra-pulmonary; 4.2% both). Infants of mothers with TB had significantly lower mean birth-weight compared to controls (2760g vs. 3140 g; p=0.028). Mean birth weight was lower in pulmonary TB than in extrapulmonary TB. Multivariate analysis explained LBW by prematurity (p<0.001) but not ethnicity (p=0.19).
Conclusion: Pregnant women with TB are at higher risk of LBW infants. This is particularly true of mothers with pulmonary TB. Mean duration of symptoms was 8.3 weeks so LBW is attributed to late presentation. Indeed patients have mild symptoms that are confused with those of pregnancy. Therefore a high index of suspicion and early referral and diagnosis is recommended.

P4970

Pregnancy: A risk for developing tuberculosis? A national cohort and self-controlled case series study using UK primary care data

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Introduction: Tuberculosis (TB) incidence has increased in the UK over the last decade. The study of TB in pregnancy is important because of adverse outcomes in mother and child. The aim of this study was to analyse the epidemiology of TB in pregnancy in the UK, and establish, whether pregnancy is an independent risk factor for TB in order to inform prevention and early detection strategies.
Methods: Using a cohort based on the UK General Practitioner Research Database (GPRD), incidence rates (IR) and rate ratios (IRR) of TB events in three time periods were compared using Poisson regression: pregnancy, a period of 6 months post-partum, and outside of pregnancy. In addition TB risk was calculated using a nested self-controlled case series (SCCS) analysis which implicitly adjusts for time-bounds covariates.
Results: Combined pregnancy and post-partum TB rates (15.4 per 100,000 person years, py) were significantly higher than rates outside of pregnancy (9.1 per 100,000 py, p=0.02). Compared to risk outside of pregnancy, TB risk was not significantly increased during pregnancy (IRR 1.29, CI 0.82-2.03), but significantly increased post-partum (IRR 1.95, CI 1.24-3.07), adjusting for age, region and deprivation. These observations were confirmed in the SCCS (IRR 1.62, CI 1.01-2.58 and 1.03, CI 0.64-1.65).
Conclusions: There is a significantly increased post-partum TB risk and this is very likely pregnancy-related, but occurs post-partum due to administrative, diagnostic or immunological delays. Our results can be used to raise clinicians' awareness and inform targeted public health policy measures to minimise this risk.

P4971

Knowledge and attitudes about tuberculosis among non-medical students in University of Novi Sad, Serbia

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Introduction: Students' knowledge and opinion about tuberculosis (TB) are very important for recognizing early symptoms and signs of disease, prevention of late in diagnosis of TB and influence on prevention and outcome of disease.
Goal: To define the non-medical students' knowledge about TB (symptoms, way of medical treatment, possible complications, comorbidity).
Material and methods: Prospective study comprised the non-medical faculties at the University of Novi Sad, Serbia. The data were obtained by the questionnaire filled in during October-November 2010.
Results: The total of 1139 students were questioned, average 19,7 year, most women (n=794, 69.7%). The majority of students had a good knowledge about TB (n= 891, 78.2%). The majority of questioned students knew that TB is infectious disease (n=1093, 96%) that the main cause of TB is bacteria (n=887, 77.9%) as well as it is curable disease (n=1079, 95.6%). Over 94% knew that cough is the main cause of TB transmission. 62% questioned students considered that risk factors can contribute the tuberculosis appearance (39.4% alcoholism, 66.3% poor nutrition, 74,7% smoking and 67.9% comorbidities). The students from Agricultural faculty showed better knowledge against other students, p<0.001.The most of the students (n=513, 45%) knew that TB incidence in the state area was decreasing.
Conclusion: Students of non-medical faculties at the University of Novi Sad showed the good knowledge about TB. The best knowledge was noticed at the students of Faculty of Agriculture. They also are well informed about TB presence in the state and the effects of national and international guidelines implementation in the country respectively.

