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# 行政院衛生署疾病管制局九十四年度科技研究發展計畫

# 接種過預防肺結核疫苗之嬰幼兒之 PPD 測試反應

研 究 報 告

執行機構：台大醫學院小兒科

計畫主持人：黃立民

協同主持人 ： 吳怡君

研究人員：詹珮君

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＊＊本研究報告僅供參考，不代表本署意見＊＊

# 目錄

## Abstract

**Objective**: to obtain the distribution of tuberculin skin test in low-risk children aged from 3 months to 15 years and to approximate the proper cutoff point for upper limit of normal size

**Methods**: Questionnaires were distributed to school children and in our health baby clinics. A Cross-sectional study with tuberculin skin test (PPD RT 23 2TU) was conducted among those who has received BCG as schedule, without history of exposure of tuberculosis, and no immunocompromised status.

**Results**: 630 eligible data was analyzed. No significant difference was observed among different size of PPD with family history of old TB more than 10 years or cough without clear cause (p= 0.3117), similar with family worked related to medical care (p=0.8546), family with foreign nationality (p=0.9855), and those who had ever had a babysitter with foreign nationality (p=0.2801) . PPD size of children aged younger than seven was affected by BCG with decreased trend when age increased. Since it was a bi-modal distribution of PPD induration size, using the same cut-off value for children of all ages was impracticable. For children younger than 6 year-old, the age specific cutoff value for normal PPD suggested by area under curve of fraction of reacting to PPD was 17~18mm. For children after 7 year-old, the approximation with ARTI historical data revealed 11~15mm were possible candidate for upper limit of normal value. Goodness of fit test disclosed that 11~12mm might be the best fit- cut-off for this age.

**Conclusions**: The study provided a normal distribution of PPD size for children who had received BCG in infancy with lower risk of TB. Though the case number for children aged under 4 year-old was small, the data provided the useful information when the available data was limited.

**Keywords**: tuberculin skin test, infant and children, induration size, tuberculosis

**中文摘要**

本研究主要是探討低危險群兒童(年齡為三個月到十五歲之間)，在嬰兒時期接種過卡介苗後，結核菌素測試的自然分布狀態為何．在學校和醫院的健兒門診間發問卷，問卷回收後,依照所設定之收案標準(包括必須在嬰兒時期按時接種過卡介苗，沒有開放性結核病的接觸史，沒有免疫不全之狀態)，使用 2TU 的 PPD RT23 做皮膚結核菌素測試．

我們對 630 個有效資料進行分析．在原本認為風險較高的情況: 家人或接觸者有十年前以上之舊結核病史，或不明原因咳嗽 (p= 0.3117), 家有醫護人員(p=0.8546)，家屬有外國籍 (p=0.9855)及孩童曾被外國籍褓姆照顧 (p=0.2801), 其結核菌素結節大小與沒有這些風險的孩童比較並沒有統計上顯著意義.在小於七歲的幼童, 結節大小的確受到卡介苗的影響， 此一影響隨年齡增大而逐漸減少. 因為結節大小分佈是一個雙峰的分佈, 如果在不同年齡層想要用同一 cut-off value 是不切實的. 對於年齡在六歲或以下的孩童來說, 利用陽性反應的百分比曲線下面積可求得正常值上限約為 17~18mm 之間. 而對於年齡在七歲級以上的孩子, 利用與估計年感染率曲線之比較可得 11~15mm 是此年齡層可能的正常值上限; 再利用 goodness of fit test 可得與 ARTI 最符合的曲線是以 11~12mm 當作陽性 cut-off

value 所做的曲線.

本研究提供了低危險, 在嬰兒時期接種卡介苗之孩童之正常結核菌素測試結節大小之分佈. 雖然年齡四歲以下的個案數太少, 以目前本土極少的兒童結核菌素研究資訊, 將是相當有用的資料.

關鍵詞：肺結核菌素測試、嬰幼兒、結節大小、肺結核

**Introduction**

在許多中度開發，或部分已開發國家，結核病仍然是公共衛生進步的一大障礙，隨著多重藥物抗藥性的結核菌出現，持續性開放性肺結核更是各國重要的公共衛生課題 (1)。防止持續性開放性肺結核的產生，最重要的步驟是減少原發性的感染以及增進抗肺結核藥物的服從性。在高結核盛行區，原發性感染常發生在嬰幼兒時期。臨床醫師判斷經結核菌暴露的孩童是否有疾病的發生，在早期的病程，是相當不容易的，受到感染的病童往往在疾病相當明顯，有持續發燒、體重減輕、營養狀態受到影響、肺部與肺部外的病灶才經培養或切片而被診斷。而要針對暴露後的未發病感染做診斷又是難上加難. 在低盛行率國家, 欲消滅結核病, 必須積極治療早期的暴露後未發病之結核感染 (LTBI, latent tuberculosis infection, LTBI), 這是預防結核再發的重要預防工作。然而在中高結核盛行區的醫師們往往面對相對多的活動型結核病患, 如何選擇適當的已暴露病童接受抗肺結核藥物的預防性投藥，是常常面臨, 但尚未有定論的日常問題。有效的診斷，篩選出高危險的病童，及早的預防性投藥，將可減少病童一生的結核發病率，及下一世代的肺結核盛行率。

