PIDSP Journ, 1990; 3:6-10

Volume 3 No 5

TUBERCULIN TEST REACTIVITY OF SCHOOLCHILDREN ATTENDING A PUBLIC SCHOOL

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ABSTRACT

In an attempt to answer the following objectives: 1) to determine the effect of the following factors on tuberculin reactivity namely: state of nutrition number of BCG scars and history of exposure; 2) to correlate tuberculin reactivity with clinical manifestations and radiological findings in tuberculosis; 3) to be able to identify predictors of tuberculin reactivity; 4) to determine an appropriate cut-off size of PPD induration for a suspected TB infection, 185 schoolchildren randomly selected from Grade 2 to Grade 6 attending a public school were intradermally tested with 5 TU of PPD. All of them also underwent a chest radiography. 61.08% were positive to the skin test. Majority belonged to the Grade 2 level. Among the factors taken into consideration, only the number of BCG scars and history of exposure were found to be significantly correlated with tuberculin reactivity at $p<0.5$. Using logistic regression analysis, 3 variables were found to be significant predictors of tuberculin reactivity: history of exposure, nutrition, and poor weight gain. Among the proposed cut-off sizes for TB infection, a >10 mm skin induration remains to be the most reasonable reference point to discriminate infected from the uninfected schoolchildren. A history of close contact to an adult with probable infectious TB is paramount in any child who will be evaluated for a possible tuberculosis infection. This risk factor together with a reactive tuberculin will be able to substantiate additional information provided for by the presence of clinical manifestations and/or radiological findings.

INTRODUCTION

The unceasing occurrence of tuberculosis in children worldwide signifies an ongoing transmission of infection among all age groups.

In the Philippines, it remains to be a major public health problem. Despite government efforts to improve disease surveillance and treatment programs, the morbidity and mortality remains to be highly significant especially among children wherein approximately 40% get the disease by 10 years.

Children with tuberculous infection are commonly asymptomatic with normal radiographic findings. Although the possibility of developing tuberculosis remains throughout an infected individual's life, children with untreated tuberculous infections are at risk for developing disease for longer periods of time than are adults, and they become a source of tuberculosis in the community.[1] Children become prone to infection if there is prolonged exposure and close contact to an adult/adolescent case. Specifically, caregivers such as relatives, neighbors, nannies or teachers have been identified to be potential sources of tuberculosis.

Poverty, with resultant poor nutrition and inadequate medical care continue to play a role in the epidemiology of tuberculosis[2] and may explain in part to the uncontrollable rise of tuberculosis in our country.

Whereas in adults diagnosis of TB is primarily bacteriologic, in children it is frequently epidemiologic and indirect. Thus, testing the latter for tuberculous infection becomes essential in identifying infected persons who can benefit from preventive therapy and perhaps in finding persons with clinical disease in need of treatment to prevent its complications and sequelae. With the high incidence of tuberculosis in the Philippines and the high risk of possible exposure to an adult with infectious TB[3], schoolchildren is one subgroup that will benefit from tuberculin testing.

A positive tuberculin skin test reaction is the hallmark of primary infection with *M. tuberculosis*. This indicates that there is a primary focus in the lung parenchyma too small to be visible on roentgenogram with associated regional lymph node involvement.[1] The best example, the Mantoux test, considered to be the "gold standard" test, involves the intradermal injection of 5 units of protein derivative (PPD) prepared from supernatant extracts of cultures of *M. tuberculosis*. In developed countries, the sensitivity and specificity of this test is estimated to be about 90% at a 10-mm reaction size. Locally, its sensitivity ranges from 10-40% and specificity of 77-100%.[4] Variable reports regarding its usefulness have been obtained due to the differences in strengths of PPD used. A great proportion of local studies have used the 2TU as a gauge of sensitivity of the Mantoux test. Recently, a study by Chan et al used the 5TU and showed a sensitivity of 59.3% but a specificity of 97.7%. With the undersupply of this test, a new commercial preparation of PPD 5TU from Japan was produced to answer the increasing demand for this test.

Utilizing the tuberculin test for recognizing children with probable TB infection enhances its value as a diagnostic tool. One limitation of the tuberculin test though is its effect on a child with previous BCG vaccination. As a preventive measure, BCG

Keywords: tuberculin skin test, Mantoux skin test
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has been routinely given to young infants and children under 8 years of age. Although BCG has been in use for quite sometime, its effectiveness is still uncertain and is believed to be from 0-80%.

