A PRELIMINARY STUDY ON THE OUTCOME OF CHILDREN SUSPECTED TO HAVE PULMONARY TUBERCULOSIS: THE PHILIPPINE CHILDREN'S MEDICAL CENTER EXPERIENCE*

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Abstract:

Objective: To determine the outcome of children suspected to have pulmonary tuberculosis presenting with signs and symptoms alone or in combination with an abnormal chest radiograph.

Setting: Philippine Children's Medical Center -TB Registry

Design: Retrospective Descriptive Study

Patients And Methods: A total of 82 children with no history of exposure, and with unreactive PPD on the initial consult were studied. Fifty four children (66%) suspected to have TB disease were symptomatic while 28 (34%) were both symptomatic with abnormal chest radiograph. Periodic follow up was done for a minimum of six months.

Results: Of the 54 symptomatics, 28 (52%) had resolution of symptoms; and 26 (48%) developed TB disease as determined by the National Consensus on Childhood Tuberculosis. Of the 28 children with symptoms and abnormal chest x-ray, 16 (57%), had resulction of symptoms; and 12 (43%) developed TB disease. Hence, of the 82 children who followed-up, 44 children (54%) became asymptomatic while 38 (46%) developed the disease. Cough, fever and poor apetite were the most common presenting manifestations. Those with prolonged cough and lymphadenopathy later developed the disease (100%). No disease progression was noted among patients with poor apetite. As early as the first three months from the initial consult, PPD became reactive (53%) and chest radiograph became abnormal (46%).

Summary: Almost half of the children followed-up eventually developed TB disease as determined by the three out of five criteria by the National Consensus on Childhood Tuberculosis.

INTRODUCTION

According to the World Health Organization, the Philippines is one of the 22 countries in the world which accounts for 80% of the world's TB cases. Routine reporting systems consistently placed tuberculosis among the top 5 causes of morbidity and mortality in

the country. In the Western Pacific Region, the Philippines ranked no. 2 with TB Case notification Rate of 272 per 100,000 population and worldwide, ranked number 4. Nearly 170,000 children die of TB every year. WHO estimates that in 1995, of all children less than 15 years of age, at least 180 million were infected with TB.²

The National Consensus on Childhood Tuberculosis recommended that a child should have at least three out of five criteria in order to satisfy a diagnosis of TB disease. Less than this may cause over diagnosis, while four or more criteria may under diagnosis TB. This study was done to evaluate the outcome of patients suspected but not meeting the three out of five criteria required in diagnosing childhood pulmonary tuberculosis.

The three out of five criteria was an arbitrary decision by the Committee of the National Consensus on Childhood Tuberculosis. Until the present time, there seemed to be no published data regarding the outcome of one or two out of five criteria in the development of the disease.

A local study by Balao-Litam, and Agrasada¹ of UP-PGH on the diagnosis of tuberculosis in children revealed that the more common clinical findings used are history of contact with an adult pulmonary TB case (43%), chronic cough (35.3%), lymphadenopathy (67%) and malnutrition 39%), chest radiograph (31.3%) Radiography and AFB Smear were the commonly requested laboratory examinations. However, these laboratory examinations carried a percentage weight of 10-25% in making a diagnosis; the specialist and pediatric groups relied on laboratory findings 20-25% while the family medicine and DOH-affiliated phycisans gave laboratory examination a 10% weight in arriving at a diagnosis.

OBJECTIVES

This study aims to determine the outcome of children suspected to have pulmonary tuberculosis presenting with signs and symptoms alone or in combination with an abnormal chest radiograph suggestive of tuberculosis.

Keywords. TB suspect, pulmonacy inhereulosis

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Specifically the objectives are:

- To describe the demographic data of children suspected to have pulmonary tuberculosis
- To identify the most common presenting signs and symptoms of children suspected to have pulmonary tuberculosis
- To determine the most common radiographic findings in children suspected to have pulmonary tuberculosis.
- To determine the timing of PPD conversion from unreactive to reactive from the time of the initial consult to subsequent follow-up
- To determine the timing of chest radiograph conversion from normal to abnormal from the time of the initial consult to subsequent followup

Study Population

All 1213 medical charts of patients suspected to have pulmonary tuberculosis, and seen at the Out Patient Department of the Philippine Children's Medical Center - TB Registry from January to December 1999 were reviewed. A total of 82 children were included in the study base on the following criteria.