結核菌素測試在兒童結核一直是一個相當實用的診斷工具, 但其敏感性及特異性常被爭論 。在接受過卡介苗接種的兒童，陽性的結核菌

素測試往往暗示著臨床醫師，此孩童有結核感染，再次感染，或者根本只是因為卡介苗所引起的免疫反應 (2)。有些報告指出結核菌素測試在施打過卡介苗可以反映近期的結核感染 (3,4)。在一歲前接種卡介苗而在兩歲大接受結核菌素測試的孩子中，有 36.6% 呈陽性反應 (5)。PPD test 是 purified protein derivative 做的結核菌素測試，它被廣泛地運用於兒童結核感染。然而，臨床上的使用，常常因為擔心結核菌素測試會被卡介苗影響而被質疑它的可信賴性。結核菌素測試的結果在接種過卡界苗的兒童的反應大小, 往往與接種的年紀, 距離接種的時間, 環境中的非結核分枝桿菌的影響, 接受結核菌素測試當時的免疫狀態, 以及接受哪一種成分劑量的結核菌素有關 (6). 在未施打卡介苗，肺結核盛行率偏低的區域，結核菌素測試確實反映了病童的結核暴露 (7)。在施打卡介苗的區域，若盛行率夠高, 肺結核菌素測試的陽性預測值就跟著上升. 在盛行率不高不低的區域，常常跟施打卡介苗到做結核菌素測試之間的間隔最有關 (8)，必須考慮年齡的因素, 以及是否在嬰兒期後追加卡介苗 (9), 較能提供高敏感或高確定的診斷意義 。結核菌素測試在這群孩童，只要 cut-off points 選得適當(10)，再加上危險因子分級，臨床的意義還是相當有用。而台灣在這方面的資料較國外缺乏.

台灣在民國六十六年改使用日本進口乾燥卡介苗接種後，曾計

畫性地使用 PPD RT23 1TU,於花蓮縣秀林鄉做有卡介苗接種疤痕之學前兒童，對結核菌素測試的影響。若以 10mm 為 cut-off point，則 0 到 1 歲嬰兒有 21.8% (29/133)呈陽性， 而在一到五歲幼兒中，陽性率為 15.2% (181/1193)。然若以 14mm 為 cut-off point 則陽性率分別為 3.8% (5/133)及 9.3% (110/1193)。此一測試因年代久遠，故無法證實當時是否有逐一詢問肺結核家庭接觸史，故暴露情形不可得。但此一結果仍具相當之流病意義，顯示山地鄉學前孩童在施打 BCG 的數個月到一年後，結核菌素反應有部份會呈陽性，但此偽陽性可因調整 cut-off point 至 14mm 而減低至臨床可使用之範圍; 然而, 在一到五歲幼兒的結核菌素測試結果可推論，當時有 6%左右的幼兒，在接種卡介苗後的四年當中，有結核暴露的經驗，成為 LTBI 的高危險群。

國際間認為 PPD RT23 2TU 與 Tuberculin PPD-S 5TU(所謂的結核菌素測試黃金標準)為 bioequivalent 的(11) 為求能與世界接軌, 故台灣自民國九十年九月起，結核菌素測試改用丹麥民間生產的 PPD RT23 2TU 做測試。零星的幼童結核菌素測試在各衛生所或小學依年級無疤及小疤學童有執行, 但缺乏完整的報告. 執行之 cuff-off value 又隨著有疤, 無疤而有所不同 (結核病年報, 2001). 若為無疤兒童, 則以大於等於 10mm 以上判陽性, 而小疤兒童則以大於等於 18mm 以上判陽性. 而新生而接種卡介苗率為 96%以上. 自民國 91 年起至民

國 94 年第三季止, 全國除北高兩市外之各縣市, 在無疤一年級學童中, 6.4%受檢者達陽性值 (5.54~7.77%), 陰性者 97.1%接受追加卡介苗. 在有疤的一年級兒童中, 11.49%受檢者達陽性值 (7.12~18.96%), 但可見其分布範圍相當寬. 自民國 92 年起至民國 94 年第三季止, 新生兒有疤 97.8%受檢者達陽性值; 幼童無疤(年齡不詳) 3.64%受檢者達陽性值 (3.16~4.7%) 陰性者 86.8%接受追加卡介苗. 整體看來新生兒剛接種完卡介苗比過去之陽性率高， 將近 100%; 而在學齡前, 無疤幼兒之陽性率為 3.64%, 到學齡兒童, 無疤學童之陽性率上升為 6.4%.

由於試劑的劑量及品質改變, 計畫性的各年齡層結核菌素測試應該再次進行，以提供臨床醫師結核菌素測試判斷陽性之依據; 然考量到衛生署不易執行嬰幼兒自願者之收案, 故本計畫將針對低肺結核暴露的大台北地區兒童，在接種卡介苗後，於年齡三個月大到十五歲大進行結核菌素測試，並詳細詢問家庭內之結核可能暴露。此研究之結果可至少提供兩點結果供參考：1．卡介苗對幼兒的結核菌素測試是否有影響？此影響為何？ 2．此年齡層，結核菌素測試可參考的 cut-off value。咸信此結果將對感染症醫師、兒科醫師、及公衛研究者提供一個相當實用的資料。

## Subjects and Methods

### Subjects

**Patient Eligibility and exclusion conditions** A healthy child with the age between 3 month to 15 year, who has received BCG as schedule, without history of exposure of tuberculosis.而未在出生施打 BCG 者，或有疑似接觸肺結核病史，在六週內若接種過 MMR (麻疹，腮腺炎,德國麻疹),水痘疫苗,口服沙賓疫苗,或得過上述疫苗所預防的疾病，或服用過類固醇(吸入型則不在範圍內)，免疫抑制劑，或因嚴重感染(細菌或病毒)而住院者，將被排除於本試驗。 若有任何先天性或後天性免疫缺陷者亦將被排除於本試驗外。另如為 3 個月大至 3 歲受試者若於出生一個月後才接種卡介苗則排除. 而 7 歲以上之受試者若能清楚出示於二年級曾追加卡介苗之紀錄，則因判讀困難，予以排除（台北市之學童結核菌素測試於國小二年級執行).