The Committee of Infectious Disease of the American Academy of Pediatrics has stated that prior BCG vaccination is never a contraindication to tuberculin testing. No reliable method exists for distinguishing tuberculin reactions caused by BCG vaccination from those caused by natural infection. Reactions are often <10 mm and should not be considered a factor in determining whether the reaction is caused by *M. tuberculosis* infection or prior BCG vaccination. In addition, reactive PPD test wanes after 3 to 5 years of vaccination and is unlikely to persist for more than 10 years in the absence of TB exposure and infection.

Revaccination with BCG however can modify the tuberculin skin test response because it produces a larger induration. In a study done by Ildirim et al in 1995 among Turkish schoolchildren, findings showed that different induration sizes were obtained in children with 2 or 3 scars. Sepulveda's study in 1990 also revealed similar results. As such, recommendations were made to use the 90th percentile values of the induration size for detecting tuberculosis infection . So far no local studies have been undertaken to reaffirm these results.

Different cut-off points have been employed to interpret the Mantoux test. The American Thoracic Society uses the "5-10-15" rule for groups with different risks of tuberculosis. For children at high risk (e.g. those who are contacts of adults with infectious TB, who are immunosuppressed, have clinical evidence of tuberculosis, or who have abnormalities consistent with tuberculosis on chest roentgenogram), a tuberculin test reaction of 5 mm or greater induration is considered positive. For infants or for children who are living with adults in a high-risk group, an induration of 10mm or greater is considered positive, for all other persons who are considered at low risk for tuberculosis, induration of 15mm or greater is classified as positive. A local study done by Chan et al showed that an induration >10 mm with PPD 5 TU was highly significant in patients with tuberculosis. The First National Consensus Report (1989) of the Committee of BCG & Tuberculin Test endorsed an 8-mm induration for indicating TB infection on the basis of the National TB Prevalence Survey results of 1983. In the recently concluded PHILCAT convention, the working group on classification and diagnosis has recommended a ≥ 5mm induration as a positive reaction whether BCG or non-BCG vaccinated in children 5 years and above. To date, there are no local data comparing these PPD sizes in children suspected with tuberculous infection.

A negative Mantoux tuberculin skin test never excludes tuberculous infection or disease. A considerable 10% of immunocompetent children with culture-documented tuberculosis do not react initially to 5 TU of PPD.[2] Host related factors such as age, poor nutrition, co-existing viral infection and overwhelming tuberculosis can likewise lower tuberculin reactivity.

with an enormous number of published studies about a very old disease certain issues remain unresolved. The objective of this study are:

1) to determine the effect of the following factors on tuberculin reactivity:
   a. state of nutrition
   b. number of BCG scars
   c. history of exposure

2) to correlate tuberculin reactivity with clinical manifestations and radiological findings in tuberculosis

3) to be able to identify predictors of tuberculin reactivity

4) to determine an appropriate cut-off size of PPD induration for a suspected TB infection

MATERIALS AND METHODS

The Antigen. A purified protein derivative from BCG Laboratories, Japan was supplied for the study. Each vial was reconstituted to contain the amount of protein equivalent to 5 tuberculin units (5 TU).

The Subjects. The study population consisted of 250 schoolchildren randomly selected and equally apportioned to each year level from Grade II to Grade VI (age range: 7-14 years old) attending a public school in Brgy. Bagong Pag-Asa, Quezon City. Parental consent, a detailed family history including a possible exposure to an adult/adolescent as well as personal medical history were obtained from each patient through the parents. In order to find out the possible sources of exposed children, parents/ guardians were asked the following afternoon fever; weight loss; chronic recurrent cough, back pain, a recent chest x-ray/AFB sputum smear; previous history of TB treatment; other adults staying with the family with similar signs and symptoms. A positive chest radiograph and/or AFB sputum smear was considered an active case. Likewise, an adult with a chest radiograph indicative of tuberculosis but with inadequate treatment was also considered an active case. Adults who had 2 or more signs and symptoms suggestive of TB were advised to have an AFB sputum and/or chest radiograph done, and were considered as TB suspects. Among the schoolchildren, special attention was given to the following signs and symptoms: cough/wheezing ≥ 2 weeks; painless cervical and or other lymphadenopathy, poor weight gain, fever ≥ 2 weeks. Presence of 2 or more of these clinical features were considered suggestive of tuberculosis. A complete physical examination was performed. The age, sex, height, weight and BCG vaccination status were all recorded. The latter was determined by the number of BCG scars in the deltoid area.