Inclusion Criteria:

- No exposure by history to an adult or adolescent with active TB from the time of consult until the next six months of follow-up.
- B. One or more signs and symptoms suggestive of TB such as:
 - Unexplained cough/wheezing of at least 2 weeks duration
 - Unexplained fever of at least 2 weeks duration
 - Unexplained painless cervical and/or other lympadenophathy
 - Unexplained poor weight gain, or weight loss
 - Unexplained poor appetite
 - Failure to make a quick return to normal health after an infection such us measles, tonsillitis, whooping cough.
 - Failure to respond to appropriate antibiotic therapy-pneumonia, otitis media
- C. Unreactive PPD 5 'TU'/Mantoux test on the initial consult
- Chest radiograph which may or may not be normal on the initial consult

Exclusion Criteria:

- A. Chest x-ray and/or PPD not done on the initial consult
- B. Live vaccine (Measles, mumps, polio, chicken pox, typhoid, pertussis) given in the last four weeks prior to PPD testing
- C. Patient had viral infection within the last four weeks prior to PPD testing
- Patients received previous treatment for tuberculosis infection
- E. Nutritional status below the fifth percentile of the growth curve.

METHODOLOGY

A total of 82 patients were included in the study and the following data were gathered: sex. age, nutritional status, history of BCG vaccination, initial signs and symptoms, presence or absence of abnormal chest radiograph on the initial consult.

Patients were subdivided into twelve small groups depending on their presenting manifestation/s on the first OPD consult. Patients were further classified as with signs and symptoms alone (Group A), and with associated abnormal chest radiograph suggestive of tuberculosis (Group B).

Periodic follow up was done to evaluate patients' symptomatology. Patients were further classified as those who became asymptomatic and those who had progression or persistence of symptoms. Patients belonging to the latter group had repeat PPD and chest x-ray. They were reclassified as TB disease once they met the three out of five criteria set by National Consensus of Childhood Tuberculosis. For our pupose, these criteria include presence of signs & symptoms and chest radiogrph suggestive of tuberculosis, and reactive PPD.

There were several residents who saw these children depending on who were rotating at the Out Patient Department during the patient's initial consult. However, each patient was followed-up by only one pediatric resident at the OPD in their Continuity Clinic.

Definition of Terms

 Pulmonary tuberculosis (TB) disease: a child with active TB had 3 or more of the following five criteria: exposure to an adult or adolescent with active TB disease, signs and symptoms suggestive of TB, positive PPD/Mantoux test, abnormal chest radiograph suggestive of TB, and laboratory findings suggestive of TB (histological, cytological, biochemical, immunological and/or molecular).

- Positive PPD or Mantoux test using 5 'TU': for children below 5 years of age, more than 5mm induration as the cut-off in a non-BCG vaccinated and more than 10 mm induration as positive for BCG-vaccinated; while for children 5 years or more, whether BCG-vaccinated or not, more than 5 mm is positive.
- Abnormal chest x-ray: Radiographic features were as follows: hilar adenopathy with or without primary focus, pleural effusion, cavitary lesions, coin shadow (tuberculoma) collapse consolidation and obstructive hyperaeration or miliary pattern.

Data Analysis

This study used descriptive analysis, enumeration of data and use of percentages.

RESULTS

Out of the 82 children included in the study, 45 were females (55%) while 37 were males (45%), with slight female preponderance. Figure 1 shows the distribution of the patients according to sex.

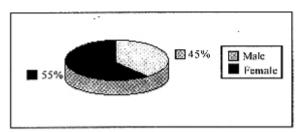


Fig. 1 Percent of cases of children suspected to have tuberculosis according to sex at PCMC. OPD from January to December 1999

The patients' age ranged from 1 to 17 years old. Majority belong to the less than 5 years, 63%; 5 to 9 years, 27%; 10 to 14 years, 6%; and 15 or more years 4%. Figure 2 shows the age distribution of patients.