1. Age under 3 year-old: healthy volunteers in well-baby clinics in NTUH. 60 children was planned to be enrolled in the group younger than 1 year-old (1-2, 2-3 year-old, 20 children will be enrolled in each age group).
2. Age of 3 to 6 year-old, cases was planned to be enrolled from volunteered students from kindergarden (3-4, 4-5, 5-6, 6-7 year-old, 20 children will be enrolled in each age group).

3. Cases was planned to be enrolled from volunteered students from elementary school and junior high school (30 children will be enrolled in each age group). A total of 270 children was planned to be enrolled from children between 7 year-old and 15 year-old.

函請教育局及社會局發文，由有意願的一兩所學校中，隨機抽樣各班座號，於每一個年齡層，按班級數發放說明及同意書，問卷調查，由收回之問卷篩選出符合受試者選擇標準之學童．與符合受試者選擇標準之家長聯繫並解釋本試驗目的及方法後，家長簽同意書由學生交回保健室．若檢查當日有發燒， 身體不適，則予以解釋暫不執行．

**Methods**

**Information collection at the enrollment** Cross-sectional study of 450 children was planned to be conducted. Children were examined and assessed for general health condition,& BCG vaccination record (2) . Possible TB exposure including elderly with chronic cough or unexplained prolonged febrile illness in household contact, any contact history with documented open TB will be thoroughly evaluated. Children with suspicious immuno-compromised status, active lung disease or exposure history of TB will be excluded and follow-up will be done.

**Procedure of PPD test** Children who fit the criteria were planned to be given 0.1 ml of PPD (PPD RT23, 2 units) intradermally, in accordance with the guidelines recommended by WHO (2) . The tuberculin for the tests was obtained from Denmark and is used throughout the country. PPD indurations was planned to be read 48 and 72 h after administration

at 90 degrees from the longest axis of the arm (transversely) and recorded to the nearest millimeter. Indurations size was recorded by one study personal. Since digit preference is a normal behavior (unconsciously prefer even number or numbers ending in digit 0 and 5), we used inversed calipers instead of ruler to reduce this bias. All size of indurations were recorded for further analysis other than arbiturary classification.

**Exclusion and Follow-up steps** Clinically, children who had induration size ≧10 mm were invited to be followed up in our clinics according to previous consensus (12) If LTBI is highly suspected, prophylaxis will be initiated. Closed contact families and care-givers were planned to be required detailed information of TB contact history and asked to take CXR for excluding asymptomatic pulmonary TB.

**Statistics**

Data were analyzed with the SAS Statistical Package (Version 9.1, SAS Institute, Cary, North Carolina). We used Chi-aquare test for categorical data. Significant differences between groups were determined by the Student's *t* test for comparison of means, and the Chi-square or Fisher exact test for comparison of proportions. Analyses were performed with the use of SPSS (Statistical Package for the Social Sciences) for Windows, version 14.0. Moving average was used to smooth the shape for small number of positive cases in each group. Chi-square with goodness of fit was used to check the different cutoff points for positivity. $P<.05$ was considered statistically significant.

## Results

A total of 1467 questionnaires were collected from baby clinics and schools. The children eligible for performing PPD test were 637 with informed consent available and information enough to identify the children. One had no birthday information and 6 were elder than 15 year-old. The final of 630 data were analyzed.

### Demographic data

The male female ratio was 312:318 (p=0.811), and age distribution (0.18 ~14.98 year-old) was summarized in table 1 (the proportion of elder-age children was more than younger age children, p< 0.0001). 55 children (8.73% of 630) had at least one family who had a job related to medical care. 28 children (4.47% of 626) got one family who had a foreign nationality. 48 children (8.61% of 588) had ever had a babysitter who had foreign nationality. All of them had BCG vaccination in early infancy but 3.79% of them initially ticked the box "can not remember'. Those who could propose the evidence of BCG booster at second grade of elementary school were excluded from our study but most of the parents did not preserve the paper-sheet. After excluding the children with contact of active TB cases, still 40 children (6.37%) had a family history of old TB more than 10 years lag from now on, and nine children (1.43%) had a family who had cough with unclear cause but TB was never diagnosed in our study period (though we encouraged them to receive differential diagnosis of asthma, smoking related or chronic obstructive pulmonary disease, etc.).

The size of PPD was compared between 48 and 74 hour-measurement and the bigger one was chosen to be analyzed. The range of

PPD was between 0~23mm. Of total, 40.79% had zero induration. 46.35%, 31.43%, 18.25%, and 3.97% of them had PPD size between 0~4 mm, 5~9mm, 10~14 mm, greater than 15mm. No significant difference was observed among these four categories of PPD size with family history of old TB more than 10 years or cough without clear cause (p= 0.3117), similar with family worked related to medical care(p=0.8546), and family with foreign nationality (p=0.9855). 45.83% of children who had ever had a babysitter with foreign nationality had a PPD size between 5~10mm compared with 30.19% of children without. The trend inversed when we compared PPD size among 10~14mm, larger than 15mm (ever had a foreign babysitter: 10.42%, 0% vs. without: 18.70%, 4.44%) and the difference was not significant (Mantel-Haenzel Chi-square, p=0.2801).