P4972

Evaluation of tuberculosis diagnostic criteria in children

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Objectives: In this study we reviewed the diagnostic citeria for tuberculosis on 198 children diagnosed with TB
Material and methods: A cross-sectional, descriptive study was conducted on a series of 525 children aged 1 to 15 years. Among 525 patients, 198 were diagnosed with TB. Date of the study were collected from the patients recoreds, chest radiographs and laboratory examinations.Demographic and diagnostic characteristics of patients were reviewed by means of the available criteria.
Results: In this study 38.9% of patients were male and 61.1% were female.Among all patients 34.5% were Iranian and 65.2% were Afghanis.In this study 82.8% of patients reported close contact with TB. Among all patients 13.1% had extrapulmonary tuberculosis, 72.7% had pulmonary tuberculosis and 14.1% had pulmonary and extrapulmonary involvement.Frequency of TST, contact, clinical symptoms, radiograph findings and bacteriology as diagnostic methods was 79.3%, 83.8%, 83.8%, 85.9%, and 58.1%, respectively. Due to our setting, 90.4% of patients fulfill the criteria.
Discussion: The result of this study indicate the high diagnostic value of smear and culture of gastric aspirate in children.How ever, it couldnt be considered as a gold standard for diagnosis of TB in children. In addition the significant accuracy of the available criteria was determined and it could be considered as an efficient diagnostic setting in childhood TB diagnosis.

P4973

Neonatal tuberculosis and cardiac inflammatory myofibroblastic tumor presenting as supraventricular tachycardia: A rarity of kinds

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This a case of a one month old female neonate who was admitted for respiratory distress. On admission, electrocardiogram showed supraventricular tachycardia. A 2-D echo showed a mass anterior to the left ventricle and the right ventricular outflow tract (RVOT). Chest radiograph showed a left upper lung haziness and computed tomography (CT) scan of the chest showed a non calcified anterior mediastinal mass with central enhancement. Intramyocardial mass biopsy revealed a large anteriorly located intramyocardial mass covering the RVOT, the great vessels and a portion of the right atrium. Final histopathology result revealed inflammatory pseudotumor, myofibroblastic in nature. Smooth muscle actin (SMA) was positive in many localized spindle cells indicative of their myofibroblastic nature while histiocyte markers- CD68 and S100 were both negative. Because of a high index of suspicion, a tuberculosis work-up was done which showed that the patient was positive for tuberculin test (18mm in diameter). Contact screening revealed 3 out of the 6 household contacts were positive for pulmonary tuberculosis. Patient was started on anti-tuberculosis medications and on the fifth month of treatment, the patient was asymptomatic, growing well and the mass regressed in size by 50%.

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P4974
Clinical and epidemiological patterns of pediatric patients with mycobacterial disease at the TB reference centre in Milan

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As in adults, occurrence of children TB has became quite rare in the last decades in Italy. We report a survey of 269 consecutive cases of mycobacterial disease (MD) in subjects under 18 yrs of age. diagnosed or referred to the Regional TB Ref Centre from 2000 to 2010.

Results: 139 were M, 130 F, 113 were Italians, 156 immigrants, 135 < 5 yrs and 58 >14 yrs.

157 had an intra-thoracic disease, 91 extra-thoracic e 21 both. Among thoracic disease lungs were involved in 97 pts, hilar-mediastinal lymph nodes in 92, and pleura in 11. Of the extra-thoracic forms, 85 were in neck lymp nodes, 9 in other lymp nodes, 8 were abdominal (peritoneal, mesenteric etc), 5 were bone disease, 3 skin, 1 genital, 1 urologic.

In 95 a microbiological confirmation was obtained: MT 55 pts, NTM 40 pts. In all other acses diagnosis was based on demographic and clinical aspects, history of contact with TB cases, histological results or immunologic tests (IGRA/TST).

Of the isolated NTM 25 were M. avium, 3 M.intracellulare, 2 M. scrofulaceum, 1 M. fortuitum, 1 M. malmoensis, 1 M. Haemofilum, 1 M. Kansasii, 1 M. Xenopi, 1 M. Lentiflavum e 4 M. could not be identified.

