

フィリピン共和国  
熱帯医学研究所プロジェクト  
巡回指導調査団報告書

昭和60年5月

国際協力事業団  
医療協力部

医 協

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フィリピン共和国  
熱帯医学研究所プロジェクト  
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国際協力事業団

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## はじめに

フィリピン国熱帯医学研究所プロジェクトは、昭和55年（1980年）10月17日署名の討議議事録（Record of Discussions）に基き、主要な熱帯病に対する応用範囲の広い予防対策の開発に資することを目的として5ヶ年の協力期間で実施されている。

討議議事録署名以来、昭和56年6月より専門家の派遣を開始し、同年3月に無償資金協力によって完成した研究所において協力活動を実施してきた。昭和59年10月以降の1ヶ年は技術協力の最終年にあたることから当事業団はこれまでの協力活動につき問題点を整理・検討するとともに、今後の協力方針についても再検討するため、巡回指導調査団を昭和59年11月17日から同26日まで派遣した。

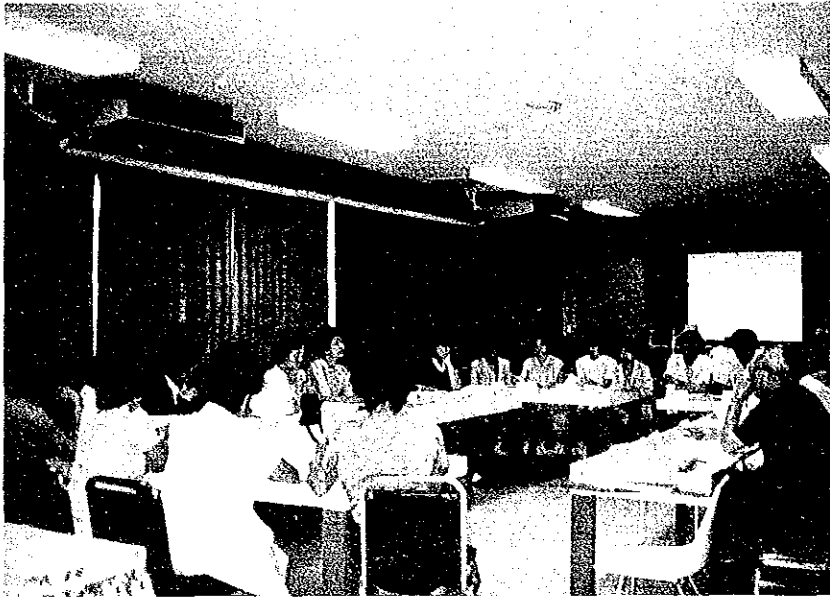
本報告書は同調査団の調査結果を取りまとめたものである。ここに、調査団各位ならびに調査団の派遣にご協力を賜った関係機関の各位に対し、深甚なる感謝の意を表する次第であります。

昭和60年5月

国際協力事業団

理事 末永昌介





RITM シニアスタッフによる  
活動報告と協議



研究室視察



林団長の講演





# 目 次

はじめに

写 真

I	調査団の構成と日程	1
I-1	調査団員	3
I-2	活動日程	3
II	調査の結果	5
II-1	総 括	7
II-2	臨床研究部	7
II-3	微生物部	11
II-4	Summary of Discussions	15
III	専門家研究報告	17
III-1	熱帯医学研究所 金子義徳	19
III-2	B型肝炎の診断試薬の作成とその応用に関する研究 金子義徳	22
III-3	フィリピンにおける小児性下気道感染症の病因に関する研究 山岡邦夫	24
III-4	フィリピンにおける小児急性呼吸器感染症の血清疫学的研究 安慶田英樹, 山岡邦夫	29
III-5	蛍光抗体法 川島豊作	36
III-6	RITM病院統計	38
III-7	フィリピン国衛生統計	46
IV	RITMから提出されたブリーフィング資料	51
IV-1	Introduction	53
IV-2	Objectives	54
IV-3	Functions, Organization and Financial Report	55
IV-4	Departmental Reports	60
(1)	Department of Pathology	60
(2)	Department of Immunology	61
(3)	Department of Epidemiology	62

(4)	Department of Medical Entomology .....	63
(5)	Department of Microbiology .....	64
(6)	Department of Parasitology .....	68
(7)	Medical Department .....	69
(8)	Nursing Department .....	70
(9)	Clinical Research Division .....	71
(10)	Department of Parasitic Diseases .....	80
(11)	Animal Research Laboratory .....	83
(12)	Medical Records Department .....	84
<i>N</i> - 5	<i>Programmes</i> .....	85
(1)	Training Programs in the Medical Service .....	85
(2)	Electron Microscopy Training Program .....	86
(3)	Training Program in Tropical Dermatology .....	87
(4)	Nursing Training Program .....	88
(5)	Personnel Development Program .....	89
(6)	Scientific Photography Training Course .....	90
(7)	The Diarrheal Disease Research Program .....	91
(8)	Acute Respiratory Infection Research Project .....	95
(9)	Project on Vaccine Preventable Diseases .....	97
(10)	Meningitis Among Filipinos .....	98
(11)	Hepatitis .....	99
(12)	Leprosy Research Project .....	101
(13)	Schistosomiasis Project .....	102
(14)	Development of Monoclonal Antibodies against <i>Schistosoma</i> <i>Japonicum</i> and <i>Wuchereria Bancrofti</i> .....	104
(15)	Malaria Research Project .....	105
(16)	Ultrastructural Research Program .....	108
(17)	Comparative Mucos L Studies in Health .....	109
(18)	RITM Census .....	111
<i>N</i> - 6	Training Programs in 1982 .....	116
<i>N</i> - 7	Abstracts of Completed Researches .....	124
A.	Interaction Between Normal Human Monocytes and <i>Schistosomula of Schistosoma Japonicum</i> .....	124
B.	Ultrastructural Studies on Schistosomiasis .....	126

C. Comparative Mucosa Studies in Health and Disease .....	129
D. Comparison of Direct Electron Microscopy, Immune-electron Microscopy, Rotazyme, and WHO--ELISA for Detection of Human Rotavirus .....	130
E. In Vitro Killing of Schistosomula Japonicum by Mononuclear Phagocytes from Normal Humans, Rat and Mouse .....	133
F. A Community-Based Clinical Trail of Albendazole in Leyte, Philippines .....	134
G. Relationship of Prevalence and Intensity of Injection to Morbidity in Schistosomiasis Japonica .....	135
H. A Preliminary Survey of Canine Schistosomiasis Japonica in Macanip, Jaro, Leyte using Serum circumoval Precipitin Test (COPT) .....	136
I. Acute Respiratory Infections in an Urban Community : Risk Factors and Proposed Tentative Solutions .....	137
J. Prospective Study of Diarrhea in Infants and Young Children of a Peri-urban Community .....	138
K. Etiology of Diarrhea in Hospitalized Children .....	139
V プロジェクト実績 .....	143
V-1 プロジェクト投入実績表 .....	145
V-2 供与機材リスト .....	149
V-3 無償資金協力による主な機材リスト(参考) .....	191
VI 機材修理班報告書 .....	239
VI-1 チームの構成と日程 .....	241
VI-2 修理状況チェックリスト .....	243



## I. 調査団の構成と日程



## I - 1 調査団員

総括	林 滋 生	国立予防衛生研究所所長
小児科	合 屋 長 英	福岡市立こども病院感染症センター所長
微生物学	山 口 恵 三	長崎大学医学部附属病院検査部講師
業務調整	北 林 春 美	国際協力事業団医療協力部医療協力課

## I - 2 活動日程

月日	曜日	内 容
11. 19	月	マニラ着 (NW 003便) Manila Peninsula Hotel 投宿
11. 20	火	10:00 JICAマニラ事務所にて岡崎職員と打合せ 10:30 日本大使館 高原一等書記官 表敬 12:00 保健大臣 Dr. Azurin 主催昼食会 金子リーダー、山岡、川島、新垣、上山専門家、高原書記官、 岡崎職員 RITM Dr. Tupasi 所長, Dr. Galon 副所長 同席 15:00 San Lazaro Hospital 病棟視察 Dr. Gonzalez 18:30 御手洗マニラ事務所長主催夕食会
11. 21	水	9:30 林団長講演 Mass Chemotherapy against Parasitic Infections 11:00 専門家と打合 13:20 Senior Staff との Meeting RITM の組織, 財政, 各部の活動報告 19:00 金子リーダー宅 夕食会 日本人専門家, Dr. Tupasi, 高原書記官 出席
11. 22	木	9:00 RITM 視察 9:30 Senior Staff との Meeting 各 Research Programme について

月日	曜日	内 容
11. 22	木	<p>13:25 Coordinating Committee  (出席者)  Dr. Flora Bayan Chief Secretary, MOH  Dr. Pacita Zara PCHRD  Dr. Tupasi Director, RITM  Dr. Galon Assistant Director  Dr. Saniel  Dr. Baccay  高原書記官  岡崎職員</p> <p>16:00 JICA 報告</p> <p>19:00 高原書記官宅 夕食会  金子リーダー, Dr. Romaldez 前所長(現フィリピン大学医学  部長), 大使館 コエズカ 経済協力班長</p>
11. 23	金	<p>9:00 議事録等打合せ</p> <p>10:30 RITM 視察</p> <p>14:30 Ministry of Foreign Affairs. Office of Asian and  Pacific にて  AI フォームの提出状況確認(北林)</p> <p>19:00 林団長主催夕食会  会議要約に署名</p>
11. 24	土	マニラ発 NW004



## Ⅱ 調査の結果



## II - 1 総括

1981年4月に開所した熱帯医学研究所(RITM)は、3年半の間に300人以上の職員を有する研究所に発展し、各種の活動を通じて保健大臣からも高い評価と信任を受けている。

1984年には初代所長のDr. Romaldezがフィリピン大学医学部長に転出し、代ってResearch DivisionのDirectorであったDr. T. Tupasiが新所長に昇格した。Dr. Tupasi自身すぐれた研究者であり、ARI等の研究に従事するとともに研究所の運営にも力をそそいでいる。Dr. Romaldezは、RITMに対する補助機関であるNSTA(科学技術庁)のDirectorも兼ねているため、今後とも引き続きRITMへの支援が期待できる。

RITMの組織自体も、これまでの臨床と研究・訓練の2部門から、Administrative, Research Paramedical, Research & Trainingの3部門に改編されたが、これは研究を主体とするというコンセプトを確立したものと見える。保健省、科学技術庁の他にも各研究者が様々の内外の機関から補助金を得ており、これはRITMの研究実施能力に対する一定の評価のあらわれを考えることができるであろう。

日本の技術協力は、研究を行うための基本的技術の導入を中心に実施されており、電子顕微鏡、ELISA、細胞培養、ジフテリア菌分離など各活動に有効に活用されている。特にウイルス学における進歩はいちじるしくフィリピンにおけるウイルス学のセンター的な役割を果たしている。

残る期間に力を注ぐべきものとしてはプロジェクト基盤整備費によって建築中の動物舎における実験動物飼育、Medical Entomology、ウイルス学におけるB型肝炎血清の精製などが考えられる。フィリピン側は臨床部門の施設、設備の充実を熱心に要請していた。

プロジェクトの延長についてはRITM所長以下スタッフの他、Azurin大臣からも望ましい旨の発言があったが、今回の調査団はその任になく、エヴァリュエーション調査団があらためて派遣される旨伝えておいた。

## II - 2 臨床研究部

フィリピン側の当初からの診療あるいは予防医学に密着した研究活動の要望を踏まえ、野外研究での住民感情による検体(特に血液試料)採取および追跡調査の困難を予測して外来・病棟(50床)および附属施設からなる臨床部門が設立され、実質的には昭和57年2月より診療を開始している。以来2年8カ月間の実状と問題点を報告する。

### (1) 外来および入院患者状況

#### ① 一般外来:

月・水・金曜の午後1~5時に一般外来診療を実施し、毎回約40~50名が来院しているが大

多数は小児の比較的軽症患者である。

58年は総数 4,866 名（月平均 405 名）で、感染症 79%・非感染症患者 21%であった。59年 1-10月では総数 4,338 名（月平均 434 名）で 8%増加し、感染症 84%・非感染症 16%（殆んど研究所職員・関係者）で本来の目的にそっている。疾患別では呼吸器疾患 47%・消化器疾患 16%・皮膚病 15%・中枢神経感染症 3%であった。

## ② 救急外来：

午後 5 時以後の一般外来診療の時間外急患に対応するもので普通約 10 名（下痢症流行時などは 30-40 名）が来院し、大多数は小児の比較的軽症患者である。

58年は総数 2,691 名（月平均 224 名）で非感染症患者 20%、重症救急患者は 13%に過ぎない。59年 1-10月では総数 3,118 名（月平均 312 名）で 40%増加し、感染症が 86%を占めているが救命救急患者は 18%に過ぎない。疾患別では消化器疾患 40%・呼吸器疾患 34%・中枢神経感染症 6.4%であった。

## ③ 入院：

集中治療 2 床を含め 50 床の病床を有し、入院患者は全て感染症患者のみである。開設された 57年 2-12月の 250 名から 59年 1-10月の 841 名に著増しており、特に小児感染症患者が全入院数の 70-80%（日本では 90-95%）を占めている（図）。

入院患者の主な疾患は急性呼吸器感染症（肺炎を含む）28%・急性胃腸炎 11%・コレラ 5.9%・化膿性髄膜炎 5.7%・結核性髄膜炎 3.5%、その他に麻疹・チフス・破傷風・敗血症・マラリア・住血吸虫症などが挙げられ、この入院患者の実態は附設診療施設の本来の目的に適合している。

開設以来の入院患者死亡数は 193 名（11.4%）で、敗血症・破傷風（何れも新生児を含む）の 40-25%の死亡率を除外しても急性肺炎（麻疹肺炎を含む）18.5%および急性胃腸炎 8.3%の死亡率は異常に高く、反対に結核性髄膜炎の低い死亡率 15%は奇異にさえ考えられる（図）。コレラ・チフスなどによる死亡が極めて少ない点は興味がある。

## (2) 臨床研究部従事者

### ① 医師

RITM の staff の他に現在 1-2 年契約の 2 名の fellow（UP-PGH 感染科より）が常勤、6-7 名の senior resident が何れも周辺大病院の小児科の感染・熱帯病研修の一環として 2 カ月単位で rotate している。即ち月・水・金曜に来院し午前中入院患者を staff, fellow と共に回診、午後は外来診療に従事する。救急外来は fellow, resident 各 1 名の当直医師があたる。開所時の数名の resident が希望者が多く現在 6-7 名に達しており、特に熱心な若手医師の研究部での見学など周辺研究機関・病院の当研究所にたいする関心と期待を反映しているものであろう。

② その他の医療従事者：

55名の看護婦およびレ線技師・検査技師・薬剤士が充足されており、現在の病院機能（入院約30床まで）はほぼ満たされている。他に2名の検査技師 internが常勤している。

夜間当直には看護婦5-6名およびレ線技師・検査技師・薬剤士各1名が当たっている。

(3) 今後の問題点と対策

① ウィルス性疾患に対する関心の促進：

RITMの研究成果として、influenza A, B・RS virus・adenovirus type 3・mycoplasmaなどのvirus性急性呼吸器感染症の流行が確認され、小児便からrotavirus・poliovirusも証明されている。このことは周辺研究機関・医療従事者の大きな関心を得ているが、結核性髄膜炎と無菌性（virus性）髄膜炎との鑑別や麻疹予防接種の実施などに対する一層の緊急重大性を認識せしめたい。

② 重症感染症患者の診療：

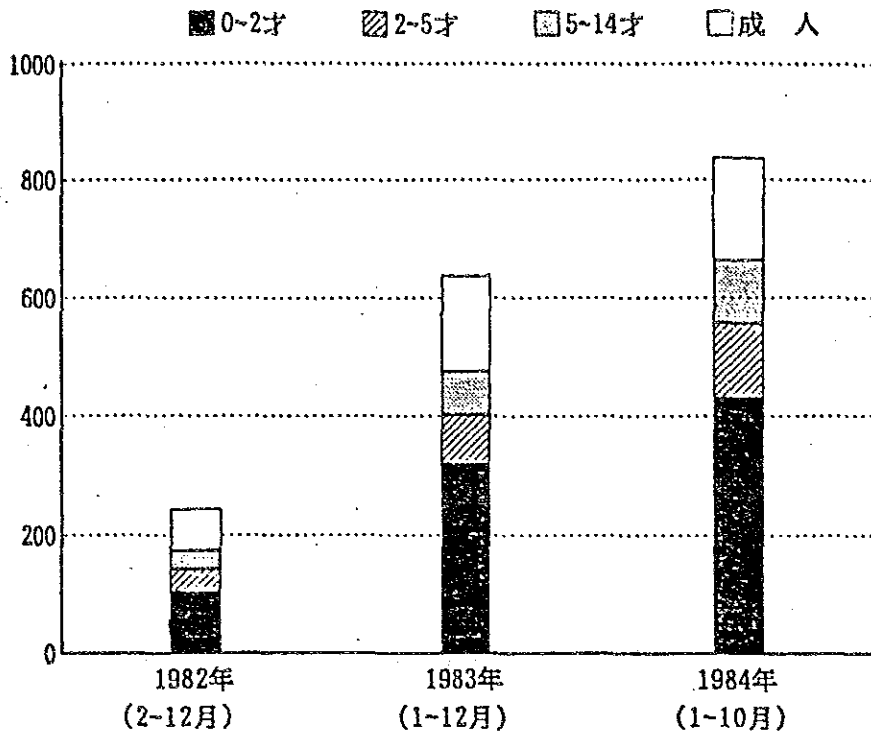
日本の感染症病棟と同様に、当臨床研究部に於いても小児患者とくに重症急性肺炎の乳児が多い。栄養不良・麻疹感染に続発するなどのhandicapはあるが死亡率は異常に高値で、特に救命救急的集中治療に於ける呼吸管理の増強が急務であろう。respirator・血液ガス分析装置の整備とともに、小児救急医療に関する高度の専門家の派遣が必須である。

③ 病床利用の今後の課題：

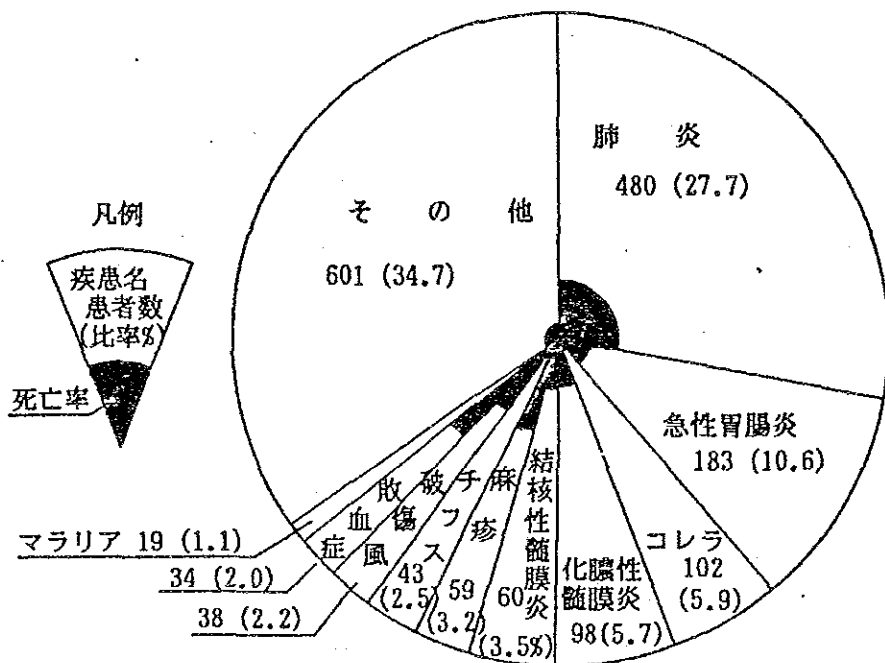
上記の如き確実な診断と重症患者の 命的集中治療を推進させれば、周辺医療施設からの紹介依頼患者が増加し、研究所にとり重要な血液その他の試料採取にも極めて有利と考えられる。他方、現在の医師・医療従事者の定員・能力では重症患者の比率が増すにつれて30床の入院患者収容が限度と考えられ、偶発的集団発生時は別として残りの20床はRITMとしての特定研究のための感染症患者収容床として温存・活用することが妥当であろう。

（合屋 長英）

入院患者状況



入院患者疾患別比率および死亡率



## II - 3 微生物部

熱帯医学研究所 (RITM) は、フィリピンをはじめとする諸熱帯地方における主要熱帯病制圧のための方法論の確立、およびこれに従事するマンパワーの育成を目的として昭和53年11月より日比両国間において検討が開始され、昭和56年4月には日本政府の援助のもとに開所の運びとなった。今回、巡回指導チームの一員として当研究所を訪れる機会を得たので、本プロジェクト開始後の実績と幾つかの問題点について臨床微生物学の立場から報告する。

### (1) 主要感染症における起因微生物の現状

感染症の診断に際しては起因微生物の検出あるいは免疫学的手法が極めて重要であり、正しい臨床診断のためには幅広い細菌学的知識と高い技術が要求される。それらの指導の一環として、我が国からは細菌、ウィルス、電子顕微鏡、蛍光抗体法などの専門家が当研究所に派遣され、現地スタッフの育成にあたっている。その結果、一般的な細菌の同定に関してはほぼ一定の水準にまで達し、また当研究所で初めて患者からウィルスが分離された事実や、電子顕微鏡操作法の熱心な指導などについてはフィリピン国においても極めて高い評価がなされている。

急性呼吸器感染症：フィリピンにおける小児の死亡率は極めて高く、中でも肺炎によるものが最も多い。このような背景をふまえて、当研究所では NSTA, BOST ID および WHO などの支持も得て Dr. Tupasi が中心となって精力的に本疾患の解析にあたっている。

細菌性のもものでは *H. influenzae* および *S. pneumoniae* に起因したものが約80%であったとの成績が得られている。一方、ウィルス、マイコプラズマ、ジフテリア感染症に関しては JICA 技協専門家の協力によって血清学的検討が行われ、これらの疾患の実態についても次第に明らかにされつつある。特にウィルスについては臨床材料から、インフルエンザ、RS、エンテロ、アデノ、麻疹ウィルスなどが実際に分離されており、これがフィリピンでの初めてのウィルス分離例であったこともあわせて非常に注目されている。

腸管感染症：Dr. Saniel を中心としたプロジェクトチームが組まれている。

Alabng 地区の小児を対象とした成績をみると、ETEC (毒素原性大腸菌) が 15.6% と最も多く、次いで *Salmonella* (10.1%)、*Rotavirus* (7.1%)、EPEC (病原性大腸菌) の順でみられたのに対して、*Campylobacter*、*Vibrio* 属の分離頻度が低かったことが注目されたが、これが地域特異性によるものなのか、あるいは分離同定技術に起因するものかは今後の検討課題であると考えられる。

本疾患群の起因微生物の解析にあたっては日本側専門家の貢献するところは大きく、その指導範囲は腸内細菌の分離同定、ETEC および EPEC の証明、ロタウィルスの酵素抗体法による抗原検出および電顕による証明など多岐に亘って行われ、高い成果が得られている。

化膿性髄膜炎：呼吸器、腸管感染症と並んで死亡率の高い疾患である。当研究所における髄

液からの細菌の分離頻度をみても、*S. pneumoniae* (30%)と*H. influenzae* (23%)によるものが最も多く、両者で全体の約半数を占めており、*Salmonella*も11%から分離されている。その他本疾患の診断を目的としたCIE (Counter immunophoresis)やCRPの定量などの導入も試みられている。一方、その他の髄膜炎として結核菌やウィルスによる髄膜炎もかなり存在することが予想され、特に結核性髄膜炎は死亡率も極めて高いことから、今後は、呼吸器感染症も含めて結核菌の分離にも力を注ぐべきものと考えられる。