The Tuberculin Test. The test was carried out in all schoolchildren with consent. A dose of 0.1 ml of 5 TU PPD was injected intradermally using a 26-gauge needle over the volar surface of the right forearm done by a single nurse.

Interpretation of Test. The reaction was read 48 hours after injection by the investigator. Interpretation was based on the presence or absence of an induration measured transversely to the long axis of the forearm.

All readings were measured to the nearest millimeter using a ballpoint to determine the edge of induration and avoid underreading when palpation is used.

A ≥10 mm induration was considered a positive reaction.

All chest radiographs were done in one hospital.

Only 1 radiologist interpreted the x-ray plates. To minimize intraobserver bias, the radiologist was blinded to the following clinical history of the child, P.E. findings as well as the PPD result.

Chest Radiograph. Both postero-anterior and lateral views were done.

Interpretation of the Chest Radiograph. Chest x-ray plates which had poor outcome were repeated before reading was done. Features like hilar adenopathy, primary parenchymal focus, or complications such as pleural effusion, cavitary lesions, coin shadow, collapse-consolidation, obstructive hyperaeration and miliary pattern were each considered as radiographic manifestations of tuberculosis.

TB Classification. In an attempt to classify the schoolchildren according to exposure infection and disease using the PPD, the following sets of definition were observed (based on ATS and Centers for Disease Control)

TB Exposure. A child who has been exposed to an adult/adolescent with active TB disease, has no signs and symptoms of TB, negative PPD and negative chest radiograph.

TB Infection. A child with or without history of exposure to an adult/adolescent with active TB, has positive PPD, no signs and symptoms of TB and negative chest radiograph.

TB Disease. A child who has active TB has 3 or more of the following criteria

1. exposure to an adult/adolescent with active TB
2. positive Mantoux tuberculin test
3. signs and symptoms suggestive of TB
4. abnormal chest radiograph suggestive of TB
5. laboratory findings suggestive of TB (histological, cytological, biochemical, immunological and/or molecular)

The following statistical tests were performed to analyze the data: Fischer's Exact Test for 2-table correlation; Mantel-Haenszel chi-square; logistic regression for predicting significant risk factors and measures of sensitivity and specificity for devising appropriate cut-off PPD size. A p-value of <0.05 was considered significant.

RESULTS

A total of 218 schoolchildren participated in the skin testing. Thirty-three students however, were excluded from the study due to non-compliance with the taking of chest radiograph. Of the remaining schoolchildren, 113 (61.08%) were positive to the skin test. The per cent of positive reactors by grade level is shown in Table 1.

Table 1. Tuberculin Reactivity in the Various Grade Levels

YEAR LEVEL	NO. OF	TUBERCULIN	%REACTIVITY	p-value
Grade 2	40	32	80.00	0.003
Grade 3	46	28	60.87	0.505
Grade 4	34	18	52.94	0.898
Grade 5	30	16	53.33	0.876
Grade 6	35	19	54.29	0.866
TOTAL	185	113	61.10	0.019

The greatest proportion of tuberculin reactors came from the Grade 2 level with an 80% reactivity. Students from the other year levels had parallel numbers of positive reactors exceeding 50% of the total number for each particular year level. Analysis using Mantel-Haenszel chi-square showed significant difference between the 5 groups on PPD response. This outcome has been greatly influenced by the large reactivity shown by the schoolchildren who belonged to the Grade 2 level.

Nutritional Status

A little more than 65% of the schoolchildren were assessed to be nutritionally stable while the rest was either classified as undernourished or overnourished based on the FNRI-PPS Anthropometric measurements for Filipino children. A Mantel-Haenszel chi-square analysis done demonstrated borderline significance between the 3 groups. As shown in Table 2, a large proportion of well nourished children produced significant tuberculin responses but many of whom, also demonstrated non-tuberculin reactivity. Overnourished children showed remarkable tuberculin reactions. Surprisingly, over 60% of children assessed to be undernourished showed positive reactions to PPD.