Medical, surgical or combined therapy guaranteed success in 239 pts, 2 had to stop treatment for adverse events,% were transferred to other centres, 3 were lost to follow up and 20 are still under treatment.

P4975
Child's tuberculosis and the socioeconomic environment

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Background: The family and socioeconomic environment influence the appearance, treatment and the supervision of child's tuberculosis. Most children of different ages are infected by household contacts with active tuberculosis, especially parents or their relatives. Children exposed to adults with pulmonary tuberculosis and AARB smear-positive sputum have a high risk for infection, and the risk increases with the degree of contact.

Methods: This is a retrospective study which gathered the 22 children with tuberculosis disease aged 0-14 years from the county of Brasov, Romania. These children received antituberculosis treatment in 2010. Most of these children were admitted to hospital and they emanate from old foci with a great number of tuberculosis sources and low treatment compliance. We have analyzed the family, social and ecomomical environment of these chlidren's living.

Results: In 59% of the studied families, both parents are not employed. Only one parent is employed in 18% of the cases and in 9% of the families one parent is floater and the other one is unemployed. Both parents are employed in 14% of the families. Many parents from the studied families are employed abroad or they are recently returned in the family and are unemployed. 45.4% of the families have low accessibility to medical assistance.

Conclusion: Child's tuberculosis is well affixed to epidemiological interest foci in which medical and social education are important. They are embedded to the ecomomical environment. Child's tuberculosis prevention is necessary as early as contact phase. Educating the people to increase treatment's compliance is able to reduce school absenteeism and the economic hospital admission costs.

P4976
Problems with poor study adherence in a tuberculosis research project in children in Tanzania

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Background: In clinical research poor follow-up has a significant effect on the validity of the data collected, affecting both the results and conclusions. For a diagnostic TB study, follow-up over time can be crucial to verify the presence or absence of active TB.

Objectives: 1) to identify factors influencing patient adherence to attend follow-up examination. 2) A qualitative evaluation of reasons for not attending follow-up examination.

Methods: 1) Baseline data such as health characteristics and demographic data from all the included patients were drawn from a TB study database. Risk factors for not attending follow-up were determined. 2) Semi-qualitative interviews of caretakers were used to investigate patients' experiences and challenges in relation to attend follow-up examination.

Results: Only 61% showed up for the follow-up examination. Being treated for active TB was a positive predictor for attending follow-up. OR: 0.24, CI: (0.12-0.50), p-value <0.001. Receiving money for the bus fare was also a positive predictor for attending follow-up. OR: 0.008 and CI (<0.001-0.06). P-value <0.001. Limited financial resources and poor communication are issues related to poor adherence.

Conclusion: Patients lost to follow-up is a significant problem. We found, that receiving money for the transport to the hospital is crucial for patient adherence. Children with active TB had a significant higher frequency of attending follow-up. All TB patients attend the TB clinic at the hospital frequently, which could explain the better adherence to follow-up.

P4977
Serial interferon-gamma release assay in children younger than 5 years with latent tuberculosis infection

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Background: Interferon gamma release assays (IGRAs) play an important role in diagnosis of latent tuberculosis infection (LTBI), but there is paucity of data about IGRA dynamic values, especially in children younger than 5 years.

Aim: To evaluate the performance of serial IGRA and tuberculin skin testing (TST) in children younger than 5 years with LTBI.

Methods: We included 11 BCG vaccinated children younger than 5 years with LTBI. The commercial IGRA (QuantiFERON TB Gold In-Tube®, QFT-GIT), Cellestis Ltd, Carnegie, Australia) was performed two times, before and at the end of 6-month chemoprophylaxis. The cut-off value for positive findings of IGRA was ≥ 0.35 kIU/L. The TST was performed using 2 IU (0.1 mL) of purified protein derivative Tuberkulin PPD RT 23 SSI (Statens Serum Institut, Denmark) according to the Mantoux method and transverse diameter of the induration was measured after 72 hours.