## (2) 本プロジェクトの評価

すでに述べてきたように、① JICA 技協 専門家の協力によって、フィリピンにおける感染症の実態が総括的に明らかにされつつあり、また一方では各種専門家の高等技術が着実に現地スタッフによって習得されつつあること、② 過去4年間に巨額の器材の供与によって研究所におけるリサーチ部門の設備が充実してきたことなどから、当研究所が今やフィリピンにおける医学の指導的研究機関として認められるようになってきたことに対して極めて高い評価がなされるべきであろう。また研究費に関しても現在までの努力と実績が認められ、すでに米国をはじめとするオーストラリア、カナダおよびWHOなどの他機関からも援助が得られるまでに至っている。このことは当研究所が自立性の面においても殆んど問題がないところまで成長したことを裏付けるものであり、今後は東南アジア地区における感染症の指導的研修センターとして機能していくであろうと期待される。また、世界各国の感染症を専門としている研究者にとっても、このように臨床部門とリサーチ部門とを兼ね備え、かつ目的に応じた症例を対象とすることが可能な研究所が存在することは、感染症の病態解明にあたって寄与するところ大と思われる。

## (3) 現時点における問題点と今後の対策

起因微生物の分離同定に関する問題点：通常の好気性菌、すなわち腸内細菌群や呼吸器感染症、髄膜炎などの起炎菌として重要な役割を果たしている*H. influenzae*や*S. pneumoniae*などはある程度まで分離同定が行われており、ほぼ満足し得る水準にまで達しているものと考えられる。しかし、① 小児における腸管感染症の起炎菌として重要な役割を果たしている微好気性菌の*C. jejuni*の分離率がやや低いこと、② 嫌気培養装置が備っているにも拘らず嫌気性菌の分離が実際には未だ軌道にのっていないこと、③ 結核菌の分離がうまく行われていないこと(2,3についてはフィリピンスタッフが日本で研修中あるいは研修予定)など、当研究所のレベルであれば最低の技術として兼ね備えられていて当然のものが未だ十分に習得されていないようにも思われる。その他、呼吸器感染症の起炎菌として頻度の高い*M. pneumoniae*はウィルス、リケッチアなどとは異なり分離も比較的容易であることから、本菌の分離技術は早急に導入すべきものと考えられる。



一方、培養に特殊技術を要するクラミジア、リケッチアおよび一部の原虫の診断に関しては現在行われている蛍光抗体法、酵素抗体法などによる免疫学的診断法が今後効果を発揮するものと思われる。

ウィルスについては、すでに分離にも成功しており、また血清学的手法も十分に消化されているものと考えられ、今後は熱帯地方に多くみられる Dengue および HBウィルスに標的を絞った技術協力が望まれる。

ジフテリア、百日咳、破傷風、麻疹に関する問題点と対策：フィリピンにおける乳児死亡率をみてみるとその原因としてこれらの疾患が一次的あるいは二次的に高く関与しているものと推定される。その疫学調査については金子リーダーのもとですでに着手されており現在迄に幾つかの興味ある成績が得られている。幸いなことにこれらの疾患群はワクチンの投与によってその発症を未然にあるいは軽度に抑えることが可能である。医療の原点である予防医学の立場からも是非これらの疾患に対するプロジェクトは今後さらに推進されるべきものであり、自国でのワクチン製造までのしっかりした基盤を作りあげるための強力な専門家の協力が望まれる。本プロジェクトは決して派手ではないが成功すれば明らかに乳児死亡率の低下につながるものと思われ、対象国の背景を考慮すれば最も重要なプロジェクトと考えられる。

臨床部門とリサーチ部門との関係：本研究所は臨床部門が併設されていることで、実際の臨床に直結したリサーチが行い易い点に特徴がある。この利点も臨床家と基礎医学者間での交流の他に、臨床家の基礎医学に対するあるいは基礎医学者の臨床に対する興味と実践があつてこそはじめて生かされるものである。短期間の滞在で軽々しく批判することにはいささか抵抗を感じるが、この点においてやや不満が残された。すなわち、この研究所の機能と設備が高い評価を受けようになるに従い、ここの病院を希望する医師数も増加し、感染症専門家の研修機関として重要な役割を果たすようになっていくにも拘らず、専任医師が本病院で診療あるいは研究に従事している時間が少ない印象を受けた。このことは専任医師が入院患者の状況について充分把握していなかった事実からも容易に推測される。しかし乍ら、その背景にはこの国特有の事情があることも考慮しておかねばならないであろう。今後は単なる診断と治療の習得のみを目的とした臨床家ではなく、その解決のため自ら実験室に顔を出し研究を行う医師が増加することが望まれる。

#### (4) まとめ

臨床と基礎の中間的な立場から今回の巡回医療指導で感じたことを幾つか述べてみた。以上のことを要約すると、以下の如くなる。

- ① 本プロジェクトは当初のマスタープランに沿って順調に経過し、ほぼ満足し得る結果が得られており、すでに当研究所の自主独立性も備ったものと考えられる。
- ② しかし乍ら、実際の技術協力は R/D が締結されてから1年半後に開始されており、実質

上の協力期間は約3年ほどである。

- ③ すでに指摘してきた如く、本プロジェクトの目的を達成するためには、さらに幾つかの技術的な問題点が残されている。すなわち、幾つかの基本的細菌検査法の充実、DengueおよびHBウィルスについての技術指導、DPTワクチン製造のための基礎作りなどがそれに該当する。また、最近着手された動物舎完成後の動物飼育のための技術指導なども残されている。

以上のことから、本プロジェクトをさらに成功に導びくためには技術協力プロジェクトの今後2年間の延長が不可欠と考えられ、この延長は将来における本プロジェクトの高い評価につながるものと結論する。

(山口恵三)

## II - 4 Summary of Discussions

The Japanese Advisory Survey Team for the Research Institute for Tropical Medicine Project (hereinafter referred to as the team) organized by the Japan International Cooperation Agency (JICA) headed by Dr. Shigeo Hayashi visited the Republic of the Philippines from November 19 to 24, 1984.

The team had a series of discussions and exchanged views with Senior Staff members of the Research Institute for Tropical Medicine (RITM) and other officials concerned of the Government of the Republic of the Philippines.

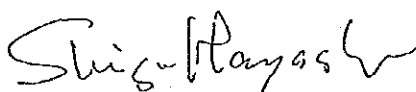
The following is the summary of discussions.

1. Detailed presentation was made by the Senior Staff members of RITM on organization and finance of RITM and activities of each Department. the Team recognized that RITM had been developed as one of the most active research institute in the Philippines in a very short time; various research and training programs undertaken shows that RITM is now greatly contributing to national health promotion and health manpower development in the Philippines.
2. RITM Staffs reported the major achievements in completed and in on-going research programs. The Team acknowledged that the present cooperation project has effectively supported technical betterment of research activities. The fact that RITM got financial support from national, international and other organizations for numbers of research programs was also confirmed by the Team as an evidence of RITM's high reputation.
3. Technical Cooperation plan until October 16, 1985 was discussed. RITM requested experts in virology (HBV and Dengue), Pediatrics, Clinical Laboratory, and provision of an ambulance, a blood gas analyzer, a blood bank refrigerator, and a portable

X-ray machine as put on high priority. The team expressed its wish to recommend JICA that the ambulance, the blood gas analyzer, and the blood bank refrigerator be included in the budget for fiscal 1984. The portable X-ray machine would be considered in fiscal 1985. The team informed that the number of counterpart personnel accepted for training in Japan would be three for Fiscal 1985. Early nomination and submitting of A2 and A3 Forms were advised.

4. At the Technical Coordinating Committee held on November 22, RITM requested extension of the period of technical cooperation for further strengthening of RITM's functions. Being not entitled to make commitment, the team promised that it would report the request along with other results of discussion to the Japanese authorities concerned. After receiving the proposal for extension through due formalities, the evaluation team will visit the Philippines to talk about extension of technical cooperation. The team advised that the proposal should be concrete, realistic and focussing on a few activities which requires more technical support from JICA.

Manila, November 23, 1984



SHIGEO HAYASHI  
Team Leader  
Advisory Survey Team  
Japan International  
Cooperation Agency



THELMA E. TUPASI  
Director  
Research Institute for  
Tropical Medicine

### III 專門家研究報告



### Ⅲ - 1 熱帯医学研究所

Research Institute for Tropical Medicine Ministry of Health

熱帯医学研究所は、昭和52年の福田総理の訪比に際し、保健省の無償プロジェクトとしてマルコス大統領からの要請にはじまる。その後数回の予備調査を通じて内容が方向づけられた。そもそもの考え方はワクチン血清等の製造検定を担当する保健省の Alabang Serum Laboratory の補強にあったが、これが UNICEF の援助をうけることになったので JICA としては、ワクチン等にも関連する問題として、フィリピンをはじめ、広く熱帯研に発生する伝染病の調査研究と、これにたずさわるマンパワーの養成の為の研究所を援助することになった。熱帯研が講義室、実習室をもつのはその為である。また熱帯研は50床の病床をもつが、それは患者に即した研究が望ましい事、併せて地域医療に寄与するという保健省の要望に答えたものである。

1. プロジェクトの経過：無償援助は昭和53年11月予備調査団を派遣し、その後数回のミッションを派遣して昭和55年3月、予算17億5000万円で建設することが決められた。また場所としては比較政府病院の少いマニラ南方アラバン地区が選ばれた。アラバンには前述のワクチン血清研究所がありその敷地60ヘクタールのうち20ヘクタールをあてることになった。6100m<sup>2</sup>の建物は昭和56年3月に完成し、フィリピン政府に引渡された。また3月25日には大統領 Executive Order No. 674 が公布され、56年4月23日開所式が行われた。

これに先立つ6カ月前、昭和55年10月17日に技術協力プロジェクト R/D が結ばれたが、期間5年、器材供与、日本専門家の派遣、カウンターパートの日本研修、研究課題、その他を内容とする。R/D は即日発効した。

2. 技術協力の進行について：(A) 日本人専門家：(昭和56年)金子義徳(東邦大、公衆衛生学、細菌学、4カ月)、布上薫(九大小児科、ウイルス学、6カ月)、(昭和57年)金子義徳(同上、2カ月)、小塚芳道(電子顕微鏡、病理学、3年)、山岡邦夫(ウイルス学、3年)、安慶田英樹(九大小児科、1年)、(昭和58年)金子義徳(同上、2年)、工藤泰雄(都衛研、腸内細菌、1カ月)、井上栄(予研、ウイルス学、1カ月)、小塚芳道(同上)、山岡邦夫(同上)、(昭和59年)金子義徳(同上)、小塚芳道(同上)、山岡邦夫(同上)、新垣民樹(琉大内科、1年)、川島豊作(蛍光抗体法、1年)、上山恵三(動物実験棟建築、5カ月)  
(B) カウンターパート日本研修：(昭和56年度) Dr. Maramuba(大臣秘書、病理学)、Dr. Romaldez(所長)、Dr. Gonzaga(病理学)、(57年度) Dr. Galon(副所長)、Dr. Baccay(病理学)、Mrs. Torres(ウイルス学)、(58年度) Dr. Gonzaga(病理学)、Mrs. Tarrayo(薬剤学)、(59年度)4名の予定。

3. 熱帯研の運営：(1) Advisory Board：Minister of Health (Chairman), Director General of NSTA, Chancellor of UP Systems Health Sciences Center. Coordinating Committee：Deputy Minister of MOH (Chairman), 熱帯研所長, 研究部長, 臨床研究部長, NEDA代表, NSTA代表, 日本専門家, JICA代表, 日本大使館オブザーバー

(2) 人員 (59年4月1日現在)：事務部 (補修, 保安, 清掃含む) …… 180名

研究部 …………… 81

臨床研究部 …………… 82 計 343名

なお所長 Dr. Romaldez は 昭和59年3月1日フィリピン大学医学部長に転出, 研究部長 Dr. Thelwa E. Tupasi が8月1日 Acting Director に就任した。

(3) 予算 (実行予算) ペソ

年	保健省	NSTA	WHO他	その他	計
1982	6,300,000	1,300,000	240,000	100,000	7,900,000
1983	5,696,363	1,154,962	189,033	100,000	7,140,358

1984年上半期は 4,300,000 Peso.

4. 研究協力活動：研究室内研究：1) 急性呼吸器疾患の疫学的, 細菌ウイルス学的, 臨床学的研究

2) 下痢性疾患の " " "

3) 日本住血吸虫症の免疫学的, 病理学的, 疫学的研究

4) マラリアの生態学的研究

5) 蛍光抗体法による病原同定法の研究

6) 予定：B型肝炎の HBS 抗原の試作, デング出血熱のウイルス学的研究

臨床的研究：1) 髄膜炎の病原学的臨床的研究

2) 感染症の臨床的研究

協力活動：1) WHO-workshop, 国内技術者の EM 操作法, 医学写真技術, 3) JOCV の健康診断, 4) その他

5. 臨床研究部の活動：1976年の年報によれば全国の病床数は76,230 (内45,000が政府立) 床で人口1万あたり17.6床である。現在, 個室10床, 4人病室10室の計50床であるが25床分の看護要員が配置され, 平均的入院患者数は20~30, 外来診療は月, 火, 金の午後もたれている。救急外来は24時間開設されている。患者数, 患者の社会経済状況は下表の如くである。



Number of patient by age-group and disease,1983

		Age	0	1-4	5-14	15-	Total
Out-patient	Infectious		844 (91.9%)	1274 (91.7%)	611 (86.3%)	1038 (62.7%)	3767 (80.7%)
	Non-infectious		74 ( 8.1%)	115 ( 8.3%)	97 (13.7%)	617 (37.3%)	903 (19.3%)
	Total		918 (19.7%)	1389 (28.7%)	708 15.2%)	1655 (35.4%)	4670 (100%)
			49.4%)				
In-patient	Infectious		211	170	95	150	626
	Non-infectious		-	-	-	2	2
	Total	No. %	211 (33.6%)	170 (27.1%)	95 (15.1%)	152 (24.2%)	628 (100%)
ER-patient	Infectious		745 (93.2%)	753 (93.0%)	253 (76.4%)	466 (46.6%)	2217 (82.4%)
	Non-infectious		21	39	49	97	206
	Others		33	18	29	187	217
	Total		799 (100%)	810 (100%)	331 (100%)	750 (100%)	2690 (100%)

Socio-economical status of patients,1983

Patient Status	In-patient	Out-patient	ER-patient	Total
Pay	27	107	83	217 ( 2.6%)
Semi-pay	4	144	21	169 ( 2.1%)
Semi-indigent I	21	214	105	340 ( 4.1%)
Semi-indigent II	117	1381	1016	2514 (30.6%)
Full-indigent	277	963	734	1974 (24.0%)
Research	160	522	240	922 (11.2%)
Personnel depend.	28	183	227	438 ( 5.3%)
Others*		1348	304	1652 (20.1%)
Total	634	4862	2730	8226 (100%)

\* No laboratory work done,not around when called, transferred to other hospital, consultation only, etc.

### Ⅲ - 2 B型肝炎の診断試薬の作成とその応用に関する研究

研究の背景：フィリピンにおいてはB型肝炎ウイルス、HBV、の研究施設はなく、したがってこれまではフィリピン大学医学部内科学教室 Dr. Domingo 教授, Dr. Lingao 助教授, RITM コンサルタント, が日本のHB研究グループの技術指導をうけ、また診断試薬の供給をうけてHBV感染の生態学的研究を数年来実施している。したがって、フィリピンにおいては、輸血用血液のHBVの検査は実施されておらず、保健大も強い関心をもっていることは小張国内委員長からも伺ったところである。一方RITM側においては所長 Dr. Romaldez は着任前のフィリピン大学医学部助教授時代から免疫研究グループに属しグループの長が肝臓疾患に深い関心をもつ上記内科学主任の Dr. Domingo であり、その助教授である Dr. Lingao を介してHBVに強い関心をもち、1982年度に Dr. Lingao を RITM のコンサルタントに迎え、HBV研究体制をつくりはじめた。チームリーダーの金子も度々将来計画について説明をうけ、又日本のHB研究グループもすでに数回 RITM を来訪し討論する機会があった。フィリピン側研究グループはすでに日本 JSPS のスカラシップをうけてすでに2名の研究員を日本に派遣し、現在も RITM から1名が日本研修中である。

RITM としては発足当時からの研究課題も進行中であり、充足すべき器材も山積している現状であるが、1982年度に、HBVの研究も考慮して超遠心機の購入にふみ切った。診断試薬の作成には長時間の遠心が必要であり、又HBV以外の目的にも使用される可能性も多分にあるので少くとも2台以上必要と思われるが、さし当って一台で、之に zonal rotar を導入して抗原試薬の作成に当る予定である。その他必要とされる低温遠心機、フラン器、恒温水槽などは即存のものが使用できるので、小型の測定器などを除けば経常経費は試薬と消耗品の供給で足りると考える。

一方これまでの研究報告では日本における健康HBV保菌者は2~3%であるのに対してフィリピンではその約10倍といわれており、したがって血漿由来の抗原の作成には極めて有利であることは明らかであり、研究の効率的な進行が期待される。たまたま WHO 西太平洋事務局が主催する Task Force Meeting on HB が、1983年11月8日~11日 マニラで開催され、金子及び Romaldez もオブザーバーとして参加した。大いに得る所があり、会議の最後の勧告案のうち本研究に関連する部分を別紙に添付する。勧告はこの他に輸血用血液のHBV検査、HBワクチンの製造とその品質管理及び基準に関する事項を含む。

又この会議では、オーストラリア、シンガポール、中国、韓国のHB研究状況が明らかになり、HBV保菌率の高い中国、韓国ではワクチンの自家製造をはじめており、一方オーストラリア、シンガポールでは米国メルク社製のものが、ハイリスク対象に任意に接種される体制にあることも報告された。しかしHB感染の検査及び実態の未だ不詳のフィリピンではワクチン接種は二次の問題であり、診断試薬の作成が緊急の研究課題であることについては関係者が一致した意見

である。

RITM発足以来実質的な研究は2年位であるが、National Projectとしての急性呼吸器疾患、下痢性疾患、日本住血吸虫症などは軌道にのり、未発表ではあるが、研究成果をあげている。HBVの研究は独立した研究室と備品があれば高額な消耗品なしに研究が進行すると思われる点から上記進行中の研究プロジェクトには支障ないと考えられる。HBV研究プロジェクトについては、政府の財政難の折にもかかわらずNSTAで承認された。又これまでWHO西太平洋地区事務局の梅内博士からは色々指導をうけ、研究室の設計についてもアドバイスをうけている。又1984年度からWHO研究費の支持も受けられる見通しである。

HB感染はフィリピンにおいても重要な問題であるが、必要な診断試薬は高価であり、予算的にはその調査研究は極めて困難であると考えられる。

RITMがこの診断試薬の作成に成功すればその意義は極めて大きいと考えられる。

研究組織：主任研究者：Dr. Baccay (RITM病理学研究室主任)

協同研究者：Dr. Tupasi (RITM研究部長)

Dr. Lingao (RITMコンサルタント、フィリピン大学内科助教授)

Dr. Saniel (RITM臨床研究部長)

Dr. 金子義徳 (JICA技協プロジェクトチームリーダー)

Dr. 山岡邦夫 (JICA技協プロジェクト専門家)

研究計画：

1984年—1) HBs, HBc, HBe各抗原の精製と診断試薬の作成

2) HBs, HBc, HBcIgM, HBe各抗体の精製と診断試薬の作成

1985年—1) 診断試薬の鋭敏度、特異性、安定性の実験室内研究

2) 上記試作品の人体応用に関する基礎的研究

1986年—1) 上記診断試薬によるフィリピンにおけるHB感染の疫学的研究

2) HBVワクチンの小規模試作と人体応用に関する研究

技術協力プロジェクトに関連事項：zonal rotarの到着をまって都臨床研の馬場氏をすでに予定しており、又RITMからも更にカウンターパートの日本研修を考えている。

### Ⅲ - 3 フィリピンにおける小児性下気道感染症の病因に関する研究

フィリピンにおいては、インフルエンザ、気管支炎、肺炎等の呼吸器感染症は、小児において罹患率・死亡率共に群をねいて、この国においても他の途上国と同様小児呼吸器感染症の研究は重要なテーマとなっている。

我々は、従来実施して来た細菌学的病因の研究に更にウィルス学的研究を加えて、その充実を計画し、実施中である。

この国の小児呼吸器感染症にしめる病因ウィルスは日本もふくめて多くの研究者が報告しているように、インフルエンザ、RS、パラインフルエンザ、アデノ、エンテロの各ウィルスであり、似たものであるが、次のように若干の興味ある知具がえられている。(図表参照)

1. インフルエンザが年間を通じて発生し、そのウィルスも年間を通して分離されている。
2. RITMがカバーする狭い地域においてすら、年間を通して、インフルエンザA型、B型両型に亘って同時に流行するという実態がウィルス分離成績からわかった。
3. 分離されたインフルエンザA型ウィルスの抗原性をみると、日本のA/Nigata/102/81とHi Titerで5倍、A/Bangkok/1/79とは2倍程度の違いであった。

このことから同定にはA/Bangkok/1/79の抗血清を使用している。

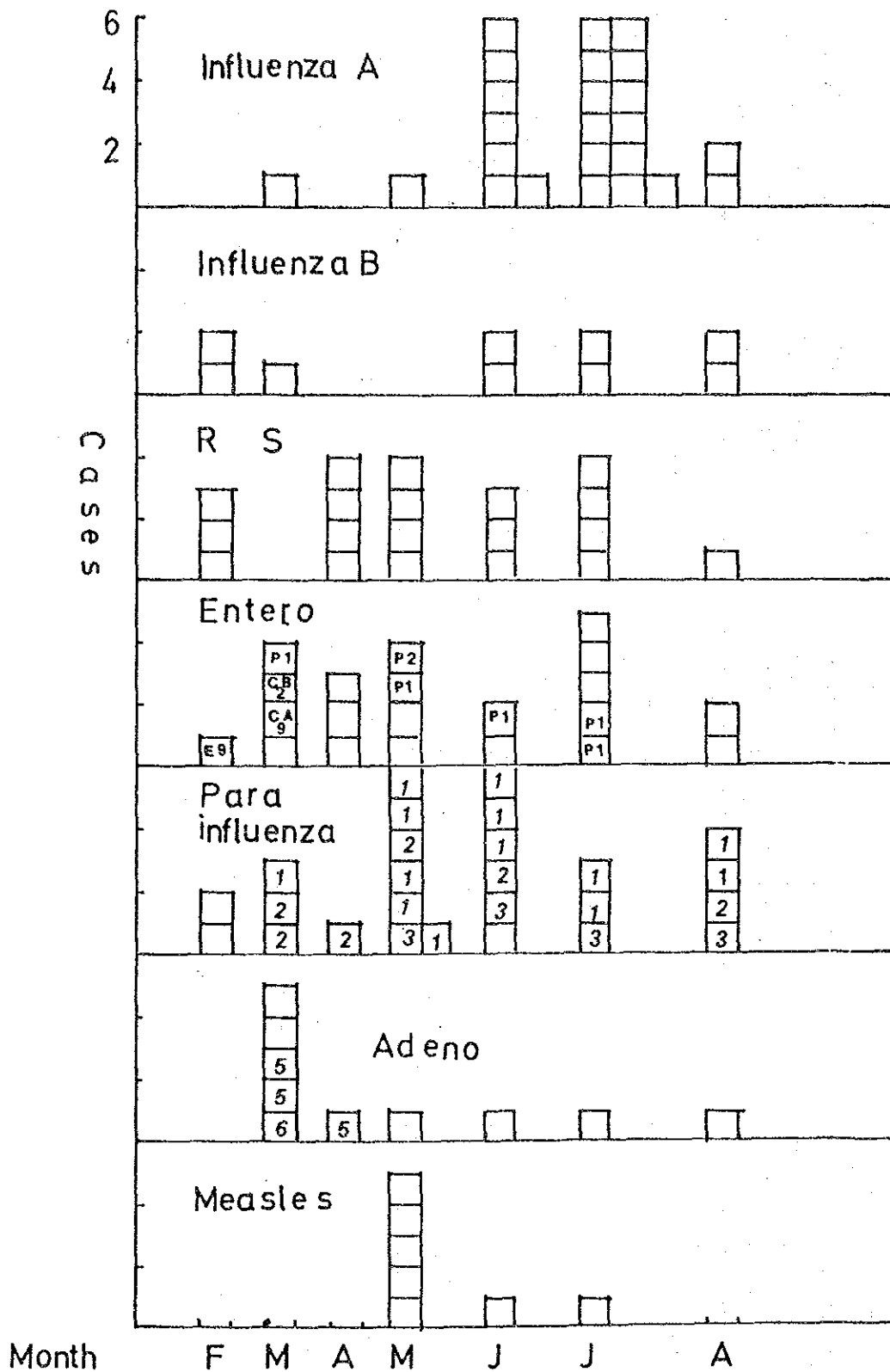
4. RSウィルスの細胞変性(CPe)が一般的に云われているようなHEP<sub>2</sub>CellでいわゆるCynritialを示さなく、ポリオウィルスのそれと似たCPeであり、CPe所見では全くRSウィルスを推定出来ないものである。
5. Enteroウィルスは年間を通して分離されている。そのうち、ポリオウィルスは高頻度に分離されている。これらのことから、ポリオワクチン投与ということになってもEnteroウィルスの流行閑期をあてるという訳には行かないであろう。