Table 2. Effect of Nutrition on Tuberculin Reactivity

NUTRITIONAL STATUS	PPD RESPONSE (-)	PPD RESPONSE (+)	TOTAL
well - nourished	53 (43.4%)	69 (56.6%)	122 (65.9%)
undernourished	15 (32.6%)	31 (67.4%)	46 (24.9%)
overnourished	4 (23.5%)	13 (76.5%)	17 (9.2%)

p = 0.062

BCG Status

Table 3. Effect of BCG on Tuberculin Reactivity

BCG STATUS	FREQUENCY	PERCENT	(+) PPD	% REACTIVITY	p - value
no BCG scar	12	6.5	3	25	0.010
1 BCG scar	78	42.2	45	57.69	0.831
2 BCG scars	95	51.4	65	68.42	0.025
TOTAL	185	100	113	61.08	

Table 3 illustrates the frequency of schoolchildren who had BCG scars and those who had none. Out or 173 who had BCG scars, 78 (42.2%) children had 1 BCG scar and 95 (51.4%) had 2. Only 25% of children with no BCG scar reacted to the test positively. Of those children with 1 BCG scar, 12 received the vaccine during infancy and 66 at Grade 1. More than 50% reacted to the test in both subgroups with comparable results. 68.42% of children with 2 BCG scars reacted to PPD positively. As the number of BCG scars increased, the number of tuberculin reac-

tors also increased. Using Fischer's Exact Test to determine differences in PPD reactivity between BCG and non- BCG groups demonstrated significant results. The presence of 2 BCG scars also revealed direct association with PPD reactivity.

The mean PPD sizes for each BCG group were as follows: 8.3 +/- 6.9; 10.4 +/- 4.7; 10.7 +/- 4.5 respectively. No significant relationship was evident between a particular BCG group and the size of the induration.

Table 4. Different Factors and PPD Outcome

FACTOR	NO. OF school children	(+) PPD	% REACTIVITY	p-value
A. Exposure				
Present	118	100	84.75	0.00000
Absent	67	13	19.40	
B.Chest x-ray				
Normal	117	106	66.57	0.406
C.Clinical manifestations				
Asymptomatic	119	70	58.80	0.285
Symptomatic	66	43	65.15	

History of Exposure

One hundred thirteen (60%) schoolchildren tested had close contact to adults suspected, others confirmed by chest x-ray of having tuberculosis. A comparison done using Fischer's exact test, to determine any difference in the PPD response of these 2 groups showed highly significant results.

Among the elicited sources of infection, parents particularly the father (28) dominated the picture followed closely by the mother (25) and grandparents (24). Most of these people live with the index reactor except for some children whose source was a next door neighbor with whom they had frequent contact.

Radiological Findings

Of the children who had undergone chest radiography, only 10 demonstrated radiographic findings suggestive of tuberculosis and 7 of whom had reactive tuberculin test. Radiological features included hilar adenopathy (2); hyperaeration (1); pneumonitis (2); consolidation (1); hazy opacities (1). The 3 non-tuberculin reactors demonstrated the following chest radiological findings: solitary, enlarged node seen only in lateral view; hilar lymphadenopathy, matted; and healed 1° TB.

One hundred seventy-five children had normal radiographic results, 106 (60.51%) of them turned positive to the skin test. Fischer's exact test showed no demonstrable significant relationship between radiological findings and tuberculin reactivity.

Clinical Features

Clinical features which included chronic cough (≥ 2 weeks); cervical lymphadenopathies and poor weight gain had been noted in 66 (35.7%) of the 185 children. The remaining 119 was assigned to the asymptomatic group. In decreasing frequency - cervical lymphadenopathies - 117 (63.2%), chronic cough - 47 (25.4%) and poor weight gain - 32 (17.3%) were observed during examination of these children. Of the 117 children with cervical lymphadenopathies, only 74 (63.25%) turned positive to the skin test. A similar turn out of tuberculin reactors was obtained in those children with chronic cough (68.08%). Although only 32 children were noted to have poor weight gain, 30 of whom (93.75%) were reactive to PPD.

Among the asymptomatic children, 70 (58.8%) were tuberculin reactors while 43 (65%) children turned positive in the symptomatic group. There was no significant difference, however, which existed between the 2 groups.