Results: IGRA values were 8.87±2.01 kIU/L and 8.02±1.99 kIU/L, before and after chemoprophylaxis, respectively, which suggests a slight, insignificant decrease (p=0.89). There was no significant difference in PPD values before (12±2 mm) and after (14±2 mm) the treatment, p=0.50.

Conclusions: Although the prophylaxis was used, both IGRA and PPD values, remained elevated during the period of 6 months in children with LTBI. Further research is needed to clarify the role of serial IGRA in children up to 5 years.

P4978
A comparison of QuantiFERON-TB Gold In-Tube test and new QuantiFERON-Microtube assay in children suspect of active TB and adults with active TB

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Background: The use of Quantiferon-TB Gold In-Tube test (QFT) in children is limited by volume of blood required. A Quantiferon Microtube (QFT-MT) using only 0.9ml of blood is being evaluated.

Objective: Comparing performance of QFT and QFT-MT for diagnosing TB infection in children and adults.

Methods: 160 children suspected for TB and104 adults with smear-positive TB were tested with QFT, QFT-MT, and TST.

Results: Among 160 children, 24 (15%) were QFT and 30 (18.8%) QFT-MT-positive, p=0.37 and 40 (25%) were QFT- and 34 (21.3%) QFT-MT-indeterminate, p=0.43.

Among 104 adults 76 (73.1%) were QFT- and 81 (77.9%) QFT-MT positive; p=0.42; 21 (20.2%) and 7 (6.7%) were QFT- and 10 (9.6%) QFT-MT-indeterminate, p=0.41. The proportions of positive, negative and indeterminate results of QFT were similar between the two IGRA.

In children clincially diagnosed with active TB, positivity rates of QFT and QFT-MT were surprisinly low; 21.4% and 31.1% (p=0.29) and much higher in adults with microscopy confirmed TB (84.6% and 95.2% respectively (p=0.05). Test performance between the two IGRAs was comparable with moderate concordance (76.3%, k=0.57) in children and 80.8%, k=0,52) in adults. The study team found it easy to use the QFT-MT system

Conclusion: Overall the performance of the QFT-MT test using 0.9ml of blood was equal to the QFT test using 3 ml of blood. The low sensitivity of both tests in children suggests difficulties in diagnosing TB in children as often desicrbed. Considering the potential benefits of QFT-MT in testing young children and infants we suggests that further investigations of the test performance are warranted.

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Contact tracing among the classmates of a 15 year old smear negative pulmonary tuberculosis

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Objectives: This study aimed to identify the infected or disease cases among contacts of the 15 year old girl with Smear Negative Pulmonary tuberculosis in an school outbreak and establish prophylaxis and treatment needed.

Methods: 52 contacts were screened by a tuberculin skin test and Chest X ray initially, Those children who had either a positive PPD or an abnormal chest X-ray were candidate for a tripled Gastric washing (Smear, Culture, Polymerase chain reaction (PCR)) and a Chest spiral CT scan.

Results: 20 contacts (38%) were considered as an infected due to either positive TST or abnormal Chest X-Ray. 28% had a positive Tuberculin Skin Test. Consequently 3 (5.7%) cases of active TB were identified through our investigations.

Conclusion: Our study suggest that even children with TB, who may have a negative smear, can transmit infection to others and therefore should be considered infectious until proven otherwise and contact tracing should be considered for contacts of all symptomatic pulmonary tuberculosis children.

P4980

Interferon-gamma release assays (IGRA) for latent tuberculosis infection (LTBI) in children

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Background: IGRA, QuantiFERON®-TB Gold in-tube (QFT-GIT) & T-SPOT.TB®(T-Spot), are widely used to detect LBTI in adults. There is paucity of data regarding their use in children (<16 yrs old), but their use in this group is increasing [1]. One of the key reported problems in children is high incidence of indeterminate results. Studies in adults have shown this can be minimized with early incubation of QFT-GIT blood samples. In Leeds there is close co-ordination between medical & nursing staff collecting bloods, and the local laboratory processing them with prompt transport of samples and the aim to incubate samples within 4 hours of collection.