When we group with PPD size with 0~4 mm, 5~9mm, 10~14 mm, greater than 15mm, there was a significant difference noted of positivity of PPD in different age groups (5~10, 11~15 year-old, p=0.0021). The difference was even more significant if we further divided age group in 0~2, 3~5, 6~9, 10~12, 13~15 year-old (Mantel-Haenzel Chi-square, p=0.0015). The distribution of positvity of PPD in our study population was bi-modal. Since the infection rate could be increased as age increased, the distributions of recorded indurations size of PPD test (shown in figure 1) were given with age grouping by 5(Fig.2) years and 3 years (Fig.3) each. We noted that the percentage of zero reaction was highest (49%) in age group 5~9 year-old and followed by 41% in 0~4 year-old, 36% in 11~14 year-old. The area under curve with 16mm induration was 99%, 98%,96% as in 0~4, 5~9, 10~14 year-old. The second peak of bi-modal

distribution were all located at 6~7 mm induration among the three age groups. In fig.3, we further divided the age group into 5 groups (0~2, 3~5, 6~9, 10~12, 13~15 year-old) and percentage of zero reaction was highest (53%) in age group 6~9 year-old and followed by 50% in 3~5 year-old, 43% in 9~12 year-old, 34% in 12~14 year-old, and 16%in 0~4 year-old. Two small peaks with a dominant peak were noted in graph for 0~4 year-old. The biggest one was still noted at 6~7 year-old, The trend is somewhat clear that, if BCG had an effect on PPD size, the third was peaked at 14 mm. Bimodal distribution though noted in age group 3~6 year-old, but the second one was a hybrid twin peak with a widening base (6~11mm). Basically the graphs of the other 3 age groups were bi-modal distributed with gradual increasing widening base as age increased. The area under curve with 16mm induration was 96%, 98%,100%, 98%, and 96% as in 0~2, 3~5, 6~9, 10~12, 13~15 year-old. The area under curve with 17 mm induration was still 96% in 0-2 year-old and reached 100% with 18mm. Similar picture was observed in age group 3~5 year-old.

If we checked the accumulative distribution of PPD induration sizes as in Fig4, we could find that if we used the same cut-off value for different age groups, false judgment would be possible especially in age group 0~2 year-old, and the bias could be reduced if the cut-off value was approaching or above 17~18mm.

The fraction of PPD reaction by age group using different induration sizes as cut-off points were shown in Fig5. After age of 5~7 year-old, the trend of the curves in line of every cut-off values were all increased with age as our knowledge of tuberculosis infection possibility. Only solid curve (18mm as cut-off) fit the possibility of 0~5 year-old age group.

Noted that the curves of 5mm and 10 mm, 15mm and 18mm as cut-off point were merged separately into the same one because of the same percentage with both of these two pairs of cutoff points after 7 year-old. To figure out the possibly- fit - curve for other age groups, we used the estimated ARTI data of grade 1 children in Taiwan (2002~2004) (Fig6, Left). School children did not received 2TU PPD RT23 as PPD test until 2002 screen (1TU was used before this). Since it was hard to collect the data of PPD size from non-BCG vaccinated children (96~98% BCG coverage national-wide), the data of children without scar or tiny scar was used to estimate the annual risk of TB infection. The solid line with full dot in the left graph of Fig5 was upper 95% CI of estimated positivity from estimated ARTI. The dashed line was lower 95% CI. To compare with the right figure of Fig6. , the curve of 12mm cut-off value was seemed to be fit best with the range estimated on left contrast to cut by 10mm or 15mm. The fitness was checked by Chi-square goodness of fit. It seemed that 11~15mm were all passed the exam with proper p value compared to < 11mm. However, 11 and 12mm had the largest sum of square which fit the estimated curve by ARTI best.

## Conclusion and Discussion

國際間以皮膚結核菌素測驗為探討的研究很多， 本研究主要是探討在高接種卡介苗區域, 結核菌素測試的分布情形, 受卡介苗影響的程度有多大. 依照父母親提供的資訊, 於問卷上表示孩童未接觸過開放性結核病病患, 家中亦無此病史之家人, 收案為低危險群兒童. 當中自然會可能有不知情的暴露, 但這都與其他正常兒童類似, 故此偏差並不影響一般兒童之皮膚結核菌素測驗大小的分布. 本研究最大的缺點在於幼童之收案困難, 在小於四歲的世代部份, 幾乎無法以一歲作為年齡層去做有意義的分析比較, 實為可惜. 來日若還有研究資源, 四歲以下的兒童增加收案到每一年齡層至少 20 名個案, 會讓本研究更臻完整. 在臨床上認為, 家中有醫護人員, 孩子被外籍保母照顧過, 或從東南亞來台灣的外籍母親, 可能會增加此一年齡層孩子的結核病感染率, 但由我們這個研究看來, 到目前為止, 這個現象並不顯著, 也未有此趨勢.

學童的父母記不清楚學童是否追加過卡介苗, 是本研究另一個偏差. 由於此次追加已不記錄在疫苗黃卡上,故除非能得到該學童小學二年級之學籍資料,再前往台北市立聯合醫院之社區傳染病院區做查核, 根本無法確認是否為 recall bias. 回溯台灣接種卡介苗的歷史, 自民國 86 年起, 除無疤或小疤兒童一年級學童經結核菌素測試陰性,

已不在進行追加.故絕大多數本研究的學童接受到第二次卡介苗接種之機會應該偏低.所以此一偏差應不至於造成推論的困難.

結核菌素測試之大小分布圖顯示, 剛接受完卡介苗的五年內, 卡介苗對結核菌素測試大小的影響力慢慢下降, 過了五到七歲, 將陽性率分別用不同 cut off value 去比較, 發現是與 ARTI curve 相當類似的. 故過了七歲以後, 若未 再追加卡介苗, 在台灣這種結核病中高盛行率的國家, 自然感染逐漸扮演腳色. 隨著年紀增加, 5~15% 的 12 歲以上兒童可能被自然感染結核而以 LTBI 來潛伏. 對於七歲以上的兒童來說, 11~12 mm 是最符合 ARTI 曲線的自然感染趨勢. 但對於 0~6 歲的幼童來說, cut-off value 無法使用與 ARTI 曲線 approximate 來取得,故由分布區線下面積對照我們認知之幼年(0~3 歲)兒童之結核病感染率(出生後約每年 1%的感染率), 則 cut-off value 設在 17~18 mm 是合理的.