Table 4A. Clinical Features and PPD Outcome

CLINICAL FEATURE	FREQUENCY	PPD OUTCOME	
		(+)	(-)
cough ≥ 2 weeks	47 (25.4%)	32 (68.08%)	15 (31.91%)
lymphadenopathies	117 (63.2%)	74 (63.25%)	43 (36.75%)
poor weight gain	32 (17.3%)	30 (93.75%)	2 (6.25%)

Combination of Factors

Individual factors which were taken into consideration were compounded based on the criteria set by the American Thoracic Society to classify suspected TB patients. Several groups were formed and schoolchildren were clustered accordingly.

Table 5. Tuberculin Reactivity of Compounded Factors

COMBINED FACTORS	NO. OF SCHOOLCHILDREN	(+) PPD	% REACTIVITY
Asymptomatic (+) Exposure	74	62	83.8
Asymptomatic (-) Exposure	45	8	17.8
Symptomatic (+) Exposure	45	39	86.7
Symptomatic (-) Exposure	21	4	19.0
Asymptomatic (+) Exposure N CXR	72	61	84.72
Asymptomatic (-) Exposure N CXR	44	14	31.81
Symptomatic (+) Exposure Abn CXR	6	5	83.33
Symptomatic (+) Exposure N CXR	39	34	87.18
Symptomatic (-) Exposure N CXR	20	4	20

This table clearly illustrates the crucial role that exposure plays in tuberculin reactivity. All asymptomatic children with history of exposure generated a high tuberculin reactivity (83.8%). Similarly, children who had manifestations with exposure begot significant reactions (86.7%). The absence of exposure in both the asymptomatic and symptomatic groups only yielded significant reactions of less than 20%. All children with significant radiological finding were symptomatic except for 2. All these 8 children had history of contact with a potential TB case. However, a number of symptomatic children with exposure had normal chest x-ray findings yet produced a high rate of positivity (87.18%).

A significant association was shown in the cluster of children who were asymptomatic with normal radiological findings and has history of contact to adult cases with tuberculin reactivity at p=0.000. These children were the ones classified under TB infection.

Table 6. Assessment of Schoolchildren

ASSESSMENT	FREQUENCY	MEAN PPD SIZE (mm)
no TB	55	[illegible]
TB Exposure	13	[illegible]
TB Infection	50	[illegible]
TB Disease	29	[illegible]

Using the analysis of variance to determine differences between PPD sizes among groups, no substantial disparity was demonstrated between those who were assessed to have infection and those who belonged to the Disease group. Significant differences, however, existed in the following at $p < 0.02$: no TB group - Infection; no TB group - Disease; Exposure - Infection; Exposure - Disease.

Logistic Regression Analysis

Using the logistic regression analysis (univariate approach), 3 of the factors considered turned out to be significant predictors of tuberculin reactivity and these were: presence of exposure; state of nutrition and poor weight gain.

This table shows the significant predictors with its resultant probable chi-square and odds ratio.

Table 7. Significant Predictors of Tuberculin Reactivity

PREDICTOR	CHI-SQUARE	ODDS RATIO
Exposure	[illegible]	[illegible]
Nutrition	[illegible]	[illegible]
Poor weight gain	[illegible]	[illegible]

If a predictor's estimated odds ratio is more than 1 then it signifies high association with tuberculin reactivity. All these predictors had odds ratio of more than 1.

The actual probability that a child has tuberculous infection using a ≥ 10 mm induration as the cut-off size for a positive tuberculin reaction was calculated using regression analysis. Results revealed non-discriminating points thus using this as reference point will entail classifying a small set of children as having TB infection when truly they have none. On the other hand, fixing the value > 10 mm will mean missing out a greater number of children with true infection.

Sensitivity and specificity testing were also done to compare the different proposed cut-off sizes and demonstrated the following results:

Table 8. Sensitivity and Specificity of Different Cut-Off Points

PROPOSED CUT - OFF SIZE FOR PPD INDURATION (mm)	SENSITIVITY	SPECIFICITY
≥ 5 mm	95.8 %	15 %
> 5 mm	91.0 %	35 %
> 10 mm	84.7 %	51 %
> 11 mm	75.0 %	57.5 %
> 12 mm	61.1 %	65.7 %

Although the ≥ 5 mm value had the highest sensitivity meaning only 4.2% of cases will be missed, difficulty will be encountered in predicting cases which are truly negative because of its very low specificity. On the other hand, setting the cut-off size at ≥ 11 mm will denote missing 25% of true cases but improving accuracy of identifying negative cases. A ≥ 10mm cut-off size had a sensitivity of 84.7% and maintained a specificity of more than 50%.