The virus isolation rates by monthly of patients  
in children with ALRI (Feb.-Aug. 1984)

Month	No. of tested	Influenza		R S	Entero	Para infl.	Adeno	Measles	Total
		A	B						
Feb	22		2	3	1	2			8 (36.4)
Mar	81	1	1		4	3	5		14 (17.3)
Apr	63			4	3	1	1		9 (14.3)
May	77	1		4	4	7	1	5	22 (28.6)
Jun	58	7	2	3	2	6	1	1	22 (38.0)
Jul	74	13	2	4	5	3	1	1	29 (39.2)
Aug	60	2	2	1	2	4	1		12 (20.0)
Total	435	24	9	19	21	26	10	7	116 (26.7)

The virus isolation rates by age of patients in children with ALRI (Feb.-Aug.1984)

Age	No.of tested	Influenza		R S	Entero	Para influenza	Adeno	Measles	Total
		A	B						
0 yr	170	4	2	10	6	10	3	3	38 (22.4)
1 yr	115	10	1	1	5	7	2	2	28 (24.3)
2 yr	70	5	2	5	8	5	2	2	29 (41.4)
3 yr	39	2	1	1	1	2	2		9 (23.0)
4 yr	27	3	1	1	1	2	1		9 (33.3)
5 yr	14		2	1					3 (21.4)
Total	435	24 (21.0)	9 (7.7)	19 (16.4)	21 (18.0)	26 (22.4)	10 (8.6)	7 (6.0)	116 (26.7) (100.00)



A result of virus isolation from  
A L R I patients ( 1984 )

The Relationship of Antigen and Antibody for  
the Identification of Influenza Virus

Antiserum Antigen	A/Nigata/102/81 (H3N2) (Japan)	A/Kumamoto/37/79 (H1N1) (Japan)	A/Bangkok/1/79 (H3N2) (WHO)	A/England/333/80 (H1N1) (WHO)	B/Singapore/222/79 (WHO)
A/Nigata/102/81	1024				
A/Kumamoto/37/79		512			
A/Bangkok/1/79			256		
A/England/333/80				128	
B/Singapore/222/79					128
A/Manila/24/84	16-32				
B/Manila/6/84			64-128		64-256



### Ⅲ - 4 フィリピンにおける小児急性呼吸器感染症の血清疫学的研究

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Thelma E. Tupasi (Research Institute for Tropical Medicine,  
Ministry of Health)

フィリピン保健省 Disease Intelligence Center, DIC の 1978 年の報告によれば, 罹患率上位 10 位までに 9 種類の感染症が含まれ, インフルエンザ, 気管支炎, 肺炎, はしか, 百日咳がそれぞれ 1, 3, 5, 7, 9 位をしめており, 死亡率の第 1 位は肺炎である。<sup>1), 2)</sup> 本研究はフィリピンのこの保健事情をふまえて, 熱帯医学研究所がフィリピン National Science and Technology Authorities, NSTA, および WHO の研究費をうけて, 国際協力事業団の技術協力プロジェクトの一課題として実施されたものである。

#### 研究対象と研究方法

1. 研究対象: Quezon 市 Apolonio Samson 地区における 5 才未満の乳幼児 228 名で, 熱帯医学研究所の ARI 研究グループが 1981 年以来調査研究をつづけている 380 家庭に属する。その年齢と WHO 基準による社会経済階級は Table 1 に示す如くである。地区は Metro-Manila の Quezon 市の一画であり, いわば都市人口に属する。検査能力に限度があったので, 対象者を 0 ~ 5 カ月, 6 ~ 11 カ月, 1 才, 2 才, 3 才, 4 才の各年齢群にわけ, 無作為に 124 検体を抽出し, その血中抗体を測定した。シック反応については Table 4 のように 219 名について実施可能であった。

2. 研究方法: 1983 年 6 月 23, 24 日に採血された。血清を直ちに分離し, 検査まで  $-20^{\circ}\text{C}$  に保存された。インフルエンザ A, インフルエンザ B, RS ウィルス, アデノ 3 型, 肺炎マイコプラズマについては Single Radial Complement Fixation (SRCF, デンカ生研) を用い, 麻疹 HI 試験用キット (デンカ生研) を用いた。尚, 麻疹 HI 抗体価は 8 倍, 16 倍, 32 倍の 3 点でスクリーニングを行ない, 抗体の有無を確認し, 終末価は求めている。

シック反応は, 国立予防衛生研究所, 東京, のシック液 Lot. No. 55 を用い, 0.1 ml を前腰屈側中央に皮内接種し, 96 時間後に発赤の径を測定し 10 mm 以上を陽性とした。陽性反応の大きさの分布は従来のものと略々同様であり, 判定に支障はなかった。

#### 研究成績

1. インフルエンザ A, インフルエンザ B, RS ウィルス, アデノ 3 型, 肺炎マイコプラズマに対する抗体について: 得られた成績を Table 2 に示す。CF 抗体は感染後約 1 年で消失すると

考えられるので、表の成績は 1982 年 6 月～1983 年 5 月の間にあった地域内流行を反映して

Table 1—Age and Socio-economic Status of the Subject

Class Age	A	B	C	Total
0 yr.		6	23	29
1	2	12	21	35
2	2	19	30	51
3	1	19	39	59
4		18	36	54
Total	5	74	149	228

いるものとする。抗体陽性率をみるとインフルエンザ A が 32.2% で最も高く 3 才児が最高であった。全体としては高い順にアデノ型 24.2%、肺炎マイコプラズマ 18.5%、RS ウィルス 10.5%、インフルエンザ B 5.6% であった。合計はこれらすべてに対する抗体陽性者を合計したものであるが、2 才児が 24.0% と最も高く感染機会の多いことを示唆した。

Table 2—Complement fixing antibody positives against Influenza A, Influenza B, RS, Adeno 3 and Mycoplasma pneumoniae by age

Antigen	CF Antibody	Age and number of tested						Total (124)
		0-5mos (7)	6-11mos (21)	1yr (24)	2yr (25)	3yr (22)	4yr (25)	
Influenza A	+	2	3	6	9	10	10	40
	-	5	18	18	16	12	15	84
	pos (%)	28.6	14.3	25.0	36.0	45.4	40.0	32.2
Influenza B	+	-	2	2	2	-	1	7
	-	7	19	22	23	22	24	117
	pos (%)	-	9.5	8.3	8.0	-	4.0	5.6
R S	+	-	2	2	4	3	2	13
	-	7	19	22	21	19	23	111
	pos (%)	-	9.5	8.3	16.0	13.6	8.0	10.5
Adeno 3	+	-	5	6	8	6	5	30
	-	7	16	18	17	16	20	94
	pos (%)	-	23.8	25.0	32.0	27.3	20.0	24.2
Mycoplasma pneumoniae	+	-	3	7	7	2	4	23
	-	7	18	17	18	20	21	102
	pos (%)	-	14.3	29.2	28.0	9.1	16.0	18.5
Total	Positives	2	15	23	30	21	22	
	No. tested	35	105	120	125	110	125	
	pos (%)	5.7	14.3	19.2	24.0	19.1	17.6	

2. 麻疹 HI 抗体について：麻疹抗体については、上記同様に無作為抽出された 186 様体について測定され、Table 3 にその成績を示した。麻疹 HI 抗体は少なくとも 10 年は持続すると考えられるので、Table 3 の数字は麻疹累積経過率も示すものと考えられる。累積陽性率は 11 カ月で 35%，1 才で 52.2% でかなり早期に罹患することが明らかとなった。

Table 3 — HI — antibody against Measles.

Age	No. tested	HI — antibody			Cumulative positive rate		
		Pos.	Neg.	Pos. (%)	No. tested	Pos.	Pos. (%)
0—5 mos.	1	—	1	0.0			
6—11 mos.	19	7	12	36.8	20	7	35.0 %
1 yr	26	17	9	65.4	46	24	52.2 %
2	40	28	12	70.0	86	52	60.5 %
3	55	43	12	78.2	141	95	67.4 %
4	45	40	5	88.9	186	135	72.6 %
Total	186	135	51	72.6 %			

3. シック反応について：5 カ月以下の乳児の一部を除いて 219 名について定法通りシック反応を行ない Table 4 の成績を得た。DPT ワクチンの接種症はテストの際に母親に聴取したものである。Table 4 で接種のない対象については、顕性、不顕性感染による獲得免疫を示すものであり、0～5 カ月の陰性者は母子免疫を示唆し、又 1 才以上については保菌者流行あるいは罹患による獲得免疫によると考えられ、当然のことながら年令の上昇とともに陰性率は高くなっている。

一方、予防接種歴のある群では、6～11 月で 50%，又各年令で高く、予防接種の効果を強く示唆している。人工免疫は時日の経過とともに低下するのは当然なので、1 才以上の上昇は顕性、不顕性感染による自然獲得免疫かあるいは年度毎の接種率の差違によるものと考えられる。

Table 4 全体としては予防接種をうけたと考えられるものは 56/219 (25.6%) にすぎず、また全体のシック陰性率 46.1% は流行を阻止するとされる集団免疫度 60% にも満たない。流行発生の可能性を強く示唆している。

Table 4 — Schick negative rate by age and history of immunization

Immunization	Schick test	Age						Total
		0-5mos	6-11mos	1yr	2yr	3yr	4yr	
No history	No. tested	4	14	23	38	43	41	163
	Neg.	3	3	4	13	16	22	61
	Neg.(%)	75.	21.4	17.4	34.2	37.2	53.6	37.4%
With history	No. tested		6	10	12	16	12	56
	Neg.		3	7	9	13	9	41
	Neg.(%)		50.0	70.0	75.0	81.3	75.0	73.2%
Total	No. tested	4	20	33	50	59	53	219
	Neg.	3	6	11	22	29	31	101
	Neg.(%)	75.0	30.0	33.3	44.0	49.2	58.5	46.1%

4. 肺炎球菌の血清型について：この研究の対象は上述の対象地区にある Quezon General Hospital の入院患者から分離された肺炎球菌で Table 5 にその由来とコペンハーゲンの国立血清研究所の血清による菌型を示した。Table 5 の中でワクチン菌型としたものは 1983 年 7 月 1 日から実施されている 23 菌型を含む肺炎球菌ワクチン<sup>3)4)5)</sup>に含まれるものである。この研究は協同者 Tupasi によって WHO の研究費の補助をうけて実施されたものである。Table 5 によれば合計 358 株のうち 290 株 (81.0%) がワクチン菌型であり、その割合は日本の最近の研究による結果<sup>10)</sup>とほぼ同様であった。しかし個々の菌型の頻度については日本の場合とやや異なっている。この調査研究は西太平洋地区ではオーストラリアと日本のみであり、貴重な結果であると考えられる。

#### 考 察

フィリピンにおいては急性呼吸器感染症 (ARI) は臨床的にも予防医学的にも重要な疾患であり、DIC の衛生統計、1978 年、によれば罹患率ではインフルエンザが第 1 位 (487.7)、気管支炎第 3 位 (455.6)、肺炎第 5 位 (248.8) であり、死亡率では肺炎第 1 位 (100.3) であり、<sup>1)</sup> 1983 年 8 ~ 11 月の熱帯研臨床研究部の外来、救急外来、入院患者をみても呼吸器疾患が 35% 以上をしめている現状である。フィリピン保健省も ARI を National Project にとりあげ、病原学的、臨床的、社会経済的にその実態を把握して対策を講じようとしている。この研究はフィリピンにおける特に小児における ARI の流行状況を血清疫学的に把握しようとしたものである。

インフルエンザウィルスの分離に関する報告はフィリピンでは殆んどみられないが、香港、シンガポールなど近隣諸国では 1983 年に A (H<sub>3</sub>N<sub>2</sub>)、A (H<sub>1</sub>N<sub>1</sub>)、B 型が分離されており、<sup>6)</sup> フィ

Table 5 - Sero-type of S.pneumoniae isolated in Quezon City, Metro-Manila  
1981 - 1983

Type Specimen Serotype	Vaccine Type			Non-Vaccine Type		
	NTA*	Blood	Others Total	Serotype	NTA*	Blood Total
19	53(20.5%)	2	1	57(19.7%)	35	8(11.8%)
23	50(19.3%)	1	1	54(18.6%)	13	10(14.7%)
6	42(16.2%)	1		43(14.8%)	28	8(11.8%)
14	18(6.9%)	6	1	25(8.6%)	21	8(11.8%)
15	15(5.8%)			15(5.2%)	16	9(13.2%)
18	9(3.5%)			9(3.1%)	34	6(8.8%)
3	9(3.5%)		1	10(3.4%)	24	4(6.5%)
33	8(3.1%)			8(2.8%)	39	2(3.2%)
9	7(2.7%)	1		8(2.8%)	48	2(2.9%)
1	7(2.7%)	3	1	13(4.5%)	42	2(2.9%)
7	6(2.3%)	2		8(2.8%)	31	1(1.5%)
11	5(1.9%)			5(1.7%)	29	1(1.5%)
10	5(1.9%)			5(1.7%)	45	1(1.5%)
5	5(1.9%)	1	1	7(2.4%)	15	1(1.5%)
20	4(1.5%)			4(1.4%)	41	1(1.5%)
8	4(1.5%)			4(1.4%)	40	1(1.5%)
2	3(1.2%)		1	4(1.4%)	27	1(1.5%)
4	3(1.2%)	1	1	5(1.7%)		
22	2(0.8%)			2(0.7%)		
17	2(0.8%)			2(0.7%)		
12	2(0.8%)			2(0.7%)		
Total	259(72.3%)	18	6	290(81.0%)	62(17.3%)	68(19.0%)

GRAND TOTAL = 358 (100%)

\* Naso-tracheal aspiration

リピンにおいても同様にA型, B型の流行があるものと考えられるが, これについては別に研究が進行中でありすでにインフルエンザA(H<sub>1</sub>N<sub>1</sub>)1株が分離されている。フィリピンにおけるインフルエンザについては田中<sup>7)</sup>の報告があり愛知/2/68(H<sub>3</sub>N<sub>2</sub>), Port Chalwars/73(H<sub>3</sub>N<sub>2</sub>), 熊本/1/75(H<sub>3</sub>N<sub>2</sub>)を用いたフィリピン妊婦のHI抗体価は日本に較べて抗体保有率, 抗体価ともに低く, フィリピンにおいては日本などの温帯地域に較べてインフルエンザの流行規模は小さいものと推察される。インフルエンザ, RSウイルスなどは日本では冬期に流行することは周知であるが, 年平均気温27.6°Cのフィリピンでこれらウイルスの流行がみられることは興味深い。大谷<sup>8)</sup>によるとタイ国では5~8月の雨期に流行が多く, 1~4月の乾期には少いと報告されている。熱帯圏におけるこれらウイルス疾患の流行学的研究は興味ある課題であろう。

アデノウイルスもARIの病原ウイルスとして重要であり, 急性熱性咽頭炎(1, 2, 3型), 咽頭結膜熱(3, 7, 14型), 肺炎(4型)などを起こすことが知られている。日本ではアデノウイルス感染症は主として夏に流行がみられるが, フィリピンにおける季節的消長や流行菌型は不明である。アデノウイルスのCF抗原はアデノウイルス群に共通であり, 一つの血清型に対するCF抗体の測定によってアデノウイルス群の感染の有無を知ることができるとされている。

肺炎マイコプラズマは日本ではほぼ4年毎に流行し, 冬に比較的発生は多いが季節性に乏しいとされている。肺炎マイコプラズマによる肺炎(原発性異型肺炎, PAP)の発生は年令的には5~15才にピークがあることが知られており, 5才以下の乳幼児の初感染像は肺炎を伴わない感冒症状や喘鳴と考えられている。今回調査した5才以下の小児の抗体保有率は18.5%で比較的高いが, 臨床症状はおそらく肺炎ではなく軽度の上気道感染症状を呈したものと考えられる。

Table 3の麻疹HI抗体の累積陽性率によれば, 1才までにすでに52.2%が罹患しており, 日本の昭和51年の患者統計から計算すると1才では34.2%であり, 侵染度前進現象が認められる。いずれにしても麻疹ワクチン接種年令に重要な示唆を与えている。Table 4についてはすでに本文中でもふれたが, 保菌者流行は明らかであり, 集団免疫度からみても流行発生の可能性を強く示唆している。Table 5はAustrian,<sup>4)5)</sup> U.S. Public Health Service Advisory Committee<sup>3)</sup>の報告からみてもフィリピンにおける肺炎球菌ワクチン接種を支持する成績である。

## 結 論

フィリピンにおける4才以下の乳幼児における急性気道感染症の流行状況を血清疫学的に調査し次の結果を得た。

- 1) SRCF法によりインフルエンザA, インフルエンザB, RSウイルス, アデノ3型肺炎マイコプラズマに対するCF抗体価を測定した結果それぞれに対する抗体保有率はインフルエンザA(32.6%), アデノ3型(24.2%), 肺炎マイコプラズマ(18.5%), RSウイルス(10.5%), インフルエンザB(5.6%)であり, いずれも少くともマニラで流行していることが確認された。またこれら病原体は1~2才の低年令層を中心に流行していることが

示唆された。

2) 麻疹 HI 抗体からみて1才ですでに 52.2%が罹患しており、4才で累積陽性率は 72.6%であり、ワクチン接種年齢に重要な示唆を与えた。

3) 予防接種率別、年齢別のシック反応結果からワクチンの効果を確認し、また保菌者流行を示唆する成績を得た。集団免疫度 46.1%は今後の流行発生の可能性を示唆している。

4) 患者から分離された肺炎球菌の血清型は、その 81%が現行肺炎球菌ワクチンに含まれることが明らかになり、同ワクチンの接種を支持する結果を得た。

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## 文 献

1. Disease Intelligence Center, Ministry of Health Philippine Health Statistics, 1978
2. 金子義徳：フィリピンにおける伝染病の疫学 医学のあゆみ：Vol.105, 1020—1025, 1978
3. U.S. Public Health Service Advisory Committee on Immunization Practices. A pneumococcal polysaccharides vaccine. Morbidity and Mortality Weekly Rep. 30: 410—412, 417—419, 1981
4. Austrian, R. Pneumococcal infection and pneumococcal vaccine. New England J. Medicine., 297: 938—939, 1977
5. Austrian, R., Gotshilich, E., Henrichsen, J., Robbins, J. B., Schiffman, G., Tiesjema, R. H. Need for agreement on a single pneumococcal vaccine formulation. Lancet i: 1354, 1980
6. CDC Morbidity and Mortality Weekly Report (MMWR) Vol. 32, NO. 8, 502—504, 1983
7. 田中利次：フィリピン妊婦についての急性感染症の血清疫学的研究 日本公衆衛生雑誌：26: 569—574, 1979
8. 大谷 明：アジアのウィルス病 佐々学編「アジアの疾病」 新宿書房, 1978
9. 国立予防衛生研究所：病原微生物検出情報, 第 40 号：1983 年 6 月
10. 福見秀雄, 金子義徳, 他：日本における肺炎球菌の血清型に関する研究 (日本感染症学雑誌, 1984 年, 印刷中)

### Ⅲ - 5 蛍光抗体法

技協の一環として免疫学に於ける役割は大きいと思考されます。比国経済状態は教育にまで波及は否めない問題かも知れないが、成書にあるペーパー上の知識は十分に持合せているが、半身不随様で基礎実験技術は貧弱極まりない状況だと思われ、要望の免疫蛍光法をモデルに進めて行きます。期間的な関連を考え合せて逆手順を踏まざるを得ないと推察、器材及び試薬類の関係あって、免疫蛍光法の実質作業開始は遅れましたが、感染症であるウィルス学、細菌学をふまえ自己免疫疾患等の応用操作を含めて行く為には他力の抗体に頼らなければならない状況です。先ずは、

- 1) 急性呼吸器疾患のウィルスについて Influenzae A, B, Parainfl I. II. III, RS, ムンプス その他麻疹、ヘルペスについて電化生研製直接法の標識抗体の使用確立を計り, Revco の故障で Prout type のウィルスが無く分離ウィルス感染細胞の組合せに依る同定使用の可能性を探索することが出来た。その中で Parainfl I. と RS (初期方針として専門家の抱える問題を第1に実施することにして、先行して調査されている SRCF で 13/124 の抗体保有児が在り乍ら抗原検出に成功していない。常夏の本疫患は疫学的にも貴重な資料になるので、現在数百の Sample が解決策を待っている) の 2 製品は非特異か蛍光抗体法以前の問題であり、未解決でなやまされている。
- 2) 免疫蛍光法の応用として ①上記標識抗体を使って臨機応変に診断に利用している。②入院患者の管理にからむ麻疹保毒問題で尿からの検索材料を本年 2 月 27 日より凍結して保存していたが、材料不適當なので廃棄、新鮮尿で 6 月 20 日より実施 6/24 の陽性であった。③百日咳菌について培養検出率が悪いので取り上げることにした。咽頭スワブ材料で東浜株による抗 K 因子/ウサギ血清を一次抗体として下記 3) の④での抗ウサギ IgG/ヤギ標識抗体を二次に間接法で 9 月 9 日より実施している。6/32 の陽性であります。
- 3) 収集抗血清を各 25~30 ml 使用して蛍光標識抗体を作成した。
  - ① 抗ヒト IgG (FC 特異) / 山羊血清 30 ml 使用。  
IgG 分画精製 × 2 FITC 蛍光色素標識精製作成。
  - ② 抗ヒト IgM (M鎖特異) / 山羊血清 25 ml 使用。  
IgG 分画精製 FITC 蛍光色素標識精製作成。
  - ③ 抗ヒト C3 / 山羊血清 25 ml 使用。  
IgG 分画精製 FITC 蛍光色素標識精製作成。
  - ④ 抗ウサギ IgG / 山羊血清 30 ml 使用。  
IgG 分画精製 FITC 蛍光色素標識精製作成。
  - ⑤ 抗狂犬病ウィルス / ウサギ血清 20 ml 使用。  
IgG 分画精製 FITC 蛍光色素標識精製作成。



注：①，②，③，④は免疫蛍光法間接法の標識抗体で第1次抗体に今後の課題があり。

⑤及び④ 直接法の標識抗体試薬である。

- 4) WHO との係わりもあるデング熱疾患について酵素抗体法である ILISA 法によってフィルター役を受持つことになっているが手がかからない状況にあり。それに新たに病態把握の一環として免疫複合体の検索をすることになり、30種程の方法の中から設備や蛍光抗体法にも関係のある Razi 細胞法で参画急遽細胞を取りよせ細胞培養を始めたが、炭酸ガス培養装置やら Razi 細胞に合相（維持に好みの）の牛胎児血清（栄研化学特殊試薬室扱，Booknek. FBS. Lot No. 378 10 本予約保存なども附加されてスムーズに運ばない。
- 5) 免疫血清（抗体）の製作着手について 免疫動物は兎を使用して ①当面3) で作成した標識抗体分画精製のチェック及び評価に当面必要なので抗ヤギ全血清／ウサギの抗体作成と免疫動物の扱い方で取組んでいる。これと別に新垣専門家によって抗コレラ及びキャンピロバクターの免疫も開始している。
- 6) 残された課題として 免疫原の物理化学的な血清蛋白の分画精製技術移行に実施して行きたいが、それには分域電気泳動装置等の機器や活用されて否ない機器の活用及び不足分の補充も必要である。