## 結論與建議

本研究只針對健康沒有接觸史的孩童進行結核菌素測試， 如想求得臨床診斷結核病感染較好的 CUT-OFF VALUE, 最好要有另一組具有家庭內開放性肺結核接觸史的孩童的結核菌素測試分佈, 才比較容易找到實用且敏感度, 特異度皆滿意的檢查異常值. 但因為開放性結核之病患之接觸兒童數量不多, 要 ENROLL 更顯困難, 可能無法以 PROSPECTIVE STUDY 來執行, 也許可以利用 CHART REVIEW 的方式來收集, 但此間施打的護士不同, 判讀的人力不同, 臨床已經懷疑是結核病也會有偏差, 這些都是很重要的偏差. 倘使今天我們想求得臨床上診斷活動性結核病的依據, 那就必須去尋找已經證實為結核病的病童來回朔其結核菌素測試之大小,除了上述的偏差外, 往往只記載 48 或 72 小時的大小, 也是一個偏差. 若能克服上述收案困難, 則結果可提供更多臨床應用的參考.

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Table 1. Age distribution in the study

| Age group | 0-1 | 1-2 | 2-3 | 3-4 | 4-5 | 5-6 | 6-7 | 7-8 | 8-9 | 9-10 | 10-11 | 11-12 | 12-13 | 13-14 | 14-15 | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Case Number | 12 | 7 | 6 | 9 | 34 | 41 | 50 | 36 | 45 | 50 | 19 | 22 | 99 | 114 | 86 | 630 |
| Percentage (%) | 1.9 | 1.11 | 0.95 | 1.43 | 5.4 | 6.35 | 8.10 | 5.71 | 7.14 | 7.94 | 3.02 | 3.49 | 15.56 | 18.25 | 13.65 | 100% |

Fig 1. Distribution of PPD sizes (histogram) among 0~15 year-old children.

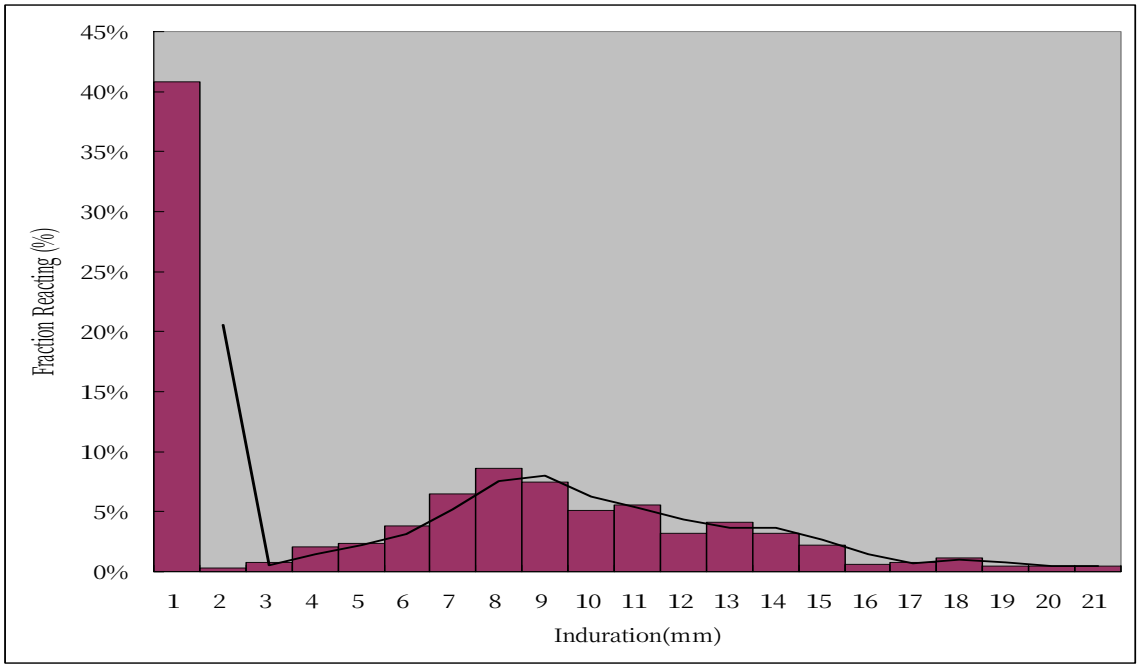

Fig 2. Distribution of PPD sizes (polygram) among 0~15 year-old children (group by 5 year-old).