DISCUSSION

The reaction to intracutaneously injected tuberculin is the classic example of a delayed (cellular) hypersensitivity characterized by 1) its delayed course, reaching a peak more than 24 h after testing; 2) its indurated character because of cell infiltration; and 3) occasional vesiculation and necrosis. A positive reaction to a Mantoux test with 5 TU PPD demonstrates that hypersensitivity to mycobacteria has developed. The larger the induration, the greater is the probability that the inflicting organism is *M. tuberculosis*. Although skin reactions may be confounded by infection to mycobacteria other than *M. tuberculosis*, these are oftentimes smaller than reactions caused by tuberculous infections. The relatively high rate of positive tuberculin test exhibited by the schoolchildren in the different year levels can help establish a probable relationship of the positive tuberculin test to infection with *M. tuberculosis*. There was a larger rate of test positivity in the younger age group than in the older ones which was in contrast to Blum's survey[7] of school age American children done in 1962 wherein tuberculin reactivity increased with increasing age. This discordance is brought forth by the practice of re-immunizing children at school entry with BCG thus producing larger reactions over the next year and gradually waning as the time lapsed from revaccination becomes longer. Apart from this, most Filipino schoolchildren maintain close contact with their parents and immediate adult relatives since they commonly live under one roof.

Malnutrition has been widely recognized to affect tuberculin response and has been considered to be one of the various host-related factors to decrease PPD response. Functional deficiency of CD4 cells and reduction of rosette forming lymphocytes are seen in malnourished states. In this study though, the degree of nutrition did not contribute significantly to the PPD outcome. In fact, a large proportion of negative reactors came from the well nourished group. Undernourished children even produced significant responses twice that of negative reactions. These findings concur with Chan's study[8] wherein degree of stunting and wasting did not produce substantial effect on PPD reactivity. Nonetheless, it has to be stressed that the degree of malnu-

trition of the participants was not severe enough to downregulate the functional capacity of the T cells. It may be inferred then that true PPD response can still be produced in mild states of malnutrition and indirectly reflect the TB status of a child.

Several reports have disclosed that revaccination produces larger induration and a greater degree of tuberculin sensitivity as compared with one vaccination.

In this study, < 42% of those with BCG scars had reactions less than < 10 mm in contrast to 75% to those without BCG. These results correspond to the findings of the Cebu vaccination campaign projects[9] done in 1965 and 1966 wherein 54% and 74% of children respectively with old scars had indurations less than 10 mm as compared to 84% and 87% without scar. Chan's results showed no significant difference between the 2 groups.

Expectedly, PPD reactivity should have waned already if BCG was received during infancy. With a background of recent contact to potential sources of active TB, more than 50% of the children (n=12) in this subgroup were tuberculin reactors which could be considered reflective of a possible tuberculous infection. Of the 66 children who only received BCG at Grade 1, 2 peaks of tuberculin reactivity was observed - first, during the 1st 2 years post-vaccination and second, 4 years post-vaccination. The former event may be a boosting effect and the latter may suggest presence of an infection considering the high proportion of children who had adult contacts with potential tuberculosis.

The presence of 2 scars substantially increased the number of reactors to the tuberculin test. Moreover, most of these positive reactors were Grade 2 children who had received BCG the previous year. Separate studies done by Ildirim [9] and Sepulveda[11] have also shown enlarging trend of skin reactions as BCG scars increased in number. Speculations arise then on the reaction size of BCG recipients to tuberculin test since various reports have stated that reactions greater than 10mm are unusual following vaccination, [3] but in this study it was shown otherwise. However, there is still no reliable test to distinguish reactions secondary to BCG vaccination from true infections so at this point, it is still reasonable to deduce that majority of the positive reactions were brought upon by the presence of a tuberculous infection because of the high prevalence of this disease in our setting and in addition, many children were found to have close contacts with adults with potential infectious TB cases. It would also be wise to recognize the fact that a number of these reactions may truly be booster effects of the BCG vaccination.

The mean PPD sizes of the different BCG groups were comparable thus there was no need to alter the size of PPD induration for detecting tuberculous infection as stipulated in Ildrim's study.