### III - 6 RITM病院統計

Number of patients at Clinical Research Division of Research Institute for Tropical Medicine, Ministry of Health, 1983

#### Out-patient

Diagnosis	Age				Total
	0	1-4	5-14	15-	
<b>I. Infectious</b>					
<b>A. Central Nervous System:</b>					
1. Cerebritis			1		1
2. Suppurative meningitis	29	24	1	3	57
3. Viral encephalitis		4	6	2	12
4. Pneumococcal meningitis				2	2
5. Cryptococcal meningitis				4	4
6. TB meningitis		28	29	12	69
7. Viral meningoencephalitis		4			4
8. Brain abscess				3	3
9. Poliomyelitis			1		1
Total:	(29)	(60)	(38)	(26)	(153)
<b>B. Central Vascular System:</b>					
1. Rheumatic Heart Disease			4	4	8
Total:			(4)	(4)	(8)
<b>C. Dermatology:</b>					
1. Atopic dermatitis	9	24	15	32	80
2. Furunculosis	5	8	7	4	24
3. Hansen's disease			3	40	43
4. Impetigo contagiosa		21	2	2	25
5. Psoriasis with secondary infection				1	1
6. Scabies		8	4	1	13
7. Contact dermatitis		3	5	29	37
8. Tinea flava		1	2	8	11
9. Verucca vulgaris			1	11	12
10. Candidiasis				1	1
11. Herpes zoster				2	2
12. Peri-inguinal verucca				1	1
13. Tinea capitis			2	2	4
14. Tinea cruris		3	2	3	8
15. Tinea pedis				5	5
16. Lichen simplex chronicus			3	19	22
17. Verucca plura			1	8	9
18. Fungal infection		1	2	2	5
19. Tinea capitis			7	9	16
20. Folliculitis	3	4	4	4	15
21. Furuncle			1	3	4
22. Herpes simplex				3	3
23. Leysiodistic eczema			2	8	10
24. Pyodermata		1	2	1	4
25. Exfoliative dermatitis				1	1
26. Ringworm				1	1
27. Suppurative hidradenitis			1		1
28. Infected lesion			2	2	4
Total:	(17)	(74)	(68)	(203)	(362)

Diagnosis	Age	0	1-4	5-14	15-	Total
<b>D. Gastro-urinary Tract:</b>						
1. Acute gastroenteritis		112	80	13	14	219
2. Amoebiasis		23	19	4	8	54
3. Enteric fever			2	4	6	12
4. Enterocolitis		5			1	6
5. Hepatitis		1	8	6	41	56
6. Liver abscess					2	2
7. Parasitism			75	28	1	104
8. Parenteral diarrhea		22	34	7		63
9. Cholera			2		4	6
10. Giardiasis			2			2
11. Ileocolitis		5	4			9
12. Schistosomiasis				1	26	27
13. Typhoid fever				18	27	45
14. Amoebic dysentery		3	2			5
15. Infectious diarrhea		15	4	2	1	22
16. Shigellosis			1	3	1	5
17. Gastrocolitis			1			1
18. Salmonellosis			1			1
19. Ascariasis			5	1		6
Total:		(186)	(240)	(87)	(132)	(645)
<b>E. Pulmonary Disease:</b>						
1. Acute respiratory infection		277	380	147	129	933
2. Bronchitis		48	63	18	69	198
3. Coryza		2	1		1	4
4. Influenza				5	16	21
5. Pneumonia		31	21	44	89	185
6. Primary complex		19	97	91		207
7. Plural effusion					1	1
8. Pulmonary tuberculosis				7	217	224
9. Miliary Tuberculosis					5	5
10. Pneumonitis				3	9	12
11. Bronchopneumonia		104	122	4		230
12. Bronchiolitis		5	1	1		7
13. Pertussis		13	11	1		25
14. Chronic obstructive pulmonary disease					8	8
Total:		(499)	(696)	(321)	(544)	(2060)
<b>F. Others:</b>						
1. Cellulitis				1	4	5
2. Conjunctivitis			2	1	3	6
3. H-fever			6	9	9	24
4. Mastoiditis			1	1		2
5. Measles		55	70	10		135
6. Mumps				2	5	7
7. Otitis externa			1	1	6	8
8. Otitis media		3	25	4	11	43
9. Oral moniliasis		19	6			25
10. Roseola infantum		1				1
11. Staphylococcal bacteremia		1	2	1		4
12. Stomatitis			1	1		2

Diagnosis	Age				Total
	0	1-4	5-14	15-	
13. Tetanus			5	2	7
14. Tonsilo-pharyngitis	21	35	25	21	102
15. Abscess		10	3	12	25
16. Cold	2	5	1		8
17. Viral infection	4	9	7	9	29
18. Gonorrhoea				2	2
19. Glossitis		1	1		2
20. Pustular lesion			1	1	2
21. Rasies			1	1	2
22. Tuberculoma		4	7	5	16
23. German measles				2	2
24. Malaria			1	10	11
25. Sepsis neonatorum	4				4
26. Sexually trans.disease				4	4
27. Tonsillar folliculitis			1		1
28. Unknown fever		3	2	3	8
29. Nasopharyngitis	3	4	3	9	19
30. Leptospirosis				1	1
31. Gingivitis		2	1		3
32. Tonsillitis		8	2	5	15
33. Arthritis		2	1	1	4
34. Lymphadenitis		1			1
35. Cystecercosis				3	3
36. Koch's adenitis		6			6
Total:	(113)	(204)	(93)	(129)	(539)
II. Non-infectious:					
1. Bronchial asthma	4	7	5	18	34
2. Asthmatic bronchitis	2	7	2	15	26
3. Dog bite	1	5	9	6	21
4. Snake bite			1	2	3
5. Others	67	96	80	576	819
Total:	(74)	(115)	(97)	(617)	(903)

Grand Total of Out-patient

Age	Age				Total
	0	1-4	5-14	15-	
Infectious	844 (91.9%)	1274 (91.7%)	611 (86.3%)	1038 (62.7%)	3767 (80.7%)
Non-infectious	74 (8.1%)	115 (8.3%)	97 (13.7%)	617 (37.3%)	903 (19.3%)
Total	918	1389	708	1655	4670
	19.7	29.7	15.2	35.4	100%
	49.4%				

In-patient

Age	0	1-4	5-14	15-	Total
<b>Diagnosis</b>					
<b>A. Central Nervous System:</b>					
1. Suppurative meningitis	45	21	4	5	75
2. TB meningitis	8	15	9	12	44
3. Encephalitis		4	3	3	10
4. Bacterial meningitis	1			1	2
5. Meningococcal meningitis			1		1
6. Brain abscess	1	2	3		6
7. Pneumococcal meningitis				1	1
8. Staphylococcal bacteremia	2	3	1	1	7
Total:	(57)	(45)	(21)	(23)	(146)
<b>B. Central Vascular System:</b>					
1. Rheumatic heart disease			(1)		(1)
<b>C. Gastro-urinary tract disease:</b>					
1. Urinary tract infection		1	3	5	9
2. Biliary tract infection				1	1
3. Gall bladder stone				1	1
Total:		(1)	(3)	(7)	(11)
<b>D. Gastro-intestinal tract:</b>					
1. Acute gastroenteritis	14	11	7	11	43
2. Schistosomiasis				18	18
3. Typhoid fever		3	8	16	27
4. Cholera		1	4	6	11
5. Hepatitis		1		6	7
6. Infectious diarrhea	3				3
7. Amoebiasis	1			1	2
8. Cholecystitis				1	1
9. Ileocolitis	1				1
10. Amoebic dysentery	1	2			3
Total:	(20)	(18)	(19)	(59)	(116)
<b>E. Pulmonary disease:</b>					
1. Bronchopneumonia	90	77	13		180
2. Pneumonia	5	4	2	15	26
3. Bronchitis	1				1
4. Acute upper resp.infect.	3	3	1	1	8
5. Pleural effusion				2	2
6. Bronchiolitis	4	1			5
7. Aspiration pneumonia		1			1
8. Pulmonary TB & Cancer				1	1
9. Pulmonary cryptococcosis				2	2
10. Miliary TB				1	1
11. Influenza				3	3
12. Pneumonitis			1		1
13. Acute laryngotrachio bronchitis	1				1
14. Acute upper resp.infect.		1	1		2
Total:	(104)	(87)	(18)	(25)	(234)

Diagnosis	Age	0	1-4	5-14	15-	Total
<b>F. Others:</b>						
1. Sepsis neonatorum		21				21
2. Tetanus			1	8	1	10
3. Diphtheria		1	3			4
4. Dengue fever			7	12	8	27
5. Fever, unknown origin		1		2		3
6. Tonsillopharyngitis			1			1
7. Jaundice, unknown					1	1
8. Neonatal hepatitis		1				1
9. Hansen's disease					1	1
10. Malaria				2	11	13
11. Septicemia		1	1			2
12. Exfoliating dermatitis					1	1
13. Staph. scalden skin		1				1
14. Systemic viral infection				1		1
15. Meningococcemia		1	1			2
16. Pustular lesions			1			1
17. Staph. bullores impetigo and septicemia				1		1
18. Snake bite				2	3	5
19. Carbuncle		1				1
20. Folliculitis		1				1
21. Staph. conjunctivitis & measles			1			1
22. Leptospirosis			1	1	2	4
23. Staph. pharyngitis				1		1
24. Pyomyositis			1	1		2
25. Tonsillitis					1	1
26. Furunculosis		1				1
27. Pulmonary embolism					1	1
28. Measles			1		1	2
29. Cellulitis				1	2	3
30. Drug sensitivity				1		1
31. Cutaneous cryptococcosis					1	1
32. Psoriasis					1	1
33. Dog bite					1	1
Total:		(30)	(19)	(33)	(36)	(118)
<b>II. Non-infectious:</b>						
1. Migrane headache					1	1
2. Adenocarcinoma, colon					1	1
Total:					(2)	(2)

Grand total of In-patient						
Age		0	1-4	5-14	15-	Total
Infectious		211	170	95	150	626
Non-infectious		-	-	-	2	2
Total	No.	211	170	95	152	628
	%	33.6	27.1	15.1	24.2	100%

ER-patient

Diagnosis \ Age	0	1-4	5-14	15-	Total
<b>I. Infectious:</b>					
<b>A. Central Nervous System :</b>					
1. TB meningitis	3	19	6	10	38
2. Encephalitis	2	1	3	4	10
3. Suppurative meningitis	31	22	6	11	70
4. Meningitis	23	8	5	2	38
5. Brain abscess			1	2	3
6. Staphylococcal Meningitis		1			1
7. Cryptococcal meningitis				1	1
8. Staphylococcal bacteremia	2	2	3	2	9
9. Poliomyelitis		1			1
Total:	(61)	(54)	(24)	(32)	(171)
<b>B. Central Vascular System :</b>					
1. Rheumatic heart disease			(1)	(5)	(6)
<b>C. Grstro-urinary tract :</b>					
1. Urinary tract infection			2	48	50
2. Acute pyelonephritis				3	3
3. Acute glomerulonephritis		2		2	4
Total:		(2)	(2)	(53)	(57)
<b>D. Gastro-intestinal tract :</b>					
1. Acute gastroenteritis	234	194	32	84	544
2. Infectious diarrhea	22	7		4	33
3. Shigellosis	2				2
4. Hepatitis A	2	3	5	17	27
5. Amoebic dysentery		1		1	2
6. Parasitism		15	2		17
7. Cholera		2	4	8	14
8. Ileocolitis	7	5			12
9. Amoibiasis	11	4	1	7	23
10. Typhoid fever			5	9	14
11. Schistosomiasis				10	10
12. Ascariasis		1	1		2
13. Giardiasis				1	1
14. Parentiral diarrhea	22	12	1		35
Total:	(300)	(244)	(51)	(141)	(736)
<b>E. Pulmonary disease :</b>					
1. Bronchopneumonia	135	128	17	4	284
2. Pneumonia		10	4	23	37
3. Lobar pneumonia	1				1
4. Aspiration pneumonia		1	1		2
5. Bronchialitis	5	6			11
6. Pneumonitis				2	2
7. Bronchitis	17	9	2	2	30

(continued)

Diagnosis	Age				Total
	0	1-4	5-14	15-	
8. Influenza		1	1	16	18
9. Primary complex		6	1		7
10. Pertussis	1	1	1		3
11. Pulmonary tuberculosis				23	23
12. Chronic obstructive pulmonary disease				4	4
13. Pulmonary cryptococcosis				3	3
14. Lower respiratory tract infection				3	3
15. Acute upper respiratory infection	142	152	36	30	360
Total:	(301)	(314)	(63)	(110)	(788)
F. Others :					
1. Tonsillitis		2	5	9	16
2. German measles				2	2
3. Infected tooth				1	1
4. Leptospirosis		1	1		2
5. Chicken pox		2			2
6. Septicemia	1	1	2		4
7. Malaria			1	14	15
8. Congenital syphilis	1				1
9. Abscess		2	2	3	7
10. Otitis media	4	5	2	1	12
11. Otitis externa				1	1
12. Measles	31	36	4	6	77
13. Tetanus		1	3	12	16
14. Conjunctivitis			1	1	2
15. Tonsillo-pharyngitis	12	34	19	16	81
16. Diphtheria	1	2			3
17. Degue fever		22	38	14	74
18. Gonorrhoea				1	1
19. Viral infection	4	7	5	11	27
20. Mumps	1	1	1	1	4
21. Benign febrile convulsion	9	10	1	1	21
22. Herpes labialis				2	2
23. Poisoning		2	2	1	5
24. Sepsis neonatorum	17				17
25. Meningococemia	1	1			2
26. Furuncle		1			1
27. Salmonellosis		2			2
28. Hansen's disease				2	2
29. Pyoderma			1		1
30. Sinusitis				3	3
31. Unknown fever	1	2	5	3	11
32. Tinea pedis			1		1
33. Oral moniliasis		2			2
34. Liver abscess			1	2	3
35. Infected fish cure puncture			1		1
36. Rhinitis				3	3
37. Carbuncle				1	1

(continued)



Diagnosis	Age				Total
	0	1-4	5-14	15-	
38. Flu				1	1
39. Arthritis				2	2
40. Chronic diarrhea			1		1
41. Rubeola			1		1
42. Pustular lesion			1		1
43. Infected wound		2	6	5	13
44. Enteric fever			6	1	7
45. Cholecystitis				1	1
46. Asthmatic bronchitis			1	3	4
47. Filariasis				1	1
48. Laryngitis		1			1
Total :	(83)	(139)	(112)	(125)	(459)
II. Non-infectious :					
1. Punctured wound		2	2	4	8
2. Lacerated wound			2	10	12
3. Non-infectious diarrhea	8	10	4	10	32
4. Rat, pig, cat bite		1	1	1	3
5. Snake bite			1	8	9
6. Obstructive jaundice	6		2	2	10
7. Dog bite	5	21	31	34	91
8. Bronchial asthma	2	5	6	26	39
9. Ureterolithiasis				1	1
10. Lupus erythematosus				1	1
Total :	(21)	(39)	(49)	(97)	(206)
III. Others :	(33)	(18)	(29)	(187)	(267)

Grand Total of ER-patient

Age					Total
	0	1-4	5-14	15-	
Infectious	745 (93.2%)	753 (93.0%)	253 (76.4%)	466 (46.6%)	2217 (82.4%)
Non-infectious	21	39	49	97	206
Others	33	18	29	187	267
Total	799 (100%)	810 (100%)	331 (100%)	750 (100%)	2690 (100%)

Ⅲ-7 フィリピン国衛星統計

(1) Ten Leading Causes of Infant Mortality

Philippines, 1978 (Rate/1000 l.b.)				Japan, 1982 (Rate/100,000 l.b.)			
Cause	Number	Rate	% of Infant death	Cause	Number	Rate	% of Infant death
1. Pneumonia	18 070	13.4	23.7	出産時外傷, 低酸素, 仮死	3 340	220.4	33.5%
2. Gastro-enteritis and colitis	7 862	5.8	10.3	先天異常	2 764	182.4	27.7
3. Avitaminosis and other nutri-defic.	7 354	5.5	9.6	不慮の事故	525	34.6	5.3
4. Anoxic and hypoxic conditions	4 875	3.6	6.4	肺炎, 気管支炎	391	25.8	3.9
5. Tetanus	2 750	2.0	3.6	詳細不明, 未熟児	374	24.7	3.8
6. Congenital Anomal.	2 636	2.0	3.5	敗血症	238	15.7	2.4
7. Bronchitis, Emphysem and Asthma .....	1 944	1.4	2.5	心疾患	209	13.8	2.1
8. Acute respiratory infection	1 580	1.2	2.1	髄膜炎	134	8.8	1.3
9. Measles	1 503	1.1	2.0	その他外面	126	8.3	1.3
10. Meningitis	985	0.7	1.3	出血, 出血性疾患	88	5.8	0.9

(2) Number of reported case and death of diphtheria

Age	Philippines, 1978				Japan, 1982			
	Case	%	Death	Case Fat (%)	Case	%	Death	Case fatal (%)
0 yr.	257		121	47.1	7		-	-
1-4	948	97.3	289	30.5		30.0%	-	-
5-14	146		36	24.7	2			
15~	38	2.7	9	23.7	21	70.0%	-	-
Total	1 389	100.0%	455	32.8%	30	100.0%	-	-

(3) Number of reported case and death of infectious diseases related to the death by acute respiratory dease, Philippines

Year	Diphtheria					Pertussis				
	Case	Rate	Death	Rate	Case fatal	Case	Rate	Death	rate	Case fatl.
1967	1 277	3.7	486	1.4	38.1%	17 771	51.3	125	0.4	0.7%
68	1 253	3.5	622	1.7	49.6	22 250	62.0	101	0.3	0.6
69	1 626	4.4	701	1.8	43.1	25 542	68.7	98	0.3	0.4
70	1 770	4.8	602	1.6	34.0	19 946	54.1	64	0.2	0.3
71	1 877	4.9	505	1.3	26.9	24 269	63.9	52	0.1	0.2
72	3 342	8.6	616	1.6	18.4	26 311	67.4	62	0.2	0.2
73	3 379	8.4	661	1.6	19.6	20210	50.2	46	0.1	0.2
74	2 884	7.0	519	1.3	18.0	22 042	53.2	58	0.1	0.3
75	1 770	4.2	601	1.4	34.0	28 231	66.4	81	0.2	0.3
76	3 371	7.7	611	1.5	18.1	27 442	62.7	117	0.3	0.4
77	2 888	6.4	562	1.2	19.5	21 403	47.6	111	0.2	0.5
78	1 389	3.1	455	1.0	32.8	15 243	33.5	80	0.2	0.5

Year	Measles					Pneumonia				
	Case	Rate	Death	Rate	Case fatal	Case	Rate	Death	rate	Case fatl.
1967	18 074	52.2	1 781	5.1	9.9%	76 799	221.6	39 320	113.5	51.2%
68	19 555	54.5	2 122	5.9	10.9	77 861	217.0	43 444	121.1	55.8
69	25298	68.1	2 515	6.8	9.9	30 109	215.6	44 689	120.3	55.8
70	20 446	55.5	1 667	4.5	8.2	86 040	233.5	43573	118.2	50.6
71	26 492	69.8	3 264	8.6	12.3	87 953	231.7	40 526	106.8	46.1
72	15 451	39.6	2 078	5.3	13.5	95 717	245.2	48 831	125.1	51.0
73	28 568	71.0	4 866	12.1	17.0	93 569	232.6	48 058	119.5	51.4
74	22 999	55.5	3 533	8.5	15.4	93 050	224.4	45 910	110.7	49.3
75	28 198	66.3	3 632	8.5	12.9	96 961	228.1	43 349	102.0	44.7
76	29 901	68.3	5 060	11.5	16.9	111 767	255.5	47 105	107.7	42.2
77	27 694	61.5	5 293	11.8	19.1	104 074	231.2	47 302	105.1	45.5
78	27 842	61.2	5 605	12.3	20.1	113 257	248.8	45 667	100.3	40.3

(4) Number of deaths by age-group and disease  
in relation to the contribution to the total, 1978

Disease	All ages	0 yr.	1-4 yr.	5- yrs.
Influenza	1 898	247	287	1 364
Pneumonia	45 667	18 734	14 175	12 758
Bronchitis	5 929	1 869	1 486	2 574
Sub-total	53 494	20 950	15 948	16 696
(%)	(18.0)	(28.3)	(44.0)	( 8.9)
Measles	5 605	1 581	3 377	647
Pertussis	80	35	38	7
Diphtheria	455	121	289	45
Sub-total	6 140	1 737	3 704	699
(%)	( 2.4)	( 2.4)	(10.2)	( 0.4)
Tetanus	3 471	2 443	119	909
TE	29 398	198	518	27 682
Gastroenteritis	15 717	6 846	5 168	3 703
All deaths	297 034	73 640	36 266	197 128
(%)	(100)	(100)	(100)	(100)

(5) Number of deaths at clinical research division and autopsied, 1983

Age	Deaths	Autopsied	%
0 yr		22	
1-4	97	17	42.3
5-14		2	
15-	13	4	30.8
Total	110	45	40.9%

(6) Number of histopathological examination, 1983

	No. Cases	No. Blocks	No. Slides
I. Histopathology			
1. Out-patients	302	287	614
2. In-patient	19	25	61
3. Cholera-EPEC	17	22	91
4. Autopsy	40	674	984
5. Exper. Animal	58	64	216
6. Leprosy	65	66	132
II. Cytopathologic exam.	522		527
III Plastic Embedding	5	5	10
Total	1 028	1 143	2 636

(7) Pathological examination of Rabies-suspected dog, 1983

	No. Cases	No. Blocks	No. Slides	No. Positives
1 Quarter	1	1	8	1
2 "	3	6	23	-
3 "	4	8	19	-
4 "	8	8	57	4
Total	16	23	107	5

出所: Health Statistics 1978



#### Ⅳ RITMから提出されたブリーフィング資料





## IV - 1 Introduction

### The Institute

Executive Order No. 674 signed on March 23, 1981 formally established the Institute. It was inaugurated on April 23, 1981. The Institute is built on a scenic 2.2 hectare area on a 20 hectare site, about 200 meters above sea level within the compound of the Division of Biologicals, Bureau of Research and Laboratories of the MOH (The Serum Laboratories) in Alabang, Muntinlupa at a cost of \$8,000,000.00 which was a grant-in-aid from the Government of Japan through the Japan International Cooperation Agency.

Construction of the building was started in February 19, 1980 and completed in March 15, 1981. The 2 storey sprawling edifice has a total floor area of 6,113.06 square meters and is uniquely equipped with a solar water heater. It has a 50 bed in-patient unit, an ICU and Operating Room, an ER unit, research and clinical equipment which includes Hitachi 300 Electron Microscope.

The primary function of the Institute is the efficient and economical implementation and performance of RESEARCH PROGRAMMES on the diagnosis control and treatment of tropical and infectious diseases. The identified scope of disease priorities are those making-up the major of mortality and morbidity in the Philippines. The RITM also provides Training and SERVICE Programmes which are in support to its research programme.

### The Project

The JICA Technical Cooperation Project (Project) was agreed upon on October 17, 1980 as shown in the record of discussion in Annex I. The purpose of the project is the strengthening of capability of the Institute to develop widely applicable control measures against the major tropical diseases in order to improve prevailing health condition. The implementation of the project is the responsibility of the Ministry of Health of the Government of the Republic of the Philippines. Accordingly, organization of the staff of the institution, expenses for maintenance and operations were borne by the Government of the Philippines. Additional funds from external agencies were endowed on the institute to augment the budget for maintenance and operations.