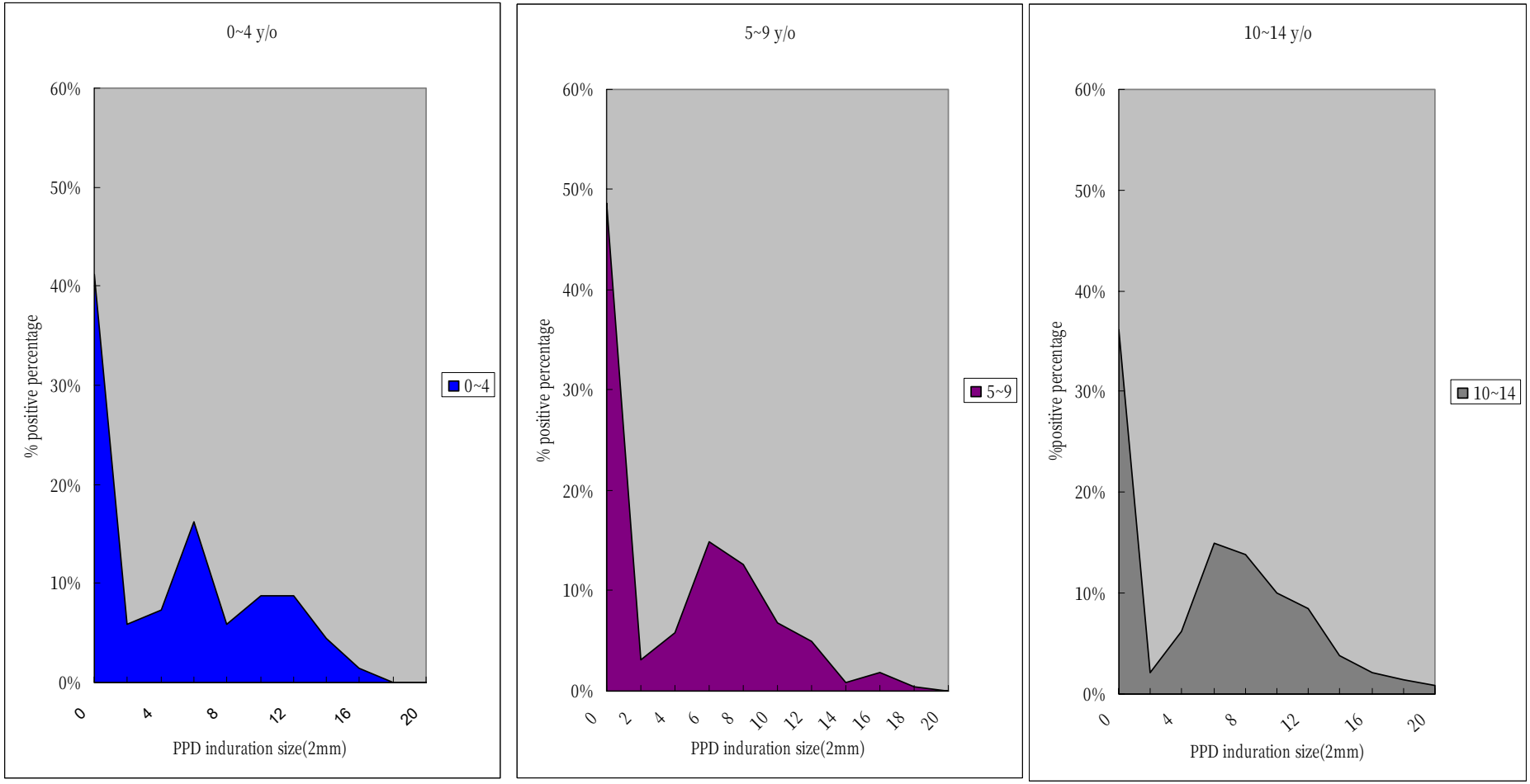

Fig 3. Distribution of PPD sizes (polygram) among 0~15 year-old children (group by 3 year-old).

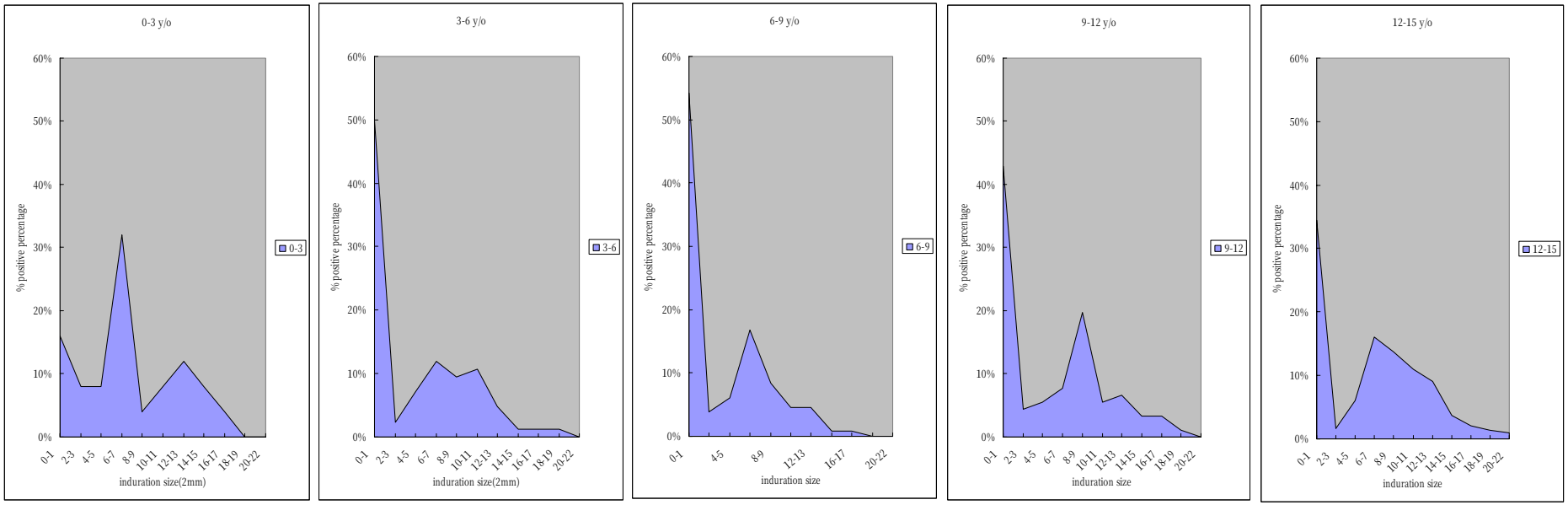

Fig4. The accumulation proportion of PPD induration sizes among different age groups.