Nutritional status was assessed to make sure that

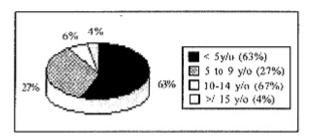


Fig. 2 Percent of cases of children suspected to have tuberculosis according to age at PCMC. OPD from January to December 1999

no patient would fall below the fifth percentile of the growth curve. This study shows that majority of the children fell under the 25th percentile with 24 cases (at 29%), p50 with 18 cases (at 22%), and p75, p90, p5 with 9 cases each (11%), p95 with 7 cases (9%), and p10 with 6 cases (7%) as seen in Figure 3.

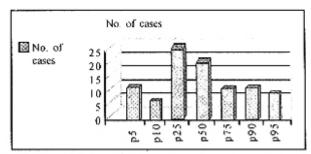


Fig. 3 Nutritional status of children suspected to have tuberculosis at PCMC, OPD from January to December 1999

Immunization history was reviewed and the BCG vaccination status evaluated. The result showed that 96% of patients received BCG while 4% did not, as seen in Figure 4.

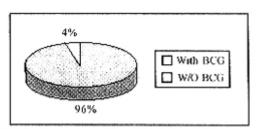


Fig. 4 Frequency of BCG vaccination among children suspected to have tuberculosis at PCMC. OPD from January to December 1999

All patients were symptomatic at consultation. The signs and symptoms noted were prolonged cough 83%; prolonged fever 48%; unexplained poor appetite 32%; weight loss or poor weight gain 22%; and painless palpable lymphadenopathy 12%; as shown in figure 5.

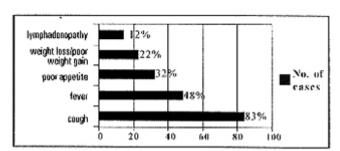


Fig. 5 Presenting signs & symptoms of children suspected to have tuberculosis according to age at PCMC. OPD from January to December 1999

The findings of all chest radiographs with consideration of pulmonary tuberculosis were reviewed. Fullness of both hilar regions suggestive of nodal enlargement was noted at 99%, while 1% had a finding of mild pleural reaction, subpulmonic effusion as shown in figure 6.

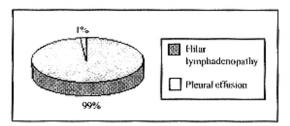


Fig. 6 Percentage of chest radiographic findings seen in children suspected to have tuberculosis at PCMC OPD from January to December 1999

Figure 7 shows the chest x-ray changes among patients including twenty-six patients with initially normal chest x-ray findings who were noted to have abnormal films on subsequent follow-up. The timing of conversion was noted to occur as early as the first three months in 12 out of 26 (46%), to as late as 13-15 months in 4 out of 26 (15%) after the initial consult.

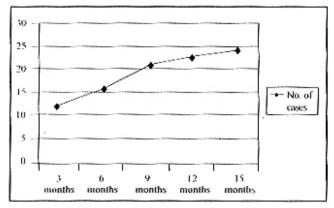


Fig. 7 Number of cases of children initially with normal chest radiographic findings that became abnormal over time, at PCMC OPD from January to December 1999

Thirty-eight children who were initially PPD negative became PPD positive on subsequent follow-ups. When the timing of conversion was reviewed, 24 out of 38 (63%) of children became PPD positive on the first three months after the initial consult, 5 out of 38 (13%) at 4 to 6 months, 4 out of 38 (11%) at 10-12 & 13-15 months, and 1 out of 38 (3%) at 7 to 9 months. Figure 8 show the following findings.

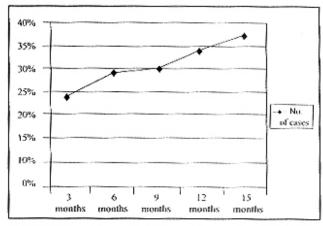


Fig. 8 Number of cases of children with unreactive PPD initially that became reactive over time, at PCMC, OPD from January to December 1999

The children were subdivided into twelve small groups depending on the presenting manifestation/s during the first OPD consult. Each of these groups was further subdivided into two depending on the result of the chest x-ray. These patients were followed up periodically, monitoring their clinical course, (whether they will improve without treatment, or symptoms will persist or progress necessitating further work-up and subsequent use of therapeutic agents).

Table 1 shows the different combinations of signs and symptoms that prompted parents to seek OPD consult. The data showed cough with low grade fever 22% (with normal chest x-ray) 10% (with abnormal chest x-ray); and cough alone 15% (with normal chest x-ray) and 6% (with abnormal chest x-ray) as the most common presenting manifestations.