## IV - 2 Objectives

### GENERAL OBJECTIVES

1. To study tropical diseases endemic in the Philippines and Southeast Asia and to develop methods of control
2. To teach and train technical and research personnel
3. To provide medical services to meet research objectives

### SPECIFIC OBJECTIVES

#### RESEARCH & TRAINING DIVISION

1. To undertake researches on the diagnosis, treatment and prevention of tropical diseases which are prevalent in the Philippines through integrated research programmes
2. To provide medical services to in-patients and out-patients in support of the Research Program and Infectious Diseases
3. To establish a manpower development program to improve research capability among the staff
4. To establish training program for field health workers and allied paramedical profession in research techniques that maybe applied in the control of tropical diseases
5. To provide research services for the Ministry of Health in the prevention and control of tropical diseases and infectious diseases.

#### RESEARCH PARAMEDICAL DIVISION

To provide paramedical services in support of the activities of the Research and Training Division specifically as it pertains to patient care.

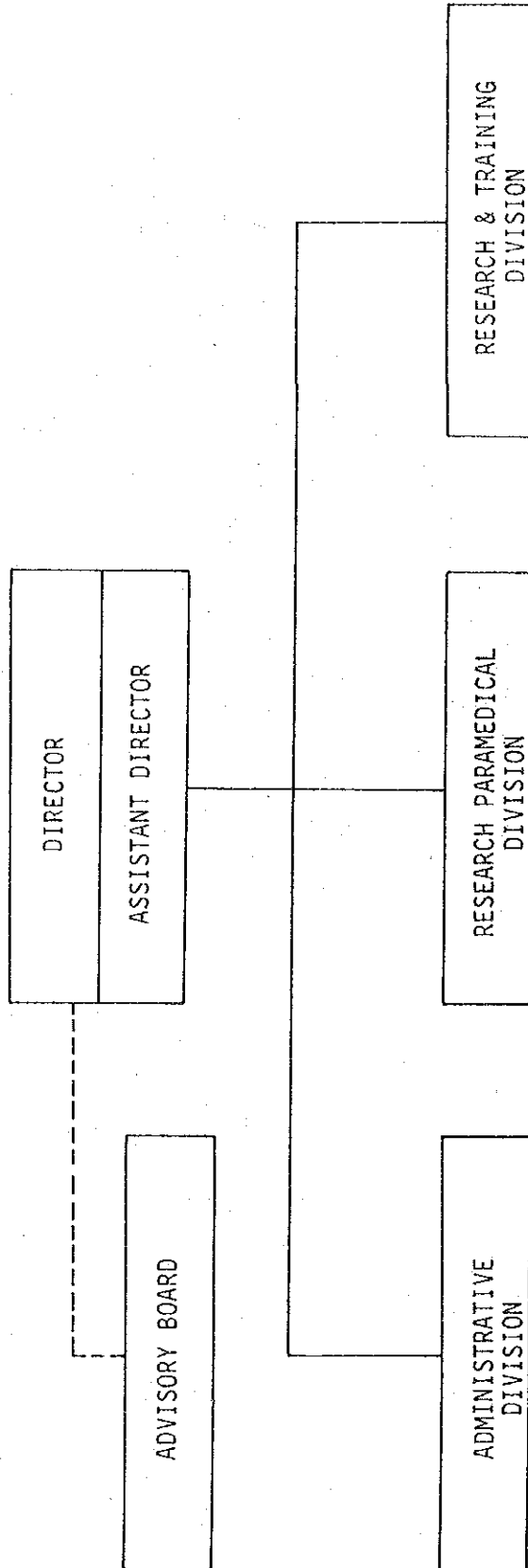
#### RESEARCH ADMINISTRATIVE DIVISION

To provide administration and services in support to health care, research and training pursuant to the objective and policies of the institution.

# IV - 3 Functions, Organization and Financial Report

Ministry of Health  
RESEARCH INSTITUTE FOR TROPICAL MEDICINE  
Aleberg, Muntinlupa, M.M.

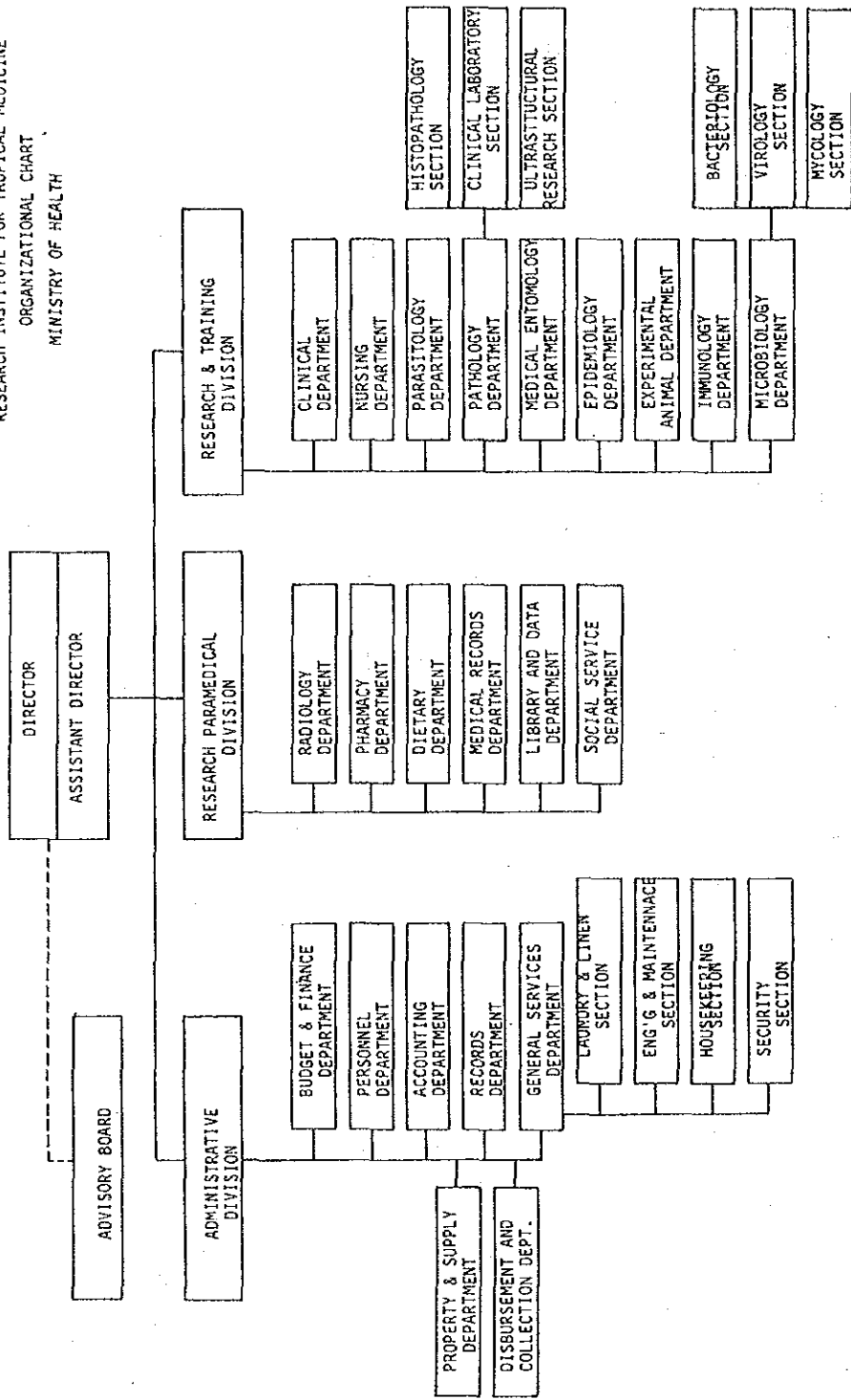
## ORGANIZATIONAL CHART



Approved:

J.C. AZURIN  
Minister  
Ministry of Health

RESEARCH INSTITUTE FOR TROPICAL MEDICINE  
 ORGANIZATIONAL CHART  
 MINISTRY OF HEALTH



PERSONNEL COMPLIMENT

PARTICULARS	1981	1982	1983	1984
<b>A. REGULAR POSITION</b>	100	196	196	196
1. Administration	47	48	48	48
2. Clinical Research Division	37	95	95	95
3. Laboratory Research Division	16	53	53	53
<b>B. CONTRACTUAL RESEARCHERS</b>				
NSIA				
1. Administration	6	6	8	8
2. Schistosomiasis	7	4	1	3
3. Acute Respiratory Infections Project	13	11	17	18
4. Diarrheal Disease Project	11	11	15	10
5. Meningitis	-	3	4	4
6. Cholera	-	6	3	5
<b>C. Contractual Support</b>				
1. Janitorial	14	14	14	14
2. Engineering	28	28	26	28
3. Security	13	13	13	13
<b>Additional Contractual Personnel under the PCRPD</b>				
1. Malaria				7
2. Hepatitis				4
3. Schistosoma				3
4. Cholera				6
5. Leprosy				1
6. GSPD				3

Republic of the Philippines  
 Ministry of Health  
 RESEARCH INSTITUTE FOR TROPICAL MEDICINE  
 Alabang, Muntinlupa, Metro Manila

BUDGETARY RELEASES\*

	1981		1982		1983		1984	
	GP	NSTA	GP	NSTA	GP	NSTA	GP	NSTA
Personal Services	₱1,001,750	₱188,106	₱3,102,684	₱159,060	₱3,118,741	₱918,216	₱3,918,995	₱997,140
Maintenance and Other Operating Expenses	1,796,755	282,730	3,150,000	555,579	3,388,000	518,844	2,710,000	710,860
(B): Special Purpose		20,000		26,600		35,000		50,000
Equipment Outlay	115,000	160,000		111,960	49,600	10,000	26,000	
Capital Outlay	2,000,000							
Sub-total	₱4,913,505	₱651,836	₱6,252,684	₱1,455,199	₱6,556,341	₱1,482,060	₱6,654,995	₱1,748,000
GRAND TOTAL	₱5,565,341		₱7,707,683		₱8,038,401		₱8,403,995	

\* NATIONAL GOVERNMENT - GOVERNMENT OF THE PHILIPPINES  
 NATIONAL SCIENCE AND TECHNOLOGY AUTHORITY

OTHER FINANCIAL SOURCES

Granting Institutions	1981	1982	1983	1984
JICA*	\$250,000	\$250,000	\$250,000	\$250,000
WHO	¥120,000	¥260,000	¥140,000	¥300,000
Edna McConnel	¥150,000	¥150,000	¥150,000	¥150,000
Australian Development Assistance Bureau			A\$ 310,000 <sup>e</sup>	
B O S T I D				\$117,400
Canadian Embassy				₱ 75,000

\* In form of Equipment and Supplies

<sup>e</sup> For a 3-year project

## IV - 4 Departmental Reports

### (1) DEPARTMENT OF PATHOLOGY

The Pathology Department, manned by 4 pathologists and 20 support staff, handles the Histopathology Laboratory, Electron Microscopy Laboratory and the Clinical Laboratory. The three sections, under a department head, function independently and simultaneously with its own set of Laboratory facilities and personnel. Each has its own research program. Moreover, every section offers a distinct service function; namely,

#### 1. Histopathology Laboratory

The section is concerned with performance of autopsy requested from the Clinical Division. Interesting and problematic cases are later discussed during the weekly clinico-pathologic conferences. Forty-four autopsy cases were performed last year. At the same time, surgical specimens from the Institute, as well as referred materials from other institutions, are processed for routine histopathologic examination and for special histologic stains. One thousand thirty eight cases were processed last year.

#### 2. Clinical Laboratory

The section serves as referring laboratory for routine urinalysis, stool examination, routine hematology and blood chemistry for in-patients as well as patients referred by the out-patient service. The section goes on a 24-hour service with on-duty personnel for emergency cases.

#### 3. Electron Microscopy Laboratory

The laboratory is equipped with an H-300 transmission electron microscope, a S-430 scanning electron microscope and several accessory equipments. With a staff of 4 trained electron microscopists and a resident Japanese expert, the laboratory can handle routine tissue processing for transmission and scanning electron microscopy. Two members of the staff have been trained in identifying rotavirus in stool; one in cytochemical techniques in electron microscopy. Two research assistance develop and print electron micrographs, perform micro and macrophotography and prepare transparent slides for conferences. With these available equipments and expertise, the laboratory is engaged in several research activities as well as handles diagnostic cases referred mostly from other medical institutions.



## (2) DEPARTMENT OF IMMUNOLOGY

The Department of Immunology is in-charged of the development of research activities where immunologic technology can be used. It is headed by Dr. Manuel M. Canlas and assisted by four (4) research assistants and one (1) medical laboratory aide. Presently, the department is involved in the use of hybridoma lymphocyte fusion technique to produce monoclonal antibodies against *Schistosoma Japonicum* and the filarial worm Wuchereria bancrofti.

The monoclonal antibody produced would be used to detect specific and cross-reactive antigenic determinants of the above parasites. The analysis of these antigenic determinants are basic in understanding the pathology of the parasitic infection and possible development of diagnostic tools and vaccine against them. The Department has also a cellular laboratory capable of determining mitogen stimulation studies to asses functional immunity of patients. The determination of complement and immunoglobulin levels, rheumatoid factor, antinuclear antibodies, enumeration of T cell and B cell counts are in the process of being developed. The above tests are important in assessing immune functions and pathology. Immunodiagnostic techniques using enzyme linked immunoabsorbent assay (ELISA) to detect infection in schistosoma and filariasis is also being developed.

(3) RESEARCH INSTITUTE FOR TROPICAL MEDICINE  
Department of Epidemiology

A. What projects have been completed by the Department ?

1. A two-year study to determine the etiology of diarrheal disease in the community. This study was done in Alabang, Muntinlupa. It found that Enterotoxigenic E. coli (ETEC) and rotavirus were the leading causes of diarrhea morbidity.
2. A two-year study to define some of the determinants of acute respiratory infections in the community. This study was done in an urban community in Quezon City. It found that important risk factors for ARI include poor housing facilities, crowding and non-compliance with childhood immunization. Malnutrition was an important poor prognostic factor leading to a high case fatality rate.
3. Epidemiologic investigation of paralytic shellfish poisoning (Red Tide) in a municipality in Samar. Investigations showed attack rates to be highest for persons who has eaten muscles during the two month duration of the outbreak. Recommendations for surveillance and prevention were made to the proper authorities.
4. Epidemiologic investigation of a cholera outbreak in an institution for mentally handicapped persons in Alabang. Recommendations for control were made to the proper authorities.

B. What research and training projects are to be undertaken?

1. A two-year intervention study to determine the effect of health education by primary health care workers on the incidence of diarrhea.
2. A two-year study to determine the various etiologies of upper and lower respiratory tract infections.
3. A one-year study to monitor cholera in an institution for the mentally handicapped in order to study the dynamics of transmission.
4. A training programme for field epidemiologists of the Ministry of Health. The possibility that this training programme be set up in cooperation with the Centers for Disease Control, Atlanta, USA is being considered.

C. What services are being planned?

1. The Department is looking to provide in the future:
  - a. Epidemiologic investigation services
  - b. Data management services

(4) DEPARTMENT OF MEDICAL ENTOMOLOGY

Functions, Objectives and Activities 1984-85

1.1. Functions

- 1.11. A research unit of RITM responsible for the study of arthropods as causes and/or vectors of disease
- 1.12. Provides diagnostic services and experimental support systems in infectious disease research
- 1.13. Provides referrals and inter/intra-agency linkages in matters relating to disease prevention and control

1.2. Objectives

- 1.21. To conduct scientific investigations on vector biology and control
- 1.22. To develop laboratory experimental models to facilitate research on chemotherapy and immunology
- 1.23. To collaborate with existing agencies on studies leading towards better understanding of the causation and/or transmission of vector-borne diseases

1.3. Activities

- 1.31. Colonization of selected anopheline species.
- 1.32. Gametocytocidal assay of antimalarials in mosquitoes.
- 1.33. Studies on vector competence of malaria vectors.

1.4. New Technologies Acquired:

- 1.41. Systematics of anopheline mosquitoes — identification of adult and larval stages of malaria vectors.
- 1.42. Laboratory and field technics in medical entomology — collection, handling, rearing and maintenance in the insectary, preparation of permanent reference materials.
- 1.43. Experimental infection of mosquitoes with malarial parasites.

(5) MICROBIOLOGY BRIEFING PAPER FOR JICA MISSION

INTRODUCTION

The present set-up of the Department of Microbiology, i.e. Bacteriology and Virology Units, collects data pertinent to on-going researches on Acute Respiratory Infections, Diarrhea and Meningitis using culture and isolation techniques, sensitivity testing, serotyping, immunofluorescence, ELIS/and IAHA. It also assists clinicians with laboratory results for the early diagnosis of the diseases of patients admitted to RITM and other referring institutions. It also serves as a training unit for diagnostic microbiology particularly infectious diseases of bacterial and viral etiology for personnels in the medical profession.

The department hopes to expand its present capabilities by setting-up facilities for Mycobacteriology, Anaerobic bacteriology, Tissue culture of Chlamydia and Mycoplasma, Mycology and Zoonotic laboratory. Furthermore, it also hopes to develop the technology for the isolation and identification of other viruses; maintenance of cell-lines for the isolation of dengue virus; isolation and maintenance of etiologic agents of zoonotic importance; preparation of bacterial, viral and parasitic antigens for use in immunodiagnosis. To be able to realize these future plans, a staff development program is imperative.

I. Technologies available at start of Institution

Bacteriology

1. Culture isolation of aerobic organism
2. Serology:
  - a. Widal test
  - b. VDRL
  - c. Serotyping of *S. pneumo* and *H. influenzae*
  - d. Biotyping of *H. influenzae*
3. Antibiotic sensitivity testing by disc diffusion

II. Technologies developed during the JICA Technology

Cooperation Project (JTCP)

- A. Bacteriology - additional technology in bacteriology was initiated by Dr. Y. Kaneko with the help of Dr. Akeda and Dr. Arakaki

1. Enteric Bacteriology

- a. isolation of enteric pathogens including campylobacter and yersinia

- b. Serotype identification with enteric pathogens including cholera and shigella
  - c. detection of toxin production of E. coli including LT and ST
2. Technology related to Respiratory Pathogens and Meningitis
- a. Single Radial Complement Fixation test for Mycoplasma (SRCF)
  - b. Culture isolation of B. pertussis
  - c. Bacterial antigen detection in body fluids
- B. Virology - initiated under the direction of Dr. Inoue and followed up largely by Dr. Yamaoka
- 1. Tissue culture for
    - a. Respiratory pathogens
    - b. Herpes virus
  - 2. Serologic Tests
    - a. ELISA for rotavirus detection
    - b. SRCF for Influenza A & B, adenovirus, Parainfluenza, measles and RSV
- C. Immunofluorescence Laboratory
- 1. Immunofluorescence techniques for identification of viral agents such as:
    - a. measles
    - b. rabies
    - c. herpes
  - 2. Indirect immunofluorescence for B. pertussis
- D. Mycology - detection of dermatophytes

### III. Technologies to be developed

- 1. Culture isolation
  - A. Mycobacteriology
    - to isolate and identify Mycobacteria
    - to perform antimicrobial sensitivity tests for Mycobacteria
  - B. Anaerobic Bacteriology
    - isolation of anaerobic microorganisms
    - identification of anaerobes by gas chromatography
  - C. Tissue Culture of Chlamydia and Mycoplasma
  - D. Virology
    - a. To develop the technology for the isolation and identification of other viruses.
    - b. To maintain cell line C6/36 for the isolation of dengue virus

E. Mycology

- a. To develop technology in antigen-antibody detection of systemic mycoses.
- b. To improve technology in identification of fungi using Biochemical tests, animal inoculation.
- c. To do sensitivity testing of fungi.

2. Biological Products

1. Hepatitis B Surface Antigen for reagents purposes
2. Typing antisera for dengue virus using monoclonal antibodies
3. Screening antisera for dengue virus using hyperimmune serum from patients or animals
4. Dengue viral antigen for serology purposes using HI and IgM capture ELISA
5. Typing antisera for enteric pathogens
6. Antisera for identification of rabies virus

3. Molecular Biology

- to develop technology for ETEC detection using DNA probing

MICROBIOLOGICAL SERVICES RENDERED  
FOR PATIENTS & RESEARCH  
JAN. - JUNE, 1984

	<u>In</u>	<u>Out</u>	<u>Total</u>
Culture & Sensitivity	2,586	858	3,444
Viral Culture	101	71	192
AFB Culture	55	1	56
AFB Smear	280	32	314
Fungal Culture	35	33	68
Gram stain	792	462	1,254
India ink smear	280	29	309
CIE	232	0	232
FAT	17	9	26
CRP	260	70	330

(6) Department of Parasitology

The Department is composed of a staff of three M.D.'s, a Ph.D. and a team of research assistants who man the schistosomiasis diagnostic parasitology laboratories.

Activities: Performs routine and specialized parasitological examinations for inpatients, outpatients, and groups of individuals for medical check-up.

Research Projects:

1. Amebiasis/giardiasis study - comparison of various staining techniques in the differential diagnosis of E. histolytica and G. lamblia.
2. The role of intestinal protozoa in the epidemiology of diarrheal diseases in the selected communities.
3. Schistosomiasis research programme.



(7) The Medical Department

I. OPD-ER Complex

A. Emergency Room:

In 1983, a total of 2,691 cases were seen, with a monthly average of 224 cases. Of these, 20% were non-infectious; and of the total, only 13% were really emergency cases. Of the total number of infectious cases seen in 1983, 45% were pulmonary infections, 33% gastrointestinal, and 9% CNS infections.

In 1984 (January to October) a total of 3,118 cases were seen, with a monthly average of 312 cases. An increase of 40% in the total number of consultations was observed. Eighty six percent (86%) of patients seen were infectious in nature, but only 18% were real emergency cases. Forty percent (40%) of the patients had gastrointestinal complaints, 34% had pulmonary problems, and 6.4% had CNS infections.

B. Out-patient Department:

In 1983, a total of 4,866 patients (average = 405/month) were seen. Seventy-nine percent (79%) were infectious in nature, while the remaining 21% had non-infectious problems. Of the infectious cases, from January to October 1984, a total of 4,338 cases were seen, with a monthly average of 434 patients. An increment of 7% was observed during this period. Eighty four (84%) of cases were infectious, and the remaining 18% were non-infectious problems, mostly of RITM personnel and dependents. Almost one half (47%) of all consultations were of pulmonary etiology. There were 590 cases (16%) who had gastrointestinal problems, and 15% with dermatologic complaints. A marked increase of dermatologic cases was observed this year, because of the HANSEN's (Leprosy) Clinic that has just been established. Central nervous system infections accounted for only 3% of cases.

II. In-patients)

A total of 50 inpatient beds including a two-bed ICU are reserved for patients with infectious diseases who require hospitalization. Since the opening of the medical service in 1982, the inpatient census has increased from 250 during the first year to 841 this year. Pediatric infectious disease cases comprise a big majority (70-80%) of all admissions. The leading cases admitted reflect some of the priority research areas being studied which include acute respiratory infections, diarrhea, meningitis, schistosomiasis and malaria.

Summaries of patients census and leading causes of morbidity and mortality are in the attached sheets.

## (8) NURSING DEPARTMENT

### I. PAST ACTIVITIES

1. Manpower development through
  - a. Training of selected nursing staff in the fields of Critical Care Nursing, Pulmonary Therapy, Physical Therapy and Rehabilitation and Operating Room Nursing.  
Done through classroom lectures and on-the-job training.
  - b. Some nursing personnel also enrolled in the masteral program in Nursing Service Administration and in other clinical specialities.
  - c. Periodic conferences in patients care management of selected cases were done.
  - d. On-the-job training of one nursing supervisor as Infection Control Nurse started.
2. Improvement of clinical facilities as in the expansion of the Intensive Care Unit, provision of a 4-bed observation room in the Emergency Room, provision of a separate dining room for patients' watchers and acquisition of more equipment.

### II. NEW EXPERTISE

More nurses were prepared to meet the need for critical care, OR Nursing, Pulmonary Therapy and Physical Rehabilitation

### III. PLANS

1. Continue with manpower development due to turnover of personnel and expanding knowledge in the sciences.
2. Formal education for the infection control nurse in a university program.
3. Hire more personnel to handle increasing patient services.
4. Involve more nurses in research projects.
5. Acquire more new equipment and repair worn-out ones. Present needs include an ambulance, a blood bank, portable x-ray machine, croupettes and oxygen hoods for pediatric and adult patients and many more.