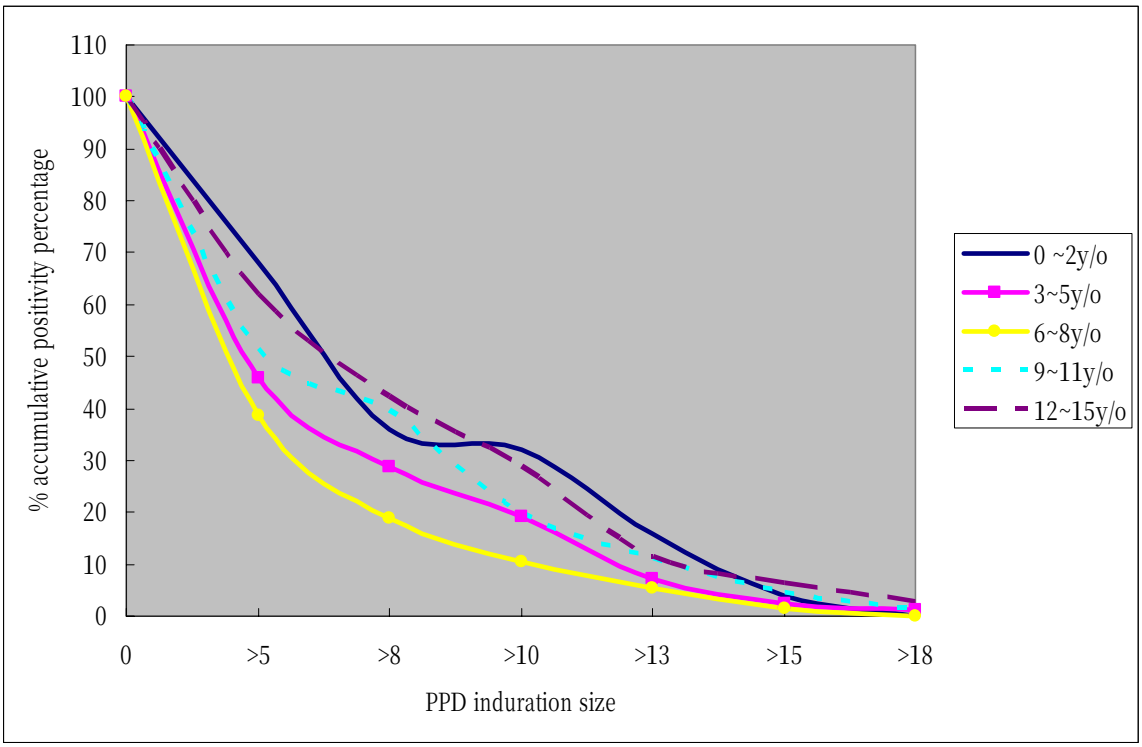

Fig5. PPD reaction by age group using induration sizes of 5mm, 10mm, 12mm, 15mm and 18mm as cut-off points. Noted that the curves of 5mm and 10 mm, 15mm and 18mm were merged separately into the same one because of the same percentage with both of these two pairs of cutoff points after 7 year-old.

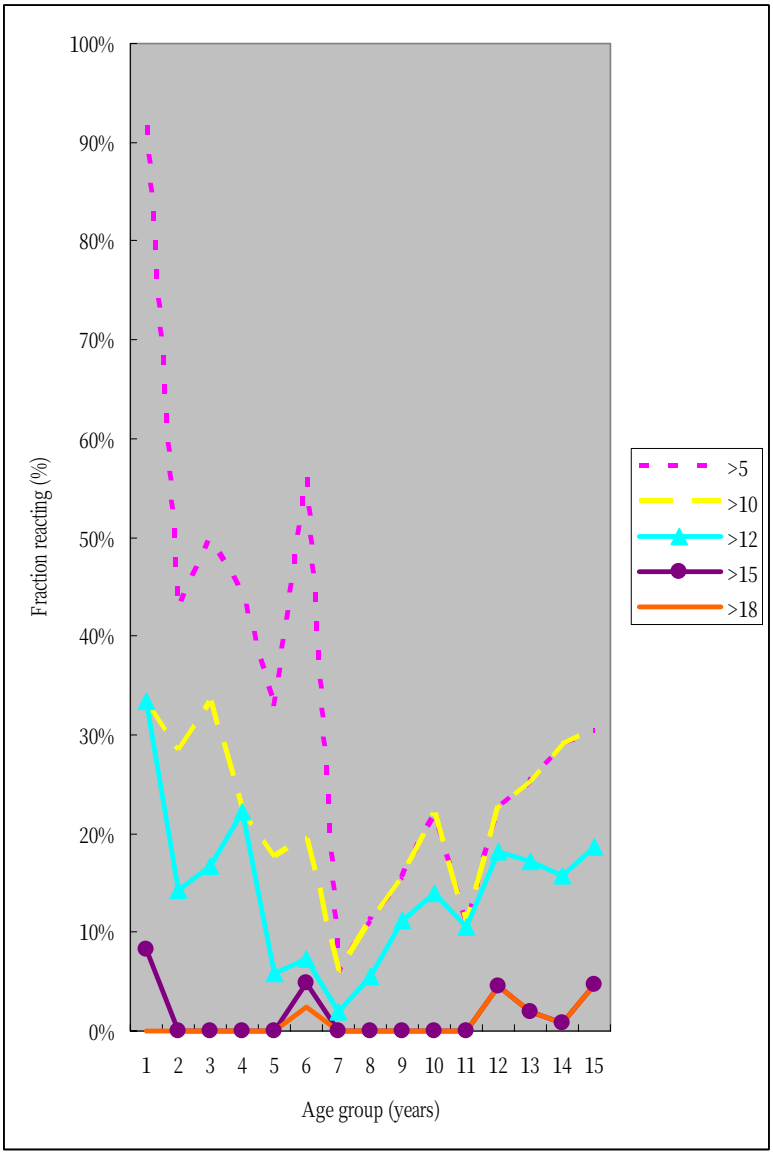

Fig 6. The PPD reaction by age group usin ginduration of 10 mm, 12 mm and 15mm as cut-off points vs. the expected risk of natural tuberculosis infection estimated from historical data on the annual risk of TB infection. With the moving average curve (cycle:3), 12mm seemed to be the curve fits ARTI best.