Methods: We retrospectively reviewed all the IGRA tests performed in children, for contact & new entrant screening, in our TB service between 2008 & 2010, to look at our indeterminate rates.

Results: A total of 188 IGRA tests were performed. T-Spot was undertaken almost exclusively in children under 1 year. None of our cohort had indeterminate IGRA results with QFT-GIT or T-Spot.

Table 1

Age (yrs)	Number of tests performed	Indeterminate Results	Negative tests	Positive tests
QFT-GIT				
<5	18	0	15	3
5–10	39	0	28	11
11–15	111	0	92	19
T-Spot				
<5	18	0	18	0
5–10	2	0	2	0
11–15	0	0	0	0
All <16	188	0	155	33

None of the children were diagnosed with active TB (multiple samples were sent for TB culture from 4 children).

Conclusion: A definitive IGRA result is achievable in otherwise healthy children with close liaison between clinical and microbiology staff, prompt transfer of blood samples and incubating QFT-GIT samples within 4 hours of collection.

Reference:

[1] Ling, D.I. et al. Immune-based diagnostics for TB in children:what is the evidence?Paed Resp Reviews. 2011;12(1):9-15.

P4981

Evaluation of QuantiFERON-TB Gold Assay in detecting latent and active infection with *mycobacterium tuberculosis* in group of Egyptian children

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Background: QuantiFERON-TB Gold In-Tube [QFG-IT] showed good diagnostic accuracy for active and latent TB in adults; limited studies have been performed in children, none in *Egypt*.

Methods: In a hospital-based prospective study, diagnostic accuracy of the tuberculin skin testing (TST) and QFG-IT were assessed in a cohort of 112 children (mean age 6.98±4.44, range 0.7-16); control not exposed (n=20), latent tuberculosis (n=42), active tuberculosis (n=50).

Results: In confirmed active TB, TST was positive in 24 out of 26 cases (92.31%), compared to 37 out of 50 cases (74%) for QFG-IT. None of the 2 tests performed significantly better than the other (p=0.109).

In latent TB infection (LTBI), TST was positive in 24 out of 26 cases (92.31%), compared to 37 out of 50 cases (74%) for QFG-IT. Despite that QFG-IT performed better than TST; this was not statistically significanct (p=0.062).

Significantly higher number of positive QFG-IT and TST were seen in children older than 5 years compared to younger children (p=0.009, and 0.007, consecutively). The 2 tests did not show significant differences between those who had confirmed pulmonary and extra-pulmonary TB (p>0.05).

The overall agreement between the 2 tests was good (84.21%, κ 0.677).

Conclusions: QTG-IT did not show higher diagnostic value in confirmed active childhood TB. Both QFG-IT and TST perform better in children older than 5 years than in younger population. Positive QFG-IT supports the diagnosis of TB in TST positive children. Negative QFG-IT does not exclude active TB. If used for diagnosis of LTBI, QFG-IT could significantly reduce the numbers of children receiving chemoprophylaxis.

P4982

Diagnostics of the latent TBC infection (LTBI) activity in children

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Material and methods: Under observation there were 118 children with LTBI and 129 diseased children with local forms of lung tuberculosis. The concentration of key cytokines IFNr, IL4, IL10, IL18 in blood serum was identified with immunoferment method.

Results: To comparatively study the correlation of functioning of Th1 and Th2 cells in the immune response, we introduced the notion of "Cytokine index". Accordingly, the secretorious activity of T-helpers of the 1 and 2 type we determined by quantitative correlation of the key cytokines IFNr/IL4 and IL18/IL10. It was determined that in comparison with a control group (30 noninfectious children) average values of IFNr content increased in diseased children in 2,4 times, in healthy with LTBI – in 3,6 times. By analogy, the values of IL18 increased in the diseased in 2,9 and in healthy children with LTBI – in 4,5 times. The obtained results underline the oneway direction of the immune response to TBC infection, appeared in organism. In diseased children the quantitative index of correlation of the key cytokines IFNr/IL4 lessened to 1,4 times (in a control group – to 2,3). In infectious children this index was equal to 1,9. The correlation of the other two nonetheless important cytokines IL18/IL10 in the differentiating of T-lymphocites in very indicative: in both groups the cytokine index appeared to be lowered to 1,4 and 1,9, which was caused by the increase of IL10 almost in 5 times as compared with the control group (2,3).