The major factor linked to infection is close contact with adolescent and adults suspected or confirmed tuberculosis cases. Results which were demonstrated in this study far exceeded the average rate (30% - 50%) given by Starke for household contacts with reactive Mantoux tests and with known exposure to infectious TB cases. Chan[8] in his study got a 71.2% for his abnormal patients. Likewise, Takamatsu[13] established history of contact in 73.3% of 359 pediatric TB cases. With a greater than 80% reactivity seen in this series among schoolage children with elicited exposure to suspected TB cases suggests an ongoing transmission of the inciting agent in the community. Sources of exposure have remained to be persons whom the children are in frequent contact with and these included parents and relatives who stay with the family.

The chest roentgenogram is often correlated with PPD and/or clinical manifestations and has been the subject of so many researches despite inconsistencies encountered among different readers and between the opinions of the same reader on different occasions. Local studies[8,14,15] have documented that the most frequent radiological findings suggestive of primary TB is nodal enlargement - retrocardiac, paratracheal or peribilar. Results of children with abnormal x-ray findings from this study conformed what had been frequently observed. Emphasis though has to be placed on the knowledge that not all normal chest radiographs will have small PPD indurations. On the other end, suggestive radiological findings coupled with a history of contact will have a probability of producing an enlarged tuberculin reaction. Different outcomes have been reported regarding this theory. In Bonus study,[14] only 46% of tuberculin reactors had abnormal chest x-ray. Chan's results demonstrated otherwise because he was able to show a significant association between PPD responses and chest x-ray. In this series, majority of the tuberculin reactors had normal x-ray findings but those with abnormal findings likewise had high tuberculin positivity (70%). Patients who belonged to the latter group were mostly symptomatic and had history of exposure. It can be deduced then that a normal chest radiograph taken in the context of other variables such as a (1) PPD skin test, a history of contact with an adult TB case and absence of symptoms has great value in assessing a child with suspected TB infection. Moreover, a significant radiographic finding with all the other parameters present can easily identify a child with TB disease.

Clinical manifestations of tuberculosis depend upon the quantity of tubercle bacilli present, the virulence of the organism, the age, immunocompetence and susceptibility of the host when initially infected. [16] Asymptomatic presentation is more common among schoolage children (80-90%) than among infants less than 1 year of age (40-50%).[17] Clinical signs are so meager and not very specific thus should always be considered in the context of other parameters for a more accurate assessment.

Among the clinical features taken into account as suggestive of tuberculosis, cervical lymphadenopathy was still the most frequently observed as has been seen in other local studies. However, there was a considerable high percentage of children (36.75%) who only presented with this sign yet had small reactions of skin test and had normal radiological findings. Apparently, no exposure was elicited from their parents thus were assessed to be free from infection. It will therefore be risky to consider a child to have clinical TB based on a sign/symptom alone because this can lead to overdiagnosis and eventually overtreatment. Poor weight gain which was found to be a significant predictor of tuberculin reactivity in this series points to a crucial role it plays as a feature suggestive of tuberculosis although this has only been shown in few studies.[5,8,15] There is still a scarcity of data regarding the predictive value of each of these

clinical features thus at this point it will be more rational to consider each suggestive manifestation in the light of other symptoms which may be present.

The use of this tuberculin test together with the other criteria (clinical features, radiological findings, history of contact) had been helpful in our pursuit of detecting children who were probably infected. In this study, history of contact with an adult with probable infectious case was foremost because this played a pivotal role in tuberculin reactivity. As has been shown, despite presence of symptoms in some children, tuberculin reactions were small and radiological findings were normal. On the other hand, a number of asymptomatic children with apparently no exposure had reactive indurations and this may be due to several reasons: time interval from BCG receipt to skin testing was short; infection with a nontuberculous mycobacteria. Children who possessed 3 criteria - clinical manifestations, presence of exposure and significant radiological findings - associated well with tuberculin reactivity.

Based on the results of this study, no exact PPD size can be suggested as indicative of infection or disease. At this point,, it will be difficult to postulate that larger indurations can be seen in diseased children.

Three factors were obtained to be significant predictors of tuberculin reactivity. These included: presence of exposure, state of nutrition, and poor weight gain. These findings are comparable with results of other studies taken together.