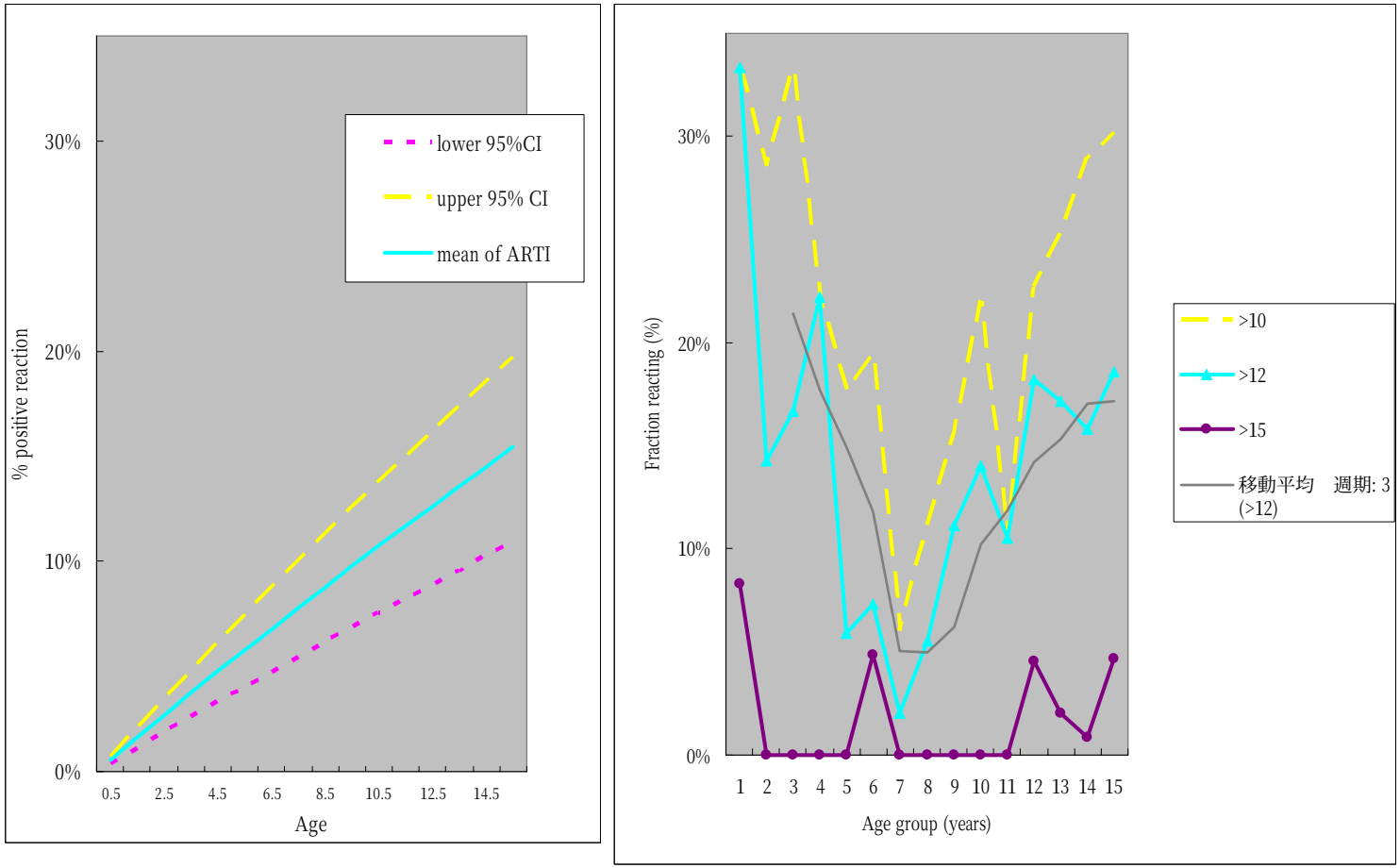

Table2. The Chi-square goodness of fit test & p value between ARTI (95%CI) and different cutoff values.

| | 10mm | | 11mm | | 12 mm | | 13mm | | 14mm | | 15mm | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | lower95% | upper95% | lowe95% | upper95% | lower95% | upper 95% | lowe95% | upper95% | lowe95% | upper95% | lower95% | upper 95% |
| Chi-square | 23.06 | 2.27 | 5.69 | 0.92 | 5.69 | 0.92 | 4.42 | 4.44 | 11.55 | 5.32 | 6.92 | 7.72 |
| p value | 0.0032881 | 0.971595344 | 0.68191 | 0.998705 | 0.681911 | 0.998705 | 0.817382 | 0.815405 | 0.172439 | 0.72289 | 0.545288 | 0.461288 |

Table3. The sum of squares for the goodness of fit test between ARTI (95%CI) and different cutoff values.

| Cutoff value | 10mm | 11mm | 12mm | 13mm | 14mm | 15mm |
|---|---|---|---|---|---|---|
| Sum of square | 32.04 | 7.99 | 7.99 | 12.91 | 20.5 | 22.06 |