The table also revealed that the combination of lymphadenopathy with cough or fever, and combination of cough, poor appetite and weight loss showed tuberculous disease in 100% of cases.

Poor appetite alone did not show development of the disease as shown in Table 1, with 100% of cases becoming asymptomatic.

Of the 82 patients studied, 66% presented with signs and symptoms alone (Group A), while 34% of children also had abnormal chest radiographs (Group B) during the initial consultation. These patients had negative PPD and had no history of exposure to adults or adolescents with active tuberculosis. On subsequent follow-ups, 52% in Group A, and 57% of Group B became asymptomatic. on the other hand, 48% in Group A and 43% Group B, developed the disease.

In summary, the outcome of the 82 children studied were as follows: 54% became asymptomatic,

and 46% developed TB disease. (As seen in Table II).

Table 1. Outcome of Children with Signs and Symptoms, with or without Abnormal Chest Radiographs Suggestive of Tuberculosis at Philippine Children's Medical Center, OPD Jan-Dec. 1999

Manifestation	Chest x-ray	Became asymptomatic	Developed the disease	Total
Cough	Normal	6	6	12(15%)
	Abnormal	3	2	5(6%)
Cough/fever	Normal	10	8	18(22%)
	Abnormal	6	2	8(10%)
Cough/wt loss	Normal	4	2	6(7%)
	Abnormal	0	0	0
Cough/poor appetite/fever	Normal	1	0	1(1%)
	Abnormal	2	[3(4%)
Cough/poor appetite/ fever/wt loss	Normal	0	0	0
	Abnormal	3	l	4(5%)
Cough/fever/wt loss	Normal	0	3	3(4%)
	Abnormal	0	0	0
Cough/poor appetite	Normal	3	0	3(4%)
	Abnormal	l.	2	3(4%)
Cough/poor appetite/ wt loss	Normal	0	1	1(1%)
	Abnormal	0	2	2(2%)
Poor appetite	Normal	3	0	3(4%)
	Abnormal)	0	1(1%)
ymphadenopathy-LN	Normal]]	2(2%)
	Abnormal	0]	1(1%)
LN/cough	Normal	0	4	4(5%)
	Abnormal	0	1	1(1%)
LN/fever	Normal	0	1	1(1%)
	Abnormal	0	0	0

Table 2. Summary of Outcome of Children Suspected to Have Pulmonary Tuberculosis with Signs & Symptoms, and Chest x-ray Findings at PCMC, OPD Jan-Dec. 1999.

	Outcome			
	Became Asymptomatic	Developed the disease	Total	
A. Signs and symptoms	28 (52%)	26 (48%)	54(66%)	
B. Signs and symptoms with abnormal chest radiograph	16 (57%)	12 (43%)	28 (34%)	
Total	44 (54%)	38 (46%)	82 (100%)	

DISCUSSION

A total of 82 patients were included in the study. There was a slight female preponderance (Figure 1). The majority of children suspected of having tuberculosis was noted to be under 5 years of age at 63%, followed by 5 to 9 years of age at 27%, 10-14 years of age at 6% and lastly by more than 15 years old at 4% (Figure 2). This was consistent with the update of Inselman, which stated that since 1985, the increase in tuberculosis among children had been mainly in those under 9 years of age, and the largest increases (36-40%) has occurred in children less than 5 years and between 10 and 14 years old age.

Malnutrition can diminish the degree of PPD induration. By excluding children below the fifth percentile of the growth curve, the possibility of having false negative Mantoux test was prevented. Majority of patients were in the 25th percentile with 24 out of 82 cases (29%).

Since TB in children is usually noninfectious, giving the BCG vaccine to children does not prevent the spread of tuberculosis. This is the reason why in this study even though 96% of the children received BCG vaccination at birth; they still develoed TB disease. The efficacy of the vaccine to prevent tuberculosis ranges from 10% to 80%, with only 38-75% protection against pulmonary tuberculosis. Its efficacy in the prevention of tuberculosis lies in its ability to stimulate local tubercle formation at an accelerated pace so that disease would not occur. It may be effective against the development of miliary tuberculosis and tuberculous meningitis in children. However, it does not prevent the acquisition of tuberculous infection.