After testing several cut-off sizes for PPD induration, a size of ≥ 10 mm would still be the most reasonable reference point to discriminate the infected from the uninfected. Although a size of ≥ 5 mm will largely improve its sensitivity, this will entail overdiagnosis and eventually overtreatment. Identifying truly uninfected children would be met with difficulty because of its low specificity. On the other hand, setting the value at ≥ 10mm will improve recognition of the uninfected However 40% of the true cases will be missed because of its diminished sensitivity. Although a 10mm induration will slightly diminish its sensitivity (84.7%) in discerning real infected children, its strength in picking out uninfected ones will be maintained at more than 50%. Based on these elucidation, setting the cut-off size at this value would still seem to be the most reasonable move.

SUMMARY

The tuberculin test using 5 TU of PPD remains to be the best diagnostic tool available to physicians to help identify children with probable TB infection. Schoolage children, the target population of this study served as the gateway to identify adults indirectly who probably continue to transmit the tubercle bacilli.

There were 185 schoolchildren who completed the study of whom 61.08% were positive to the skin test. Majority of the tuberculin reactors came from the Grade 2 level and recipients of BCG the previous year.

Malnutrition producing a state of anergy to the tuberculin test was not shown in this study. Inasmuch as the degree of malnutrition should be considered, mild forms of such can still generate a reactive PPD response.

The number of BCG scars had markedly affected tuberculin reactivity leading to a larger number of positivity as it increased. Since this influenced interpretation, especially that tuberculin testing was done a year after receipt of BCG vaccination, explanations were taken in the context of the epidemiology and prevalence of the disease in our setting and possible booster effect of the vaccine.

Among these 3 criteria considered - exposure, chest x-ray findings and clinical features - only history of exposure correlated well with tuberculin reactivity.

Presence of cervical lymphadenopathies continued to be the predominant manifestation but did not necessarily signify presence of infection.

With the aid of this new tuberculin test combined with the other criteria, schoolchildren were ably classified as to TB exposure, infection and disease. Most of them belonged to TB infection.

The 3 significant predictors of tuberculin reactivity included: history of exposure to an adult with suspected TB; state of nutrition and poor weight gain.

An induration of ≥ 10mm utilizing this new preparation of PPD 5TU remained to be the most reasonable cut-off size to distinguish between the infected and the uninfected schoolchildren.

RECOMMENDATIONS

In the light of the results of this study, we recommend the use of PPD 5 TU as a diagnostic tool in schoolchildren to detect TB infection and possibly identify adults indirectly, who may be potential sources of infection.

We propose that a similar study be done on a larger scale and include schoolchildren attending private schools to validate these results. Younger age groups, < 5years of age attending preschool or day care centers could be another population which can be thought of to do parallel studies since this subset is at higher risk of developing disease.

Since BCG may possibly have a boosting effect on PPD or in situations where risk factors may be present, prevaccination tuberculin testing at school entry may be done by giving it between 4 and 11 years of age or between 6 and 11 years old.

The availability of this new preparation should be welcome news to physicians. Comparative studies should be undertaken on to re-affirm the results with a similar preparation.

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Instructive Case

Monoarticular Knee Joint Inflammation in a Newborn

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CASE REPORT

A 23-day-old baby girl was admitted because of right knee swelling. History revealed she was born full term, adequate for gestational age by ceasarean section for fetal distress. Patient was meconium stained, vomited on the 1st day of life thus was started on ampicillin and amikacin for possible sepsis. Antibiotics were shifted on day 3 of medications when she developed abdominal distention, hypoactive bowel sounds, *pneumatosis intestinalis* on plain abdomen and occult blood on fecalysis. The patient completed 2 weeks piperacillin tazobactam and amikacin for necrotizing enterocolitis stage II-A. Blood culture grew nothing. She underwent phototherapy and was on parenteral nutrition via a peripheral vein until breast milk feedings were tolerated. She was sent home improved on the 20th day of life. A day after discharge, the patient's right knee was noted to be swollen and she would cry when the affected leg was moved. This prompted consultation and readmission.

Maternal history showed regular prenatal check-ups, cough on 4th month of pregnancy but no intake of antibiotics which recurred on the 8th month for which she took amoxicillin. The family history, nutritional, developmental, immunization, personal and social histories were non-contributory. Review of systems revealed no trauma, fever , diarrhea and no fussiness or irritability. Physical examination showed a slightly pale infant with good suck, cry and activity. Vital signs, abdominal and neurological findings were essentially normal except for a swollen, erythematous and warm right knee which was tender when touched. Complete blood count on admission revealed WBC within normal limits for age, anemia and thrombocytosis. Radiographs of both knees showed soft tissue swelling only of the affected right joint.