(9) DEPARTMENT/SECTION: Clinical Research Division  
Dietary

PROJECT LEADER: Miss Nieves C. Serra

SUMMARY OF ACCOMPLISHMENT:

DOCTORS

(Rotating Residents and RHPP'S)

Month	Number of Persons	Total Cost
January	131	P 541.66
February	126	498.96
March	155	633.82
April	144	660.16
May	187	771.68
June	222	935.74
July	188	622.93
August	233	851.26
September	228	823.68
October	222	605.61
November	236	832.32
December	216	865.08
TOTAL	2,288	P 8,642.90

DEPARTMENT/SECTION: Clinical Research Division  
Dietary

PROJECT LEADER: Miss Nieves C. Serra

SUMMARY OF ACCOMPLISHMENT:

MOTHER'S CLASS

Month	Number of Persons	Total Cost
April	71	P 17.75
May	164	49.20
June	185	61.05
July	129	43.86
August	193	96.50
September	181	99.55
October	129	83.85
November	145	108.75
December	<u>135</u>	<u>108.00</u>
TOTAL	1,332	P 668.51

DEPARTMENT/SECTION: Clinical Research Division  
Dietary

PROJECT LEADER: Miss Nieves C. Serra

SUMMARY OF ACCOMPLISHMENT:

IN-PATIENT

Month	Number of Persons	Total Cost
January	602	P 2,274.78
February	886	3,351.48
March	849	3,418.28
April	830	3,324.72
May	879	2,979.52
June	989	4,948.03
July	1,164	4,722.61
August	1,717	7,249.88
September	1,530	6,375.18
October	966	3,490.56
November	921	4,180.64
December	<u>1,196</u>	<u>5,293.64</u>
	16,575	P 51,609.32

DEPARTMENT/SECTION: Clinical Research Division  
Radiology

PROJECT LEADER: Vicente V. Romano, M.D.

SUMMARY OF ACCOMPLISHMENT:

IN-PATIENT

1. Number of X-rays done
    - a. Chest . . . . . 593
    - b. Others\* . . . . . 148
- TOTAL            741

OUT-PATIENT

1. Number of X-rays done
    - a. Chest . . . . . 871
    - b. Others\* . . . . . 203
- TOTAL            1,074

\*Other Examination Includes:

A. Special Examination (with Contrast Media)

1. Percutaneous Transhepatic Cholangiogram
2. Endoscopic Retrograde Cholangiography Pancreatography
3. KUB-IVP
4. Esophagogram
5. Biopsy (under fluoroscopy)
6. Upper GI Series
7. Oral Chole
8. Barium Enema

B. Non Contrast Examination

- |                               |                          |
|-------------------------------|--------------------------|
| 1. Extremities; Upper & Lower | 6. Mastoids              |
| 2. Pelvic Girdle              | 7. Paranasal Sinuses     |
| 3. Hip Joints                 | 8. Vertebral Column      |
| 4. Pelvimetry                 | 9. Plain KUB and Abdomen |
| 5. Skull                      | 10. Optic Foramen        |

DEPARTMENT/SECTION: Clinical Research Division  
Pharmacy

PROJECT LEADER : Mrs. Minerva G. Tarrayo

SUMMARY OF ACCOMPLISHMENT:

A. Patient Care

1. In-Patient

a) Number of patients served	820
b) Number of prescriptions filled	<u>22,635</u>
TOTAL	23,455

2. Out-Patient (ER included)

a) Number of patients served	4,292
b) Number of prescriptions filled	<u>6,573</u>
TOTAL	10,865

B. Total Expenditures of Drugs and Medicines (Jan.- Dec. 1983)

a) January	16,670.12
b) February	23,646.58
c) March	24,206.19
d) April	33,663.86
e) May	28,258.22
f) June	38,751.90
g) July	32,270.69
h) August	38,367.68
i) September	49,960.79
j) October	24,849.43
k) November	28,993.65
l) December	<u>28,207.14</u>
TOTAL	P 367,846.25

C. Total Cost of Inventory for Drugs and Medicine

a) Antibiotics	177,934.01
b) Dextrose & Sets	114,139.64
c) Other Medicines	<u>13,504.31</u>
TOTAL	P 305,577.96

DEPARTMENT/SECTION: Clinical Research Division  
Social Services

PROJECT PROPONENT/LEADER: Miss Florivin A. Alfonso

SUMMARY OF ACCOMPLISHMENT:

I. Total number of patients classified . . . . .	3,927
Number of In patient . . . . .	642
Number of Out-patient . . . . .	3,285
II. Total number of Intake Interviews made . . . . .	2,777
III. Total number of referrals made to other hospitals . . . . .	120
Certification for Indigency Assistance . . . . .	120
a. CT Scanning at Makati Medical Center . . . . .	78
b. Electroencephaogram at PGH . . . . .	14
c. VP Shunting at PGH . . . . .	1
d. Thoracostomy at Makati Medical Center . . . . .	1
e. Liver Scanning at Makati Medical . . . . .	1
f. Ultrasonography at UST . . . . .	1
g. Esophagoscopy at PGH . . . . .	1
h. Blood assistance at PNRC . . . . .	3
i. Medicines at MSSD . . . . .	17
Kapwa Ko Mahal Ko, medicines . . . . .	3
TOTAL . . . . .	240
IV. Total number of Transfers/Placements made . . . . .	41
a. Marillac Hills, for unwed mothers . . . . .	2
b. MSSD, Muntinlupa, case-work assistance . . . . .	20
c. Perpetual Help Hospital, SS assistance . . . . .	1
d. Alay Ng Puso, placement . . . . .	1
e. Tala Leprosarium, placement . . . . .	1



f. Makati Medical Center, SS assistance . . . . .	6	
g. PGH, Social Service assistance . . . . .	.8	
	<u>        </u>	
TOTAL	41	
V. Total number of Communications received/responded . . . . .		85
a. Barangay Unit . . . . .	56	
b. MSSD Muntinlupa . . . . .	12	
c. Malacañang Social Service.. .	1	
d. Lung Center, Social Service .	1	
e. NKFP, Social Service . . . . .	5	
f. MSSD Cavite . . . . .	1	
g. AKAF . . . . .	8	
	<u>        </u>	
TOTAL	85	
VI. Total number of Fieldwork activities . . . . .		33
a. Home Visits . . . . .	21	
b. Agency contact . . . . .	12	
	<u>        </u>	
Total	33	
VII. Total number of Personalized Services made. . . . .		3,522
a. Counselling . . . . .	3,419	
b. Discharged planning/Home	<u>103</u>	
Total	3,522	

Total number of patients classified:  
 1. Inpatient: 642

C L A S S I F I C A T I O N										
MONTH	PAY	SEMI	SEMI-	INDIGENT	RESEARCH	PERSONNEL	TOTAL			
:	:	:	:	:	:	:	:	:	:	:
:	:	PAY I	PAY II	INDIGENT	:	DEPENDENT	:	:	:	:
December	: 0	: 0	: 1+4*	: 3 + 4*	: 24 + 3*	: 6 + 2*	: 0	:	:	: 47
November	: 4+5*	: 1	: 2 + 3*	: 6 + 7	: 33+ 4*	: 7	: 1	:	:	: 73
October	: 3+1*	: 0	: 0	: 5+5*	: 28	: 9+2*	: 2*	:	:	: 55
September	: 2+1*	: 0	: 0	: 7+	:	:	:	:	:	:
August	: 2	: 0	: 1	: 8+7*	: 36+7*	: 9+2*	: 2*	:	:	: 70
July	: 3	: 0	: 1	: 6+1*	: 20	: 19+1*	: 3*	:	:	: 55
June	: 0	: 0	: 1	: 3+3*	: 12+4*	: 15+3*	: 1+1*	:	:	: 41
May	: 1	: 0	: 1	: 4+1*	: 9+2*	: 19	: 2+2*	:	:	: 41
April	: 1*	: 0	: 3*	: 8+4*	: 12	: 18	: 1+1*	:	:	: 48
March	: 0	: 1	: 3*	: 3+1*	: 22+3*	: 14	: 2	:	:	: 49
February	: 1	: 0	: 0	: 4+2*	: 17	: 7	: 2	:	:	: 33
January	2+1*	1	3	10	12+1*	3	1			42
	27	3	23	117	239	159	27			TOTAL= 642

2. Out-Patient/Emergency = 3,265.

C L A S S I F I C A T I O N

Month	: PAY : A :	: SEMI- : PAY I : B :	: SEMI- : PAY II : C :	: SEMI- : INDICENT : D :	: INDICENT : E :	: RESEARCH : R :	: PERSONNEL : DISPENDENT : P/SD :	: TOTAL :
December	: 15 :	: 4 :	: 36 :	: 121 :	: 49 :	: 27 :	: 21 :	: 273 :
November	: 17 :	: 14 :	: 46 :	: 163 :	: 101 :	: 27 :	: 43 :	: 421 :
October	: 22 :	: 5 :	: 21 :	: 178 :	: 83 :	: 26 :	: 50 :	: 355 :
September	: 16 :	: 4 :	: 11 :	: 194 :	: 129 :	: 31 :	: 25 :	: 413 :
August	: 12 :	: 14 :	: 28 :	: 123 :	: 67 :	: 18 :	: 24 :	: 285 :
July	: 10 :	: 5 :	: 17 :	: 136 :	: 108 :	: 19 :	: 28 :	: 323 :
June	: 7 :	: 4 :	: 15 :	: 125 :	: 77 :	: 31 :	: 16 :	: 275 :
May	: 12 :	: 3 :	: 13 :	: 103 :	: 56 :	: 13 :	: 12 :	: 204 :
April	: 7 :	: 5 :	: 8 :	: 73 :	: 109 :	: 10 :	: 21 :	: 233 :
March	: 5 :	: 3 :	: 14 :	: 54 :	: 97 :	: 12 :	: 15 :	: 200 :
February	: 4 :	: 2 :	: 20 :	: 58 :	: 60 :	: 9 :	: 10 :	: 163 :
January	: 3 :	: 2 :	: 15 :	: 48 :	: 37 :	: 3 :	: 4 :	: 112 :
	130	67	244	1,381	973	226	274	TOTAL=3,285

(10) DEPARTMENT OF PARASITIC DISEASES

INTRODUCTION

The Department is currently involved in 3 areas of endeavours: laboratory research, field studies and a service area utilizing parasitological diagnostic procedures. Laboratory researches are mainly concerned with the immunology of parasitic diseases especially those aspects of host-parasite relationships established during infection. Field studies involves researches on the epidemiology and methods of intervention of control of parasitic diseases. The service component includes routine parasitological examinations as well as special diagnostic procedures for patients seen in the hospital and outpatients service of the Research Institute.

I. Technology available at the start of the project:

Routine diagnostic procedures

1. direct fecal smears
2. stool concentration techniques
  - a. Acid-ether concentration technique
  - b. Formalin-ether concentration technique
  - c. Merthiolate-iodine-Formaldehyde concentration technique
3. Cellulose tape peri-anal swab
4. Morada-Mori Culture Method for Hookworm

II. Technology developed during the JICA Cooperation Project

A. Immunodiagnostic Procedures

1. circum-oval presipitin test for schistosomiasis
2. Enzyme-linked immunosorbent assay for schistosomiasis
3. Indirect Hemagglutination for amoebiasis

B. Maintenance of Schistosoma japonicum life-cycle in the laboratory

1. Breeding of field-collected Oncomelania, quadrasi snails
2. Isolation of miracidial from infected livers by egg-hatching technique

3. Infection of snails
  4. Isolation of cercarias from infected snails
  5. Loop method of percutaneous infection of rabbit and mice
- C. Schistosoma japonicum adult worm and egg antigen production
1. Perfusion technique for recovery of adult schistosomes from mesenteric vasculature
  2. Drypsin/Pepsin digestion of infected livers and intestines for recovery of eggs
  3. Lyophilization
  4. Dialysis and protein determination (BIORAD assay)
  5. Purification of antigens
- D. Cellular Immunology Techniques
1. Induction of Lymphocyte Blastogenesis by antigens and mitogens (PHA, COM-AO)
  2. Isolation of Peripheral Blood mononuclear cells by Ficoll-Hypaque sedimentation
    - a. isolation of B & T lymphocytes
    - b. isolation of monocytes
  3. In-vitro cultivation of effector cells and target organisms (i.g. schistosomula)
- E. Hybridoma Technology in the production of monoclonal antibodies
1. Propagation of myeloma cell lines
  2. Fusion of NS-1 cell with spleen cells
  3. Maintenance of hybrid cells
  4. Assay for antibody production
- F. Hematoxylin/Eosin Staining of tissues for histopathological examination of schistosome egg granulomas
- G. Inbreeding of BALB/C, C57/BL and Swiss Webster Mice
- H. Stool Culture for Protozoan parasites

I. Special Staining for Amoebas and other protozoans

1. Chlorazol Black E Technic
2. Buffered Methylene Blue Technic

J. Malaria Research (Section of Medical Entomology)

1. Collection of adult and larval mosquitoes from natural habitats
2. Attempts to produce laboratory-bred colonies by natural and artificial mating procedures
3. Standardization of procedures for biting experiments with gametocyte-positive patients
4. Design and fabrication of membrane-feeding device to facilitate in vitro experimental infection.

III. Technology to be developed:

1. Radio immunoassays
2. Fluorescent Antibody Techniques
3. Recombinant DNA Technology
4. Vaccine Development
5. Bio-assay of Malarial gametocytes
6. In vitro cultivation of malarial parasites

(II) ANIMAL RESEARCH LABORATORY  
Research Institute for Tropical Medicine

Activities in the Laboratory

The laboratory is presently staffed by one veterinarian and two animal caretakers who are concerned with breeding, nutrition and care of conventional laboratory animals. As such, the unit maintains an inbred line of Balb/c and C57Bl/6J mice and outbred Swiss Webster mice and Sprague-Dawley rats. The other species of animals including rabbits and guinea pigs are being kept solely for experimentation purposes and not for breeding. Another activity of the unit revolves around provision of comprehensive care for breeders as well as for those being utilized in experimental procedures. The projects being served by the laboratory includes those on diarrhea, cholera schistosomiasis and malaria. Future projects will include dengue, amoebiasis, giardiasis, rabies and hepatitis B.

Future Plans:

Manpower training will be geared to develop a staff trained in the maintenance of non-conventional laboratory animals including specific pathogen free, gnotobiotic and hopefully axenic animals. Other technologies to be acquired are those on laboratory animal genetics and animal nutrition. With the provision of an animal feed mill in the Institute, the quality of nutrition will be upgraded through research.

(12) MEDICAL RECORDS DEPARTMENT

The Medical Records Department, which supervises the Admitting/ Information Section, is at present has the following personnel a Medical Records Officer, a Junior Statistician, three Telephone Operator and two Science Research Aide.

The Department has 12 filling shelves divided into six shelves, which can accomodate 600 records per shelves. At present four of the twelve filling shelves have been filled-up by patient's records. Six remaining shelves are being used for storage of medical records forms.

In 1983, 3,762 patients records have been processed and filled-up as against 3,764 records from January to October, 1984. If we are to project, there will be a 20% increase of patients records that will be processed until the end of this year.

Based from the retention period of 25 years for Medical Records forms there will be no place for incoming records, hence a new trust, to resort to computerization of medical records, not only for safe-keeping but also for accessibility of patient's records most especially the laboratory results of examination performed on patient's which is one of the perennial problems of the department.

Other plans includes the introduction of problem-oriented Medical Records (POMR) and a training in coding of diseases based on the International Classification Diseases by WHO.



## IV - 5 Programmes

### (1) TRAINING PROGRAMS IN THE MEDICAL SERVICE

#### TRAINING PROGRAMME

1. Fellowship training program in infectious diseases and tropical medicine

This two-year program is a joint undertaking of the RITM and the Section of Infectious Diseases, Department of Medicine, Philippine General Hospital (University of the Philippines) and is open to M.D.'s who have finished three years of residency in internal medicine or pediatrics. It incorporates clinical, laboratory and research training under the supervision of the infectious diseases faculty of UP-PGH and RITM.

Since its expansion as a joint undertaking in 1982, a total of four fellows have graduated from the program. Two more trainees are due to finish by the end of December, 1984.

2. Rotating residency program

Since 1982, senior residents in medicine and pediatrics who are interested in short-term training in clinical infectious diseases have rotated in RITM. Affiliate institutions for this program include both government and private hospitals such as National Children's Hospital, Jose Fabella Memorial Hospital, Children's Medical Center, Makati Medical Center and Manila Sanitarium Hospital. More government and regional hospitals are encouraged to participate in this program in the future.

3. Rural health practising physicians (RHPP) program

From July to December 1984, a total of 5 rural health practising physicians were assigned to the Research Institute. These are medical graduates awaiting the results of the Professional Regulations Commission Board Examinations.

While training at the research institute for 3 months, these graduates will be able to contribute to the improvement of community health care delivery by providing means for better and accurate diagnosis and management of infectious and tropical diseases.

While rotating at the Muntinlupa Health Office for 3 months, these medical graduates will be exposed to the implementation of the primary health care program in a typical rural health unit.

The RHPP's will rotate 3 months at RITM, and 3 months at the Muntinlupa Health Office.

## (2) ELECTRON MICROSCOPY TRAINING PROGRAMME

### TRAINING PROGRAMME

#### 1. Fellowship:

Through the JICA assisted program, the Institute sent a pathologist for a training course in basic electron microscopy in Japan in 1981. In 1984 the same pathologist was sent to Japan to further his training on the application of electron microscopy in the different on-going projects.

#### 2. Training Courses in the Department:

##### 2.1. Title of the course: Biomedical Application of Transmission and Scanning Electron Microscopes.

This is a six-month training course started in 1982 with Dr. Yosimichi Kozuka, a Japanese technical expert as the training officer. The course consists of lectures and laboratory sessions aimed at providing the necessary knowledge on the basic principles and operation of electron microscopes and accessory equipments, the theoretical and practical aspect of specimen preparation and interpretation of electron micrographs. The first course was composed of trainees from the different departments of the Institute and provided the core group proficient in the preparation and examination of specimen for electron microscopy. Subsequent courses included trainees from other institutions. At present ten (10) participants, three from the University of the Philippines are undergoing such training.

##### 2.2. Title of the Course: Scientific Photography

This is a three-month training course with the primary objective of providing manpower among research personnel in documenting research materials for conferences. The training officer Dr. Yosimichi Kozuka emphasizes close-up and macrophotography, light microscope photography and preparation of slides for presentation. The first course offered last summer attracted 18 registrants from the different departments. Seven completed the course. At present two of them are working in our photography section developing and printing of electron micrographs and preparing transparent slides for scientific conferences.

### (3) TRAINING PROGRAM IN TROPICAL DERMATOLOGY

At present there are seven physicians who are training in dermatology who come to the Institute every Monday. These doctors are exposed to the facilities of the Institute specifically in the laboratory bacterial, viral, fungal and parasitic infections. They are taught the proper technique of obtaining specimens from patients for inoculation into different culture media. Special emphasis is given to doing skin biopsies and smears for acid-fast bacilli.

The doctors are encouraged to attend relevant clinical conferences and participate in discussions. They also see patients confined in the hospital with dermatologic problems. In the afternoon, a skin clinic is open to the community for out patient consultations in infectious dermato-ogic disorders. This clinic provides a venue for training in clinical evaluation and management of tropical skin diseases.

#### (4) NURSING TRAINING PROGRAMME

##### SUMMARY OF ACCOMPLISHMENT:

1. March to May 1983 - three nurses sent to Makati Medical Center for Pulmonary Therapy Training
2. Weekly clinical conferences on nursing needs and intervention of selected patients
3. October 1983 to January 1984 Lecture series (2 hrs/week) on critical care nursing including ECG taking and interpretation, arrhythmias, etc.
4. November to December 1983 - Lecture series on care of patients (pedia and adult) with pulmonary problem
5. November 7-18, 1983 - Training in Operating Room Nursing at Singian Hospital. Attended by 3 nurses and 1 midwife
6. Three nurses among the Staff are pursuing graduate studies at the UPCM towards masters in Nursing, expenses personally shouldered by the said nurses.
7. Monthly conferences with supervisors and headnurses in matters related to administration and supervision
8. On-thejob training of one nursing, supervisors as infection control nurses. She acts as secretary to Infection Control Committee also.
9. Participation of nurses and other nursing personnel in different sports activities of RITM and of the Philippine Nurses' Association
10. Participation by some nurses in conferences on the Psycho-social aspects of patient care-once a month

(5) PERSONNEL DEVELOPMENT PROGRAMME

SUMMARY OF ACCOMPLISHMENT:

	<u>No. of Personnel</u>
1. Course Career Executive Service Development Program of the Development Academy of the Philippines	1
2. 5-day non-residential Civil Service Counsellor's Course at the Technological University of the Philippines	1
3. Seminar Workshop on Research Management at the University of the Philippines at Los Banos	1
4. In-vitro testing of chloroquine sensitivity in Plasmodium falciparum malaria cases training	1
5. Diagnostic research techniques in Parasitology Institute of Public Health Training	1
6. Course in Electron Microscopy in Japan	1
7. Training in Clinical Pharmacy in Japan	1
8. Principles and Application of Problem Oriented Medical Records	30
9. Seminar on Performance Appraisal System	30
10. Basic Statistics Seminar	15
11. Workshop on Clinical Aspects & Control of Diarrheal Diseases	5

(6) SCIENTIFIC PHOTOGRAPHY TRAINING COURSE

A course in Scientific Photography, a three-months training course which consists of lecture/workshop (2 session/week) started first week of April. Registrants endorsed by the Head of the different Departments of the Institute totalled 18:2 regular medical research staff, 6 rotating medical residents and 10 laboratory research staff.

Application of photography to science is the primary objective of the course. For its specific objectives techniques on the following are included in the relevant to scientific researches: 1) close-up macrophotography 2) light microscope photomicrography 3) preparation of transparent slide for presentation.

A camera unit is required for every registrant to assure individual participation in the workshop. Photographic materials/supplies needed in the course are available at the Dept. of Pathology through the able support of Dr. Y. Kozuka (JICA, consultant) who is also the principal trainer.

(7) The Diarrheal Disease Research Program

Mediaroa C. Saniel, M. D.

I. Objectives

- A. To study the epidemiology of diarrheal diseases among Filipino children in the community and to determine the causes of these illnesses
- B. To determine the clinical and laboratory features of diarrhea secondary to bacterial, viral and parasitic agents in hospitalized children, and to evaluate the laboratory procedures used for identifying enteropathogens.
- C. To develop a comprehensive health education program for the community as an intervention strategy for controlling diarrhea, and to develop mechanisms for evaluating such a program
- D. To develop and evaluate modified solutions for oral rehydration in the treatment of diarrhea

II. Past and Current Activities

A. Researches

1) Epidemiology

A two-year community-based study describing the patterns of disease, risk factors and etiologies of diarrhea in infants and young children has just been completed. In addition, a hospital-based study of etiologic agents and clinical features of pediatric diarrhea was recently published. The attached reports give summaries of the etiologies of diarrhea in these two researches. A review of diarrhea cases in RITM is ongoing.

2) Laboratory

An ongoing project which aims to compare the specificity and sensitivity of the following laboratory procedures for rotavirus detection is nearing completion: ELISA using the Rotazyme and WHO Kits, electron microscopy and immune electron microscopy. In addition the detection rate is compared when rectal swabs vs. stool specimens are tested.

B. Manpower Development and Acquisition of New Technology

- 1) In the detection of diarrhea pathogens, the following procedures and tests have been adopted:

1. Rotavirus

- a) antigen determination in stools using ELISA and RPHA
- b) electron microscopy (direct and IEM)
- c) serology using complement fixation and IAHA

2. Bacteria

- a) routine identification of Salmonella, Shigella, Campylobacter jejuni, Yersinia, enterocolitica, vibrios, Aeromonas, Plesiomonas, and EPEC
- b) ETEC identification using infant mouse assay for stable toxin and RPLA for labile toxin
- c) EIEC detection using the Sereny test

3. Parasites

- a) E. histolytica
  - b) G. lamblia
- } refer to report of Department of Parasitic Diseases

## 2) Manpower Development

Drs. Inoue, Nunoue and Kudoh visited RITM as short-term consultants under the auspices of JICA to introduce and transfer technologies in relation to rotavirus and enterobacteriaceae identification.