The National Prevalence Survey on Tuberculosis in 1997 showed that the proportion of patient with a BCG scar was 66% and among these without BCG scars, the prevalence of tuberculous infection was 63.4%⁵

True tuberculin reactivity usually appears 3 to 6 weeks after infection but may take as long as 3 months to develop. Since approximately 10% of children with culture-proven tuberculosis is Mantoux test negative, a negative Mantoux test never rules out the diagnosis. Host factors such as immune deficiency (including HIV infection), malnutrition, young age, coexisting viral infections (varicella, measles and influenza) and overwhelming

tuberculous disease, all diminish the degree of induration. Locally, sesitivity of Mantoux test ranged from 19 to 41% and a specificity of 77-100%. This study revealed that 38 out of 82 (46%) children who were previously PPD negative became positive. Sixty-two per cent of conversion cases occurred after the first three months of the initial consult. However, the frequency of conversion after this time becomes variable as noted in Figure 8. Another reason for conversion of the Mantoux test is the boosting phenomenon that is presumably caused by stimulation of a waned immunologic response to M. tuberculosis or to cross-reactions with nontuberculous mycobacteria or Mycobacterium bovis used to manufacture BCG. The boosting represents an increase in the reaction to a skin test in a person already sensitized to mycobacterial antigens caused by repetitive tests. The incidence of the booster phenomenon increases with age in geographic areas where exposure to nontuberculous mycobacteria is common, and in children previously vaccinated with BCG. In this study, 96% of the subjects received BCG. The booster phenomenon can be seen on a second test dose as soon as a week after testing study in the same it showed that PPD conversion occurred up to 15 months after the initial PPD testing. However, booster phenomenon was ruled out since all patients previously treated with anti-tuberculous medications were excluded from the study. It is therefore presumed that PPD conversion in this study is due to a new infection.

Among immunocompetent hosts, radiologic features include hilar adenopathy in up to 29% of cases with or without parenchymal focus'. Less common features arise from complications due to hilar adenopathy or progressive primary focus; pleural effusion, cavitary lesion, coin lesion (tuberculoma), collapse consolidation and obstructive hyperaeration. A third manifestation is a miliary pattern. Chest radiographs may be normal, however, in up to 10% of patients who have proven primary tuberculosis.8 The diagnosis of primary TB on the basis of isolation of M. tuberculosis, with x-ray findings of hilar lymphadenopathy showed a sensitivity and specificity of 83 and 36% respectively. In this study. the most common chest radiographic finding was hilar lymphadenopathy at 99%, with one case developing pleural effusion (1%). The timing of

conversion from a normal to an abnormal radiograph was noted to be 46% occurring on the first three months after the initial consult (Figure 7).

A chronic cough, significant weight loss, sweats and chills, fatigue and body malaise, and fever are found in over half of patients. These clinical signs should raise the possibility of TB. Of the 82 symptomatic children included, cough occurred most frequently at 83%, followed by fever 48%, poor appetite 32%, weight loss or poor weight gain 22%, and lymphadenopathy at 12% (Figure 5). Two clinical studies were done to determine if a specific clinical sign and symptom could discriminate for a disease. PTB was diagnosed by smear and/or culture in the study by Cohen.9 Diagnosis was through culture in the study of Samd.12 There were no significant differences in the occurrence of anorexia, weight loss, fever and dyspinca between patients with TB and those with non-TB respiratory disease. In both studies, a chronic cough occurred with significantly greater frequency in PTB patients.

The combination of cough and fever occurred most frequently at 32%, (22% with normal CXR, and 10% with abnormal CXR), followed by cough alone at 21%, (15% with normal CXR, and 6% with abnormal CXR), and cough with weight loss at 7%. However, when these patients were followed-up, only about 50% developed TB disease.

When the signs and symptoms were analyzed based on which ones will develop TB disease, it revealed that lymphadenopathy alone or in combination with cough or fever developed TB disease in 100% of cases. Combination of cough, fever and weight loss also showed development of TB disease in 100% of cases. Patients with poor appetite alone or in combination with cough became asymptomatic on follow-up. Poor appetite, in combination with cough and weight loss, showed development of the disease in 100% of cases.