Conclusion: The IL18/IL10 obtained results allow of IL18/IL10 introducing into clinical practice quantitative evaluation of correlation of Th1 and Th2 hence to diagnose the LTBI progress.

P4983

Tuberculosis detection in children and adolescents using diagnostic testing based on tuberculosis recombinant protein E SAT6-CFP10 (diaskintest)

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Background: Until recently, the tuberculin skin test (TST) has been the only diagnostic method for latent tuberculosis infection (LTBI). However, the specificity of TST is low, because the purified protein derivative (PPD) used for TST contains numerous M. tuberculosis (MTB) antigens that are almost identical to BCG antigens or similar to non-TB mycobacterium (NTM) antigens. Of those 99% BCG vaccinated in Russia it is very difficult to diagnose LTBI. DIASKINTEST (DST) consists of two MTB-specific antigens - ESAT-6 and CFP-10, which are absent in all *M. bovis BCG* substrains and most of NTM antigens. Aim was to evaluate to evaluate the role of DST in TB detection.

Method: 1675 children and adolescents with converted tuberculin reaction, reaction size increased by more than 6 mm, hyperergy, TB contacts (social and household) received the Mantoux test with 2 TU PPD-L and DST 0.2 mkg/0.1 ml.

Result: 95,8% -TST-positive. 349 (20,8%) - DST- positive, all - chest X-rayed plus computer tomography (CT). TB was diagnosed in 148 (42,4%). Out of them 6 were initially DST negative but after 3 months DST was repeated and resulted positive- active TB was diagnosed. In 19 (5,5%) TB was in the calcination phase. 9 TB contacts with established TB were DST-negative. All had BCG vaccination. 4 children one year old, probably, had not developed immunity. Two had contacts with TB/HIV parents.

Conclusion: DST allows detecting TB in 42,4% of cases. DST negative reaction could be in early aged TB patients – when immune response has not been developed yet. DST positive reaction may develop later in vaccinated children.

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Diagnostic value of non-specific humoral immune changes in children investigated for tuberculosis by skin test and bacteriology

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It was suggested that repeated skin tests (IDR) used to diagnose childhood tuberculosis (TB) potentially change the immune response of the host. Adaptive cell-mediated immunity is the most important in protection against TB, but there is no information on the changes in the dynamics of immune globulins (Ig) and circulating immune complexes (CIC) in these patients. We hypothesized that the changes would be dependent on both the skin test results and bacteriological (BK) category of the subjects. The study was carried out in three groups of children, 1 to 17 years old, positive to both skin test and bacteriology (IDR+BK+, n=18), positive to the skin test but negative for bacteriology (IDR+BK+, n=12) and negative to skin test, but positive for bacteriology (IDR-BK+, n= 9). Serum samples were subjected to total immunoglobulin (Ig) and immune complexes measurements (CIC), carried out by 0.24% zinc sulphate and 4.2% polyethylene glycol precipitation tests, respectively. Optical densities (optical density units, ODU) were red spectrophotometrically. The statistical significance of the results was estimated by Student's t test.

Table 1-Total Ig and CIC levels of children tested for tuberculosis

ODU	IDR+ BK+	IDR+ BK−	IDR− BK+
Total Ig	0.408±0.126	0.375±0.099	0.586±0.141*
CIC	0.014±0.013	0.014±0.004	0.024±0.009*

*p<0.05.

The highest concentration of immune globulins and circulating immune complexes, statistically significantly different (p<0.05), found in the IDR-BK+ group indicated the dependence of humoral changes on the presence of bacteria, rather than related to IDR, suggesting an added diagnostic value by use of these non-specific serological tests.

P4985

WITHDRAWN