Pe Leano and Dr. Marilla Lucero were trainees in ICDDR-B Dacca in microbiology and epidemiology related to diarrheal diseases.

## III. Future Plans

### A. Researchers

#### 1) Intervention Program

A three-year community-based program for diarrheal disease control focused on promotion of breastfeeding, improved weaning practices and personal and domestic hygiene will start in January, 1985.

#### 2) Epidemiology

The factors in transmission of disease due to ETEC in the community will be studied. Sero-epidemiologic research on rotavirus infection has been started.

#### 3) Clinical Trial

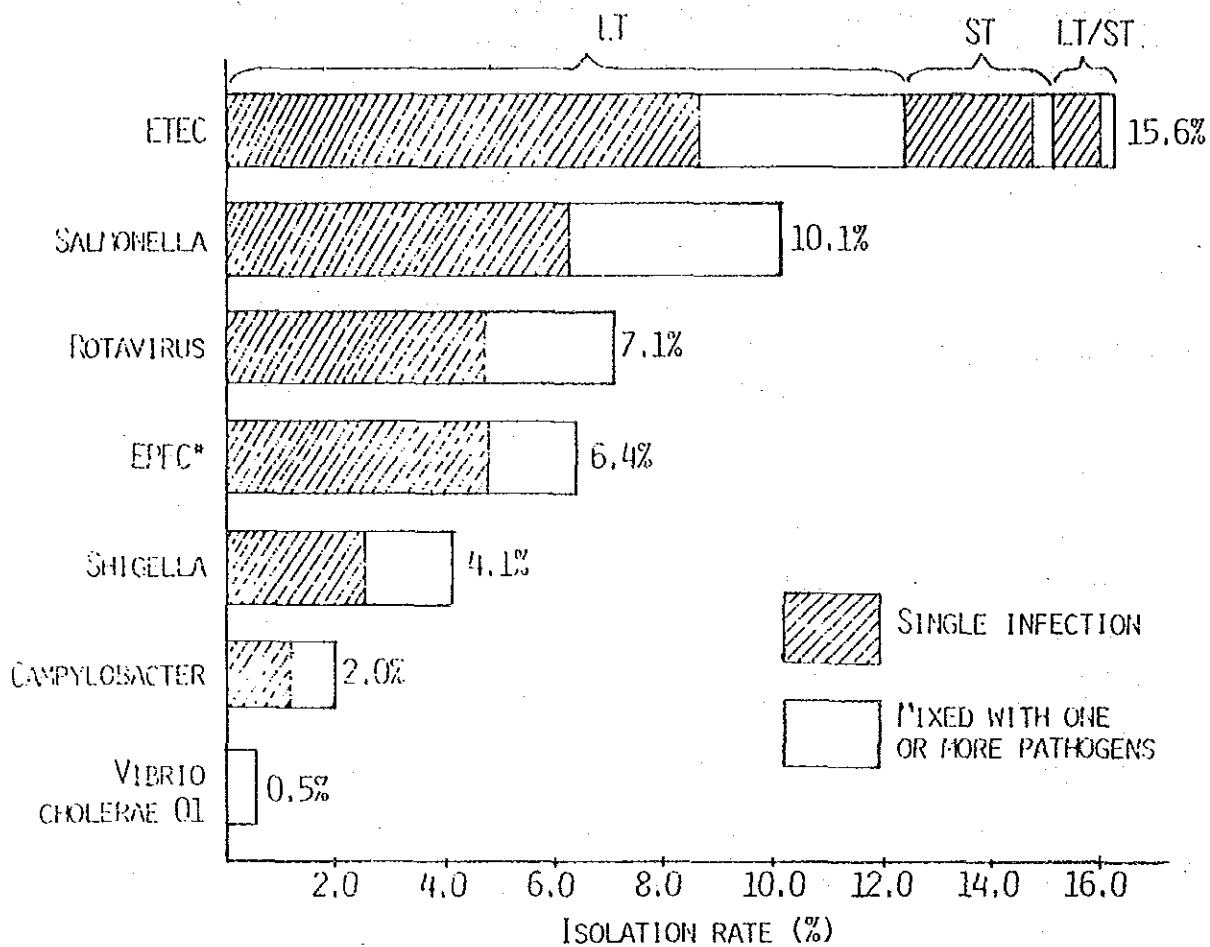
The efficacy of an oral home-made solution (rice-water) in preventing the development of moderate to severe dehydration in pediatric diarrhea will be evaluated.

### B. Manpower Development and New Technology

Capabilities to do the following laboratory procedures will be developed:

- 1) Environmental microbiology, including analysis of water and food specimens for fecal contamination and specific enteropathogens
- 2) Procedures involved in investigating bacterial foodborne diseases, including those due to *Clostridium perfringens* and *Bacillus cereus*, and antibiotic-induced pseudomembranous colitis such as identification of *C. difficile* and its toxin in stools
- 3) Other rapid tests for identifying ETEC including the Biken test, ELISA and use of DNA probes
- 4) Production of diagnostic antisera and reagents
- 5) Rotavirus isolation by tissue culture techniques and electrophoretic analysis
- 6) Phage typing of *Vibrio cholerae* and some of the enterobacteriaceae
- 7) Identification of new parasitic agents such as *Cryptosporidia*





PATHOGENS ISOLATED FROM 556 STOOL SPECIMENS  
OBTAINED FROM CHILDREN WITH DIARRHEA IN ALABANG  
(JULY 1982 - JULY 1984)

\*311 SPECIMENS WERE TESTED FROM CHILDREN < 3 YEARS

Isolation Rates of Enteric Pathogens in National Children's Hospital  
from Cases and Controls, June 1982 to May 1983

Pathogen	Cases n = 422 (%)	Controls n = 326 (%)	p Value
*Rotavirus	17	7	p < 0.001
Salmonella	18	20	/ NS
†ETEC	9	7	NS
‡EPEC	5	2	NS
E histolytica	4	0	p < 0.001
Shigella	1	2	NS
V cholerae	2	0	p < 0.01
G lamblia	1	0	NS
C. jejuni	1	0	NS
Yersinia	0	0	-

\* 620 cases and 517 controls tested

† 193 cases and 167 controls tested

‡ 150 cases and 130 controls tested

/ NS = not significant

(8) Acute Respiratory Infection Research Project

Theлма E. Tupasi  
ARI Study Group

SUMMARY OF ACCOMPLISHMENTS:

In the descriptive phase of the study of ARI, attack rates for ALRI was highest in the age group 1 - 4 years followed by infants under 1 year. Risk factors in the occurrence of ARI was analyzed in these children. Low socio-economic state, crowding and lack of DPT vaccine were significant risk factors in this population.

In 473 children less than 5 years admitted at the QCGH, Case Fatality Rate (CFR) was significantly higher in malnourished children compared to well nourished children. In malnourished children prognosis was worse if the children had either prolonged illness prior to hospitalization and/or complicating factors associated with illness. Bacteria pathogens were isolated in the majority of these children and H. influenzae and/or S. pneumoniae were predominant organisms isolated. These organisms were present alone or in combination in approximately 78.8% to the patients. Previously observed higher mortality rates due to ARI in developing countries as compared to developed countries had been attributed primarily to a bacterial etiology in the majority of cases in the former compared to viral etiology in the latter. Having identified the high risk population group to or children under 5 years belonging to low socio-economic status, we plan to investigate more precisely the etiology of ARI in this population and to relate it with other risk factors, clinical presentations and clinical outcome.

PRESENT ACTIVITIES:

1. Study on Etiology of Acute Respiratory Infection (ARI) in Childhood

This is a 2 year study consisting of a community-based and hospital-based study on ARI. All children under 5 years of age consulting at the out-patient department for moderate ALRI and those admitted into the hospital

for severe ALRI have been enrolled in the study. The patients shall be investigated for etiology of their illness. Accordingly, the following examinations shall be done:

1. Blood culture
2. Virological studies on respiratory secretion including:
  - a). virological cultures
  - b). detection of viral antigens by ELISA and IF test
3. Bacteriological studies on body fluids including:
  - a). Washed Quantitative culture of respiratory secretions
  - b). Bacterial antigen detection in body fluids
4. Quantitative C-Reactive Protein

In a random sample of Alabang Barangay, a subset of children under 5 years of age shall be monitored for the occurrence of acute lower respiratory infection. In case ALRI occurs, respiratory secretions and blood, if feasible, shall be obtained for etiologic examinations similar to those described for in-patients. Additionally, a sero-epidemiologic survey shall be done semi-annually to detect new cases in the monitored population using SRCF kits for RSV, Influenza A and B, Parainfluenza 1, 2, and 3, and Adenovirus.

## 2. ARI Project in Bohol

The ARI study group is lending technical support to the ARI Research team in Bohol. Briefly, the ARI Project in Bohol aims to evaluate the feasibility and impact of the implementation of an ARI Control Programme which consists of: improved case management at all levels, immunization, and health education of the community. The impact will be measured by the mortality reduction in children under 5 years of age.

(9) Project on Vaccine Preventable Diseases

Marilla Lucero, M.D.

SUMMARY OF ACCOMPLISHMENT:

A sero-epidemiology of measles was undertaken in an urban poor community in Quezon City. The result of the HI antibody survey (Table I) indicates that 70% of children by age 2 years and 65% of children by age 1 year had positive titers. No measles immunization was administered in this community.

Schick testing to determine immunity to diphtheria indicates a coverage by childhood immunization of at least 20 - 30% of the target population.

PRESENT ACTIVITIES:

The role of measles and pertussis in the causation of severe lower respiratory infection (ALRI) shall be studied in patients under 5 years of age admitted at the RITM. All patients shall be investigated for pertussis by means of:

- 1). culture on B-G for Bordetella Pertussis
- 2). Immunofluorescence detection of B. pertussis

A control group of patients with mild to moderate ALRI shall be similarly studied.

Patients with measles rashes shall be investigated for measles by:

Immunofluorescence test to detect measles in urine.

The case fatality rate in patients with severe ALRI admitted at RITM will be determined and compared in the following subsets:

- 1). ALRI with measles
- 2). ALRI with pertussis
- 3). ALRI without measles or pertussis

Table I - Hemagglutination Inhibition (HI)  
Antibody against Measles in children  
under 5 years in an urban slum population

Age	No tested	HI-antibody		Cumulative (%)
		No.	(%)	
0-5 m.	1	0	(0)	(0)
6-11 m.	19	7	(36.8)	(35.0)
1 year	26	17	(65.4)	(52.2)
2	40	28	(70.0)	(60.5)
3	55	43	(78.2)	(67.4)
4	45	40	(88.9)	(72.6)
T o t a l	186	135	(72.6)	

(10) Meningitis Among Filipinos: Clinical Features, Diagnosis and Management

Lita C. Vizconde, M.D.

SUMMARY OF ACCOMPLISHMENT:

The clinical profile of gram negative patients admitted to Research Institute for Tropical Medicine with diagnosis of meningitis were evaluated.

The different etiologic agents causing acute suppurative meningitis and their antibiotic susceptibility patterns were analyzed and used as basis for subsequent antibiotic recommendations.

New laboratory techniques, like CIE and quantitative CRP, were set to improve identification of causative agents.

Table I - Etiologic Agents in Bacterial Meningitis

	Number	(%)
<i>S. pneumoniae</i>	18	30
<i>H. influenzae</i>	14	23
<i>Salmonella</i>	7	11
<i>A. lwoffii</i>	3	5
<i>S. epidermidis</i>	3	5
<i>S. aureus</i>	2	3
<i>E. coli</i>	2	3
<i>Proteus specie</i>	2	3
<i>A. faecalis</i>	2	3
<i>E. cloacae</i>	2	3
<i>Klebsiella sp.</i>	2	3
* Others	5	8
T o t a l	61	

\* One each of *P. aeruginosa*, *M. kengii*, *F. meningosepticum*, *C. typhimurium* and *N. meningitidis*.

(II) H E P A T I T I S

Evelyn Dy, M.D.

The Hepatitis Study Group is a recent addition to the activities of the R.I.T.M. It was started on July 1983 with the approval of the project "Local HBsAg production for Research and Vaccine Use."

Hepatitis B virus infection is a major problem in the Philippines is that 60% of adult population have been exposed and about 8-22% are HBsAg (+) carriers. As shown by foreign and local studies, HBV also plays an important role in the development of hepatocellular carcinoma.

The control of HBV infection in the country would entail the use of great quantities of reagents and expensive vaccines. At present the cost of these reagents and vaccines is too high for use in a mass scale. Local production of HBsAg would bring down the cost of these reagents and vaccines to a manageable level and would also promote more opportunities for research.

I. PRESENT ACTIVITIES:

1. Sero-epidemiological survey of Vigan, Laguna, Batangas, Cebu, Roxas City. This will help us determine the pool size of the source by establishing the following:

1. age prevalence of HBsAg positivity
2. rate of sero-conversion from positive to negative
3. incidence rate of carrier stage.

PRELIMINARY RESULTS OF SERO-EPIDEMIOLOGICAL  
STUDY OF VIGAN CITY

Total Number of Samples----868

Number of samples of age group 21 - 50 years	----	298
Number of samples (+) for sAg (RIA)	43/298 =	14.8%
Number of males tested (21-50)	-----	163
Number of male (+) sAg (RIA)	24/163 =	14.7%
Number of female tested (21-38 yrs.)	-----	127
Number of female (+) sAg (RIA)	19/127 =	14.9%
Number of samples with HBsAg with titer <sub>2</sub> ≥ 9-10	-----	7/43 = 16.28%
Number of samples with HBsAg with titer <sub>2</sub> ≥ 11	-----	15/43 = 34.88%

II. Collection of HBsAg + plasma from PNRC and commercial blood banks.

While establishing the HBsAg<sup>+</sup> pool size from identified rural communities, collection of HBsAg<sup>+</sup> plasma from PNRC and commercial blood banks has been started. This will insure us enough materials for the pilot study on purification and recovery of HBsAg from local sera.

FUTURE PLANS

1. Pilot study of purification and recovery of HBsAg by early

next year.

This activity will need the advice and guidance of a Japanese consultant on this field, to ensure that the right technology is applied since the cost of running an ultracentrifuge is too high and enough HBsAg<sup>+</sup> plasma for purification process takes time to collect.

2. Local production of reagents - RPHA, PHA to provide commercial blood banks with low cost reagents for screening.
3. Local production of vaccines.
4. Vaccination of newborns from HBsAg(+) mother and also mass vaccination of susceptibles in the communities.

### III. EQUIPMENTS NEEDED:

1. Plasmapheresis unit - this will enable us to collect more HBsAg<sup>+</sup> plasma while preserving the much needed RBC of the donors.
2. Ultracentrifuge exclusive for hepatitis use.
3. Chromatography column

### IV. Space for Expansion of the hepatitis laboratory.



## (12) Leprosy Research Project

Roberta C. Romero, M.D.

### SUMMARY OF ACCOMPLISHMENT:

A protocol for the evaluation and management of patients with leprosy was established among institutionalized patients and those found in the community around Alabang. Appropriate anti-leprosy medications were given and regular follow-up patients was done to boserve for drug toxicity or leprae reactions. Initial laboratory work-up also included processing of biopsy specimen for electron microscopy studies.

One hundred fifty-eight patients so far have been recruited in the study with the following types of Leprosy:

Paucibacillary	=	38
Multibacillary	=	120
Total		<u>158</u>

Of these 32 patients have completed the Drug Regimen and have been released from control.

Dr. Masahide Abe, Director of National Institute for Leprosy Research visited RITM and expressed willingness to help set-up serologic studies in Leprosy.

### New Technologies and Expertise Acquired

1. Acid fast staining of skin smears and histopathologic specimens
2. Electron microscopic method for morphologic evaluation of *M. leprae* bacillus and after therapy.

### Plans for future activities:

1. To establish a laboratory method to detect antibody levles against *M. leprae* using the Fluorescent Leprosy Antibody Absorption Test (FLA-Abs) of Dr. Masahide Abe.
  - 1.1. Train a medical technologist with Dr. Abe at the National Institute for Leprosy Research in Tokyo, Japan.
  - 1.2. Acquire reagents and equipment needed to run test.
  - 1.3. Hire the appropriate personnel for seroepidemiologic studies.

(13) Schistosomiasis Project  
RITH RESEARCH IN SCHISTOSOMIASIS  
Department of Parasitic Diseases  
Remigio Olveda, M.D.

Research activities in schistosomiasis are divided into 2 areas: laboratory research and field studies on the control of schistosomiasis japonica. Laboratory researches are mainly concerned in the study of the immunology of the disease especially those aspects of host-parasite relationships established during infection. During earlier phases of research, we initiated the maintenance of the life-cycle of *S. japonicum* by alternate passage of the infection in laboratory animals (mice and rabbits) and field-collected oncomelania quadrasi snails. Subsequent to this, we also started maintaining inbred strains of BALB/c, C57/BL and Swiss Webster mice as well as the laboratory breeding of O. quadrasi snails to facilitate the maintenance of the life-cycle of the parasite.

The earlier researches conducted included the study of the natural course of *S. japonicum* infection in BALB/c mice. Innate and non-specific resistance to the infection was also studied by determining in vitro killing of schistosomula by normal monocytes. The study was further extended to investigate the role of macrophages from peritoneal exudate cells of mice and rats in the killing of schistosomula. Follow-up investigations concerning the ultrastructural changes which occur during interaction mononuclear phagocytes and schistosomula were also done. At present, we are studying the mechanisms of schistosomula killing by the mononuclear phagocytes using both electron microscopy and assay of biochemical mediators from supernates cultures.

WE are evaluating suppressor splenic cell activity in patients with advanced hepatosplenic schistosomiasis japonica undergoing elective splenectomy. We are using cell mixing experiments to assess the effect of mitomycin-C treated spleen cells on antigen and mitogen-induced <sup>3</sup>H-thymidine incorporation of responder cells.

Cell purification procedures are being done to determine the actual suppressor splenic cell population by nylon-wool adherence technique and rosetting of neuraminidase-treated sheep erythrocytes. Such suppressor splenic cell population may modulate splenic and peripheral blood lymphocyte responses in patients with hepatosplenic schistosomiasis.

As another aspect in immunology research, we are currently demonstrating adoptive transfer of modulation of granuloma formation and hepatosplenic disease in murine schistosomiasis japonica by serum from chronically infected humans. In this study, the course of the disease is being examined and other disease manifestations are being evaluated. This is to find out whether granuloma formation and hepatosplenic disease can be suppressed by serum from infected humans.

Field studies in the control of infection are also being undertaken using the drug praziquantel. We are currently in our last year of treatment and follow-up of patients in three communities in Leyte. Field-related activities include the regular collection of O. quadrasi snails in Oriental Mindoro.

Very recently, we started research on the production of monoclonal antibodies using hybridoma technology against the different life-cycle stages of S. Japonicum. A sterile tissue culture room has been established for this purpose. Work has been going on despite the lack of facilities such as: laminar flow hood and inverted microscope inside the sterile room. We hope to acquire such equipments in the near future. We are presently working using an improvised sterile bench and so far, tissue culture work has progressed quite well.

(14) DEVELOPMENT OF MONOCLONAL ANTIBODIES AGAINST  
SCHISTOSOMA JAPONICUM AND WUCHERERIA BANCROFTI

Manuel M. Canlas, M. D.

Overall Objective:

This proposal is designed to utilize hybridoma monoclonal technology to get monospecific antibodies against the different stages of S. japonicum and to analyze on a molecular level the antigenic structures from the different life-cycle stages of the parasite.

Specific Aims:

1. Production of monoclonal antibodies against distinct developmental stages of S. japonicum (cercariae, schistosomula and adult worms).
2. Use of these monoclonal antibodies to identify and isolate relevant antigens which stimulates protective immune responses.
3. Use of these monoclonal antibodies to identify antigens unique and common to the different stages of the parasite.

Summary of Accomplishment:

At present, the cell culture laboratory has been semi-equipped with the essential equipment and materials for tissue culture work. Studies in the production of monoclonal antibodies against Schistosoma japonicum have already begun with the initial propagation of NS-1 myeloma cell lines. The research staff involved in the investigation are now in the process of fusion of myeloma cells with spleen cells from immunized animals to produce the hybrid cell. Subsequent cloning of hybridomas and assay of supernatants for antibody production are some of the major activities in the near future.

(15) MALARIA RESEARCH PROJECT

ACTIVITIES:

1. Experimental infection of mosquitoes with malarial parasites involving:
  - 1.1 Periodic collection of malaria vectors from natural habitats.
  - 1.2 Maintenance of laboratory -bred colonies under insectary conditions.
2. Assessment of gametocytocidal action of antimalarials in experimentally infected mosquitoes.
3. Malariometric survey of selected endemic communities for mass drug administration with primaquine as a supplemental control strategy in malaria including G6PD study.

SUMMARY OF ACCOMPLISHMENTS:

1. Experimental Infection of Mosquitoes with malarial parasites. December 1, 1983- 1985

Larvae of *Anopheles litoralis* were collected from salt-water beds in Las Pinas paranaque area. These were held in white enamel pans with saline water and fed a 1:1 mixture of sustagen and Tetramin (fish food food preparation). Adult mosquitoes which hatch from these larvae under insectary conditions of 25-26 degrees centigrade and 75-85% relative humidity were fed on cotton wads soaked in 5-10% sugar solution with supplemental vitamins.

Current activities include observation on longevity of adults, blood feeding and induced mating technic to establish laboratory -bred colonies and in preparation for experimental infection.

2. Glucose 6Phosphate Dehydrogenase Deficiency in Hospital Patients with Malaria and in a Malaria Endemic Community. December 1, 1983- November 30, 1984.

Prevalence of G6PD deficiency in Eastern-Central Luzon Provinces in the Philippines is 2.3-15.3%, 5.26 in 76 Malaria patients, 3.95% in 76 non-malaria patients. Future activities include completion of target number of hospital patients (174) control (174), and community (161) assays using Heinz body test as screening Method.

Table I Prevalence of G6PD Deficiency in Hospital Patients with Malaria

Hospital	Total No. of Subject	No. of Deficient	%
V. Luna	51 (15 Vivax) (36 Falciparum)	3 (2 F) (1 V)	6.12
RITM	24 (10V) (14F)	1 (V)	3.85
JAYONILLO Clinic	1 (vivax )		
TOTAL	76	2(F) 2(V)	5.26

Table II. Prevalence of G6PD deficiency in OPC and in-patients without Malaria

Hospital	Total no. of subject	No. Deficient
V. Luna	9	0
RITM	12	0
UERMMC	6	3
Javonillo Clinic	9	0
APARRI	12	0
UP-PGH	28	0
TOTAL	76	3(3.95%)

Table III. PREVALENCE OF G6PD DEFICIENCY IN A MALARIA ENDEMIC COMMUNITY

PROVINCE	COMMUNITY	NO. ASSAYED	% OF TOT. POP.	DEFICIENT No. %
Quezon	Dibut Bay	218	98%	5 2.3
Rizal	Calawis	51	51/518	7 13.7
	St. Joseph	41	41/227	3 15.3
	Mainit	13	13/267	2 7.3
Isabela	Diadi	16		0
TOTAL		339		2.3-15.3

(16) ULTRASTRUCTURAL RESEARCH PROGRAM  
Normando Gonzaga, M.D.

A. Completed Institutional And Collaborative Researches:

1. Interaction between Normal Human Blood Monocytes and Schistosomula of *Schistosoma japonicum*: An Ultrastructural Study. (See Appendix A) - awarded first prize for senior category in the Dean Proceso Gabriel Award by the Philippine Society of Pathologists in February, 1983; presented at the 3rd Asia-Pacific Conference on Electron Microscopy held at the National University of Singapore in August, 1984 and subsequently published in its proceedings.
2. Ultrastructural Studies of the Cyst Wall of *Sarcocystis* Spp. in the Philippine Carabaos. - a collaborative study with the College of Veterinary Medicine, Univ. of the Phil. and published in the Phil. Journal of Veterinary Medicine, Vol. 23, No. 1.
3. Light and Electron Microscopic Studies of Pituitary Gonadal Differentiation in *Tilapia nilotica*. - another collaborative research presented by Prof. Annabelle Herrera for her doctoral dissertation at the Univ. of the Phil., College of Arts and Sciences last June, 1984.