Limitation of the Study

The study design was retrospective hence certain variables pertinent in the study were not adequately controlled. These variables include the following:

 a) the number of examiners who followed up the patients;

- the time when PPD or CXR should have been repeated (from the time of initial presentation of signs and symptoms and not from the time of initial OPD consult);
- c) TB exposure screening of all family members with chest radiograph, and sputum examination or PPD, and not merely by history taking. There was only a handful of cases included in each grouping hence results obtained were non-conclusive.

SUMMARY

Based on this study, cough, fever, and poor appetite are the most common presenting manifestations of children suspected to have pulmonary tuberculous disease. However, patients with cough and lymphadenopathy eventually developed TB disease while those with poor appetite did not. PPD became positive and chest radiograph becomes abnormal on the first three months after the initial consult at the OPD. Almost half of the children suspected to have tuberculosis but did not meet the three out of five criteria eventually developed the disease as early as the first three months after the initial consult.

RECOMMENDATIONS

Physicians should always maintain a high index of suspicion in children suspected to have pulmonary tuberculosis who do not meet three out of five criteria since they may eventually develop the disease in forty six percent of the time as noted in this study.

It is also recommended that a similar study be done with a prospective design in order to validate the result of this research.

This study included only children with signs and symptoms, with or without abnormal chest radiographs in patients suspected to have pulmonary tuberculosis. Early diagnosis and treatment of tuberculosis in the sick child can decrease morbidity. Even with widespread pulmonary disease, children may be asymptomatic. Case finding of asymptomatic children is an important component of any tuberculosis elimination strategy, hence, it is recommended that similar study be done, this time using asymptomatic children with history of exposure.

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INFECTIOUS DISEASE MARKERS AMONG DONORS AT PHILIPPINE GENERAL HOSPITAL BLOOD BANK**

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Abstract

Objectives. Preventing transmission of infectious diseases through blood transfusion is one of the greatest challenges of transfusion medicine. This is a cross-sectional study which aims to describe the frequency of infectious disease markers in the blood obtained from commercial blood banks before May 1998 as well as to compare the frequency of infectious disease markers between voluntary and replacement blood donors.

Study Design and Methods. All blood donors presenting at the Philippine General Hospital (PGH) blood bank are routinely screened for hepatitis B surface (IIBs) antigen, hepatitis C virus (HCV) antibody, rapid plasma reagin (RPR) for syphilis, human immunodefeciency virus (HIV) scrology and malaria. Blood donors are classified as replacement (those recruited by the patient, families and friends), volunteer (walk-in donors and mass blood letting) and paid or professional donors coming from commercial blood banks. To determine differences in proportion of infectious disease markers in replacement compared to volunteer donors chi square test was used for HBs and HCV while Fisher exact test was used for RPR, HIV and malaria.

Results. A total of 86,079 blood donors screened from April 1997 to December 1999 were included in the study. Donors from commercial blood banks comprised 67% (26,281) of the total number of blood units (39,215) transfused to PGH patients from April 1997 to May 1998.

Replacement donors (58,933) made up 98.5% while volunteer donors (865) comprise only 1.5% of the total blood donations from April 1997 to December 1999. Prior to the implementation of Republic Act 7719 otherwise known as National Voluntary Blood Services Act (NVBSA) of 1994, the prevalence of having a positive HBs antigen marker was 0.09% and that of having a positive hepatitis C antibody marker was 0.01%. There was no blood unit which was positive for RPR, HIV and malaria after testing. From April 1997 to December 1999, the prevalence of HBs antigen positive was 7.05% and 7.69% in volunteer and replacement donors respectively (p=0.479). The prevalence of HCV positive blood units was higher among volunteer donors compared to replacement donors (0.92%) versus 0.67%) but this was not statistically significant (p=0.375). There was likewise no difference in the prevalence of RPR, HIV and

Conclusion. Blood units from all donors are potential sources of transfusion-transmitted infectious diseases. The low proportion of infectious disease markers in blood from commercial blood bank reflects a selection bias considering that these units had undergone screening prior to being delivered to Philippine General Hospital. There was no significant difference in the frequency of infectious disease markers for hepatits B, Hepatitis C, syphilis, HIV and malaria among volunteer donors compared to replacement blood donors.

OBJECTIVES

A. General

To determine the frequency of infections disease

signments: Mond doners, infectious disease number

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