B. On-going Projects:

1. Ultrastructural Studies on Schistosomiasis. (See Appendix B).
2. Comparative Mucosal Studies in Health and Disease: Profile of Secretory Immune and Enzyme System in Normal, Acute and Chronically Infected Small Intestine. A Light, Electron Microscopic, Immunohistochemical and Tissue Enzyme Study. (See Appendix C for preliminary EM findings).
3. Comparison of Direct Electron Microscopy, Immune-electron Microscopy, Rotazyme and WHO-ELISA for Detection of Human Rotavirus. (See Appendix D).

C. On-going Collaborative Researches with UP-PGH Study Groups:

1. A Comprehensive Study of Glomerulonephritis in the Philippines by Means of Multidisciplinary Approach.
2. A Study of the Evolution of Optic Neuritis Caused by Ethambutol in Rabbits.



(17) COMPARATIVE MUCOSAL STUDIES IN HEALTH AND DISEASE:  
PROFILE OF THE SECRETORY IMMUNE AND ENZYME SYSTEMS  
IN THE NORMAL ACUTE AND CHRONICALLY INFECTED SMALL  
INTESTINES

A LIGHT MICROSCOPIC IMMUNOHISTOCHEMICAL AND TISSUE  
ENZYMES STUDY B

\*EXPANDED BIOPSY STUDY PROTOCOL (STUDY A)  
REMOVABLE INTESTINAL TIE: ADULT RABBIT DIARRHEA  
MODEL FOR CHOLERA AND ETEC INFECTION STUDY B

Marietta C. Baccay, M. D.

Accomplishments:

A total of 76 healthy volunteers (no symptoms with and without parasites) have been screened and thirty biopsies taken. Data now being presented are from 22 small intestinal biopsies.

The visual impressions of the normal range of mucosal morphology includes an irregular villus morphology in almost all biopsies: Villi being wider, leaf, lobed or ridged in proximal biopsies and finger-like, branching and narrower in more distal biopsies. The enterocytes lining the free portion of the villi are columnar with parallel to nuclei with intact villus tips and uniform discrete microvilli tips on EM. Migrating plasma cells or neutrophils. Roughly 2-3/20 enterocytes (1 visual field) are counted. In some biopsies artifactual villus hemorrhage not seen in basal mucosa give wide and shorter villi. Lamina propria cellularity when prominent is made up of small and medium size lymphocytes with frequent eosinophils and in frequent to rare plasma cells. Basal glands (5/oil power field) contribute to most of basal mucosal diameter. In the younger subjects, prominent lymphoid nodules make the basal mucosa wider. Brunner type glands above lamina muscularis mucosa when included in the biopsies from proximal duodenum.

More data is needed to establish the relationship of parasitism socio-economic background (T.4) to mucosal morphology. So far by our light microscopic parameters no consistent correlation is noted.

Biopsies from diarrhea cases: 2 Cholera patients in their second to third day of infection and one Giardiasis case showed in 2/3: high migrating WBC counts and wide basal glands and sub-glandular diameters. Free villus height is not so dependable parameters because of the range and consistency of values obtained.

Table : THE SPECTRUM OF NORMAL FILIPINO SMALL BOWEL MUCOSA VERSUS OTHER NORMALS

PARAMETER	FILIPINO BIOPSIES (Non-diarrheic)	NIHON Range	WESTERN DATA
Free villus height	220 - 480 u 84 % of cases (16/19) 220 -372 u	289 - 403 u 338 (M)	
Villus Width/Height Relationship	Width 24-40% of height	(-)	Width 25% of height (Whitehead)
Basal gland Diameter	102.5-352.5 u 85% of cases (12/14)-100-252 u 57% of cases (8/14)-202-252 u	152-186 u 177 (M)	(-)
Basal gland/Villus Height relationship	1:1-3	(-)	1 - 5 Whitehead
Sub-glandular mucosal diameter	21.7-126 u 61.3% of cases (8/13) -21.7-58 u	computed 60 u	(-)
WBC/100 enterocytes	5-42/100 94.7% (18/19)	(-) 5-32/100	8-40/100 Whitehead

(18) Research Institute for Tropical Medicine

CENSUS

1982 (Feb-Dec) : 1983 (Jan-Dec.) : 1984 (Jan-Oct.)

A. In-patients -

Infectious 0-2 yrs.	105	321	433
2-5 yrs.	41	84	127
5-14 yrs.	33	74	108
Above 14	71	162	173
Non-infectious	0	0	0
Total	<u>250</u>	<u>641</u>	<u>841</u>

B. Out-patient Department

Infectious	2,155	3,826	2,615
Non-infectious	785	1,035	705
Total	<u>2,940</u>	<u>4,861</u>	<u>4,320</u>

C. Emergency Room

Infectious	708	2,224	2,668
Non-infectious	170	467	454
Total	<u>878</u>	<u>2,681</u>	<u>122</u>

10 Leading Causes of Morbidity at  
OPD

February-December 1982			January-December 1983			January-October 1984		
	Cases	%		Cases	%		Cases	
1. Upper respiratory infection	305	10	1. Acute respiratory infection	933	19.2	1. Acute respiratory infection	487	
2. PTB	120	4.2	2. Pneumonia	4-6	8.35	2. Pneumonia	330	
3. Parasitism	86	3	3. Acute gastroenteritis	230	4.7	3. PTB	246	
4. Bronchopneumonia	83	2.8	4. Pulmonary TB	229	4.7	4. Bronchitis	143	
5. Influenza	76		5. Primary complex	205	4.2	5. Tonsillopharyngitis	128	
6. Acute gastroenteritis	62	2.1	6. Bronchitis	176	3.6	6. Hansen's Disease	124	
7. Bronchitis	58	2.0	7. Measles	134	2.7	7. Parasitism	111	
8. Systematic viral infection	49	1.7	8. Tonsillopharyngitis	89	1.8	8. Measles	76	
9. Primary complex	43	1.5	9. Parasitism	88	1.8	9. Acute gastroenteritis	75	
10. Typhoid fever	41	1.4	10. Urinary tract infection	67	1.37	10. Urinary tract infection	62	

10 Leading Causes of Morbidity (Inpatients)

February-December 1982		January-December 1983		January-October 1984	
				Cases	%
1. Pneumonia	19.9%	1. Pneumonia	29.9%	1. Pneumonia	238 28
2. Acute gastroenteritis	15.6	2. Suppurative meningitis	10.6	2. Acute gastroenteritis	105 12
3. Typhoid fever	8.8	3. Acute gastroenteritis	6.1	3. Cholera	74 12
4. Cholera	6.6	4. T.B. Meningitis	5.6	4. Measles	49 .08
5. Measles	4.0	5. Hemorrhagic/Dengue Fever	4.2	5. Suppurative Meningitis	30 .04
6. Acute protracted viral infection	3.2	6. Typhoid Fever	3.3	6. Sepsis Neonatorum	27 .03
7. Fever of unknown origin	1.6	7. Sepsis Neonatorum	2.7	7. Meningitis	24 .028
8. Schistosomiasis	1.6	8. Tetanus	2.7	8. TB Meningitis	20 .02
9. Tetanus	1.6	9. Viral encephalitis	2.0	9. Malaria	19 .02
10. TB Meningitis	1.6	10. Cholera	1.7	10. Tetanus	17 .01

10 Leading Causes of Morbidity at ER

1. Gastroenteritis	152	17.3	1. Acute gastro-	646	24	1. Acute gastro-	782
2. Bronchopneumonia	75	8.5	2. Acute respiratory tract infection	360	13.4	2. Bronchopneumonia	456
3. URTI	36	4.1	3. Bronchopneumonia	316	11.4	3. AURI	315
4. Diarrhea	30	3.4	4. Meningitis	137	5.1	4. Pulmonary tuberculosis	172
5. Measles	29	3.3	5. Measles	105	3.9	5. Meningitis	117
6. Typhoid Fever	17	1.9	6. Acute tonsillopharyngitis	86	3.2	6. Infectious Diarrhea	111
7. Cholera	12	1.3	7. Hemorrhagic Fever	74	2.7	7. Measles	85
8. Bronchealitis	10	1.1	8. Urinary tract infection	50	1.9	8. Acute tonsillopharyngitis	68

9. FUD	10	1.1	9. Bronchitis	54	1.3	9. Urinary tract infection	66
10. Meningitis	9	1.0	10. Hepatitis	30	1.1	10. Amoebiasis	54

10 Leading Causes of Mortality (In-Patients)

<u>February-December 1982</u>			<u>January-December 1983</u>			<u>January-December 1984</u>		
1. Broncho-pneumonia	9	3.6	1. Pneumonia	37	42.5	1. Bronchopneumonia	43	
2. Diphtheria	2	0.8	2. Suppurative Meningitis	10	11.5	2. Measles	19	
3. Septicemia/peritonitis	1	0.4	3. Tetanus	7	8.1	3. Acute Gastro-enteritis	13	
4. Encephalopathy probably viral encephalitis	1	0.4	4. TB Meningitis	7	8.1	4. Sepsis Neonatorum	6	
			5. Acute gastro-enteritis	6	7.1	5. Infectious Diarrhea	5	
			6. Sepsis neonatorum	4	4.6	6. Suppurative Meningitis	4	
			7. Septicemia	3	3.4	7. Tetanus Neonatorum Metabolic Acidosi Rabies	3	
			8. Encephalitis	2	2.3	Pneumonia	3	
			9. Disseminated intravascular ocagulation	2	2.3	8. Encephalitis Meningitis	2	
			10. Diphtheria	1	1.2	TB Meningitis	2	

CAUSES OF MORTALITY AT ER

March to December 1982	January to December 1983	January to July 1984
1. Pneumonia (2)	1. Measles/Bronchopneumonia (2)	1. Diarrhea with severe dehydration (3)
2. Vehicular accident (2)	2. Severe dehydration 2° acute gastroenteritis (1)	2. Measles with severe dehydration (1)
3. URI with malnutrition (1)	3. Meningococemia (1)	3. Intestinal obstruction (?) (1)
4. Diarrhea (1)	4. Meningitis (1)	4. Congestive Heart disease (1)
5. MI (1)	5. Septicemia (1)	5. Cervical CA (1)
	6. Pneumonia (1)	
	7. Acute CHF (1)	
	8. MI (1)	
	9. Cardiac arrest (1)	
	10. DOA - undetermined cause (2)	

## V - 6 Training Programmes in 1982

### TRAINING PROGRAMMES 1982

#### 1. LABORATORY RESEARCH DIVISION

##### 1. NATIONAL WORKSHOP ON RESEARCH DESIGN AND METHODOLOGY IN BIOMEDICAL AND HEALTH SERVICES RESEARCH (August 24th- September 2nd, 1982)

This workshop was undertaken to develop research capabilities of the senior staff of the Ministry of Health in order for them to provide leadership in promoting a scientific approach to clinical and public health problems. Participants were divided into: 1) bio-medical research including clinical research; and 2) health services research including behavioral research.

The workshop aimed 1) to develop knowledge and skills in bio-medical, clinical research and health services research, utilizing a methodology which is scientifically sound and appropriate to the work and resources and 2) formulate, plan and draft protocol proposals for scientific research review board of international standards. The participants included the Senior Technical personnel of the Ministry of Health and related institutions, Regional health Directors, representatives of neighboring countries, participants from the PCHRD and some observers. The course director was Dr. Daniel Dennis, Epidemiologist, WHO Regional Centre for Research and Training, Institute of Medical Research, Kuala Lumpur, Malaysia.

##### 2. BASIC AND ADVANCED PHOTOGRAPHY COURSE FOR RESEARCH PERSONNEL

A three-months course in basic photography, darkroom, macro-photography and photomicrography techniques was held in June-August 1982 with 15 registrants: 6 from the RITM Research Staff, 5 from the Medical Staff of affiliate institutions and 4 personnel dependents. The course methods included lectures with hand-outs, audio-visual presentations, and wet clinics with a faculty from the Professional Photographer's Association of the Philippines. The course was funded by participants or their sponsoring institutions, and the NSTA.

##### 3. EM TRAINING COURSES IN TRANSMISSION AND SCANNING ELECTRON MICROSCOPY.

A six-month regular training program was started in the 3rd quarter of 1982 with eight trainees (3 research assistants, 3 research specialists, 1 consultant, 1 rotating resident from an affiliate hospital) with the objective of training more personnel in ultrastructural research. The training provided necessary knowledge on 1. basic principles and operation of the electron microscope and accessory equipments; 2. theoretical and practical aspects of specimen preparation; and 3. interpretation of the electron micrograph and



correlation with the results obtained by light microscope. At present 6 of these trainees have a working knowledge on electron microscopy and are working on research projects.

Most of the trainees shall have completed requirements in April. Problems initially encountered have been resolved by a JICA funding of the course supplies and materials. A second course shall start late this second quarter. Subsequent courses would include use of the scanning electron microscope.

#### 4. PATHOLOGY /RESIDENCY TRAINING

The University of Santo Tomas Hospital, Division of Anatomic Pathology, an affiliate hospital sent a resident who has undergone rotation in RITM, Department of Pathology and has trained in electron microscopy and special staining techniques.

### II. CLINICAL RESEARCH DIVISION

#### 1. FELLOWSHIP IN INFECTIOUS DISEASES AND TROPICAL MEDICINE

Currently there are five second year and two first year fellows undergoing training under the integrated program of the RITM and UP-PGH Section of Infectious Diseases. This two-year program involves clinical, research and laboratory training relevant to the objectives of the Institute.

#### 2. ROTATING RESIDENCY PROGRAM

Since January 1983, senior residents at the second and third year levels from the Department of Medicine, Makati Medical Center and the Department of Pediatrics, Jose Fabella Memorial Hospital have been assigned to the Institute for a two-month subspecialty rotation in infectious and tropical diseases. The plan is to extend this rotating residency program to other affiliate institutions in the near future. During this rotation, residents are trained in the systematic approach to the diagnosis and management of infectious and tropical diseases.

#### 3. PROGRAM FOR RURAL PRACTISING PHYSICIANS (RHPP'S)

In September 1982 the Institute started a program for RHPP's. In addition to activities directed towards primary health care in the different health centers of Muntinlupa as organized by the municipal health office, the RHPP's are also assigned to assist in the management of cases seen in the OPD, Emergency Room and in-patient facilities of the Institute.

#### 4. NURSING DEPARTMENT

In 1982, efforts of the department were directed towards preparing its personnel for effective clinical nursing. Most of its personnel were on their first experience in hospital nursing. Hence, the need for post-basic training. This included the following activities.

1. Selected nurses were sent to PGH and Lunsod ng Kabataan for training in critical care nursing both for adults and pediatric patients. While these nurses learned from their experiences they still expressed the need for longer and more intensive training program along this line.
2. On October 20-22, 1982, Mrs. W. Estimoso, acting supervisor was sent to a Seminar-Workshop on Clinical Management of Diarrheal Diseases. This was sponsored by the MOH and conducted at the San Lazaro Hospital. An echo-seminar, with emphasis on the use of Oresol in the management of patients with diarrhea, was held at RITM afterwards.
3. Weekly clinical conferences on the nursing management of patients with various tropical diseases were conducted.
4. A bi-monthly conference among the chief nurse, supervisors and head nurses was conducted to thresh out problems in management and supervision as well as improve their skills and knowledge in this field of work.
5. To augment the staff in the OR, 5 nursing aides underwent training in OR nursing particularly on the duties and responsibilities of scrub nurses. This group of aides will form part of the nursing pool from which "on-call" personnel needed for surgical procedures will be taken.
6. Three nurses were sent to Makati Medical Center for a three-month training in Pulmonary Therapy in answer to RITM's need for pulmonary therapists. An echo-seminar will be conducted by them sometime in 1983 for the benefit of the other RITM nurses.

#### III. ADMINISTRATIVE DIVISION

##### 1. SEMINAR/WORKSHOP ON MONITORING AND EVALUATION FOR RITM PROGRAMS/PROJECTS

A seminar/workshop on monitoring and evaluation was conducted by NEDA on March 17 and 18, 1983 at the Conference Room of RITM.

Director Jesus Enriquez discussed the Project Development Cycle, its various aspects as planning, programming, implementation, monitoring and post-evaluation; Mrs. Teodora B. Reyes lectured on Indicators and Target Setting for Planning and Implementation; Engr. Evaristo Varela, Jr. introduced Program Evaluation and Review Technique (PERT) and Critical Path Method (CPM). Workshop on PERT/CPM was supervised by Engr. Varela where participants were presented different cases to work on. Forty-two personnel representing different sections/departments attended the seminar/workshop.

## 2. PERFORMANCE APPRAISAL

In pursuant to the Civil Service Commission's Memorandum Circular re: IMPLEMENTATION OF THE NEW PERFORMANCE APPRAISAL SYSTEM (NPAS) a seminar/workshop was conducted by the Civil Service Commission to the department/section heads of the Research Institute for Tropical Medicine on August 16 and 17, 1983. Ms. Maria Luisa I. Aberin and Ms. Maria Teresa Sison, both Civil Service Commission representatives, lectured the minimum requirements to be observed in the establishment of the performance appraisal plan.

## IV. PERSONNEL DEVELOPMENT PROGRAMMES

### JICA STUDY AND TRAVEL GRANTS

DR. M. CARPIO-BACCAY - Head, Department of Pathology went on an individual observation and study tour of Pathology and Electron Microscopy Laboratories and Animal Research Centers in Tokyo, Fukuoka and Okinawa, Japan from August 17 to September 26, 1982.

DR. MARGARITA M. GALON - Deputy Executive Director went on an individual observation and study tour of Research Centers and Institutes in Tokyo, Fukuoka and Okinawa, Japan. Emphasis of tour was on Research Administration: October to December, 1982.

MS. CLEOTILDE TORRES - Science Research Specialist IV presently in Japan training in Virology: December 2, 1982 to December 13, 1983.

### WHO FELLOWSHIP AND TRAVEL GRANTS

MRS. FE LEANO - Science Research Specialist III Attended the Inter-Regional Training Course on Diarrheal Diseases, Laboratory aspects: March 3-26, 1982, ICDDR, Dacca, Bangladesh.

- Dr. Marilla Lucero - Medical Specialist I Attended the Inter-Regional Training Course on Diarrheal Diseases, Epidemiologic aspect, September 20-October 1, 1982, ICDDR, Dacca, Bangladesh.
- Ms. Bella Almario - Science Research Specialist III Attended a National Training Course in Biostatistics and Epidemiology, October 3-16, 1982, Kuala Lumpur, Malaysia.
- Dr. Ofelia Calubiran - Head, OPD and Emergency Section Attended the WHO workshop on Immuno-pathology of Parasitic Diseases, September 1 -October 15, 1982, Lusanne, Switzerland.

#### V. NATIONAL WORKSHOPS

1. THE PHILIPPINE BIOCHEMICAL SOCIETY 1982 SEMINAR-WORKSHOP SIMPLIFIED LABORATORY TECHNIQUES IN BIOCHEMICAL INSTRUCTION AND RESEARCH, JUNE 1-4, 1982, UNIVERSITY OF THE PHILIPPINES AT LOS BAÑOS, LAGUNA.

Participants: Minda A. Teleg, M.D.  
 Angelita de las Alas  
 Rebecca M. Marquez  
 Fe M. Flores

2. NATIONAL WORKSHOP ON DESIGN AND METHODOLOGY IN BIOMEDICAL AND HEALTH SERVICES RESEARCH:

Participants: Drs. R. Carreon-Romero  
 R. Olveda  
 M. Saniel  
 L. Vizconde

3. WORKSHOP ON CONCEPTS AND DYNAMICS OF RESEARCH MANAGEMENT - U.P. AT LOS BAÑOS, FEBRUARY 14-25, 1983.

Participant: Dr. M. Margarita M. Galon

RESIDENTS ROTATING AT RESEARCH INSTITUTE  
FOR TROPICAL MEDICINE

COPY FOR Dr. Tupasa

1983

- |                      |   |  |
|----------------------|---|--|
| JANUARY TO FEBRUARY  | - | 1. MMC - Dr. Alfredo Bisnar<br>2. MMC - Dr. Belen Matias<br>3. JFMH - Dr. Guillerma Castillo   |
| MARCH TO APRIL       | - | 1. JFMH - Dr. Susan Aduana<br>2. MMC - Dr. Celerino Magbuhos<br>(up to 1st wk. of April)<br>3. POLY - Dr. Josephine Tan<br>(started on April 18) |
| MAY TO JUNE          | - | 1. POLY - Dr. Josephine Tan<br>(up to June 15)<br>2. MMC - Dr. Estrella Lopez<br>3. JFMH - Dr. Evelyn Cordero<br>(started in June)               |
| JULY TO AUGUST       | - | 1. MMC - Dr. Thelma Dimalanta<br>2. JFMH - Dr. Eunice Bucsit<br>3. MLA. SAN. - Dr. Jesse Guadiz  |
| SEPTEMBER TO OCTOBER | - | 1. MMC - Dr. Eloisa Pastores<br>2. JFMH - Dr. Elvira Santos<br>3. MLA. SAN. - Dr. Ruth Sombilon<br>(started in October)                          |
| NOVEMBER TO DECEMBER | - | 1. JFMH - Dr. Vivian Lofranco<br>2. MMC - Dr. Greg Tan<br>3. MLA. SAN. - Dr. Ruth Sombilon   |

TOTAL/YEAR = 16 rotating residents

JANUARY TO FEBRUARY

- 1) Makati Medical Center  
Dr. Sonia Alarcon  
Dr. Emelyn Abundo-Rivera
- 2) Mariano Marcos Memorial Hospital  
Dr. Estrella Abundo
- 3) Children's Medical Center  
Dr. Daisy Gonzales
- 4) National Children's Hospital  
Dr. Editha Miguel
- 5) Jose Fabella Memorial Hospital  
Dr. Lea Dilag

MARCH TO APRIL

- 1) Children's Medical Center <sup>Qtr</sup>  
Dr. Daisy Gonzales (up to March)
- 2) National Children's Hospital  
Dr. Florida Senen
- 3) Manila Sanitarium Hospital  
Dr. Elizabeth Fajardo
- 4) Makati Medical Center  
Dr. Rebecca Littaua
- 5) Jose Fabella Memorial Hospital  
Dr. Felino Fernandez
- 6) Children's Medical Center <sup>April</sup>  
Dr. Beatriz Marquez (up to June)

MAY TO JUNE

- 1) Children's Medical Center  
Dr. Beatriz Marquez
- 2) Makati Medical Center  
Dr. Estela Zagala Cabrera
- 3) Jose Fabella Memorial Hospital  
Dr. Marilyn Guzman
- 4) National Children's Hospital  
Dr. Myrna Valencia

RESIDENTS ROTATING AT RESEARCH INSTITUTE  
FOR TROPICAL MEDICINE 1984

JULY TO AUGUST '84

- 1) Children's Medical Center  
Dr. Thaddeus Evangelista
- 2) Makati Medical Center  
Dr. Ma. Ramona N. Pablo
- 3) Jose Fabella Memorial Hospital  
Dr. Emma Cortez (up to July)
- 4) National Children's Hospital  
Dr. Jose Merencilla, Jr.
- 5) Manila Sanitarium Hospital  
Dr. May Ann Segovia-Lao (up to Sept.)

SEPTEMBER TO

October '84

- 1) Makati Medical Center  
Dr. Marivyl Javato
- 2) National Children's Hospital
- 3) Children's Medical Center (up to Sept.)  
Dr. Thaddeus Evangelista
- 4) Manila Sanitarium Hospital (up to Sept.)  
Dr. May Ann Segovia-Lao
- 5) Children's Medical Center  
Dr. Ana Cruz (start - October)

NOVEMBER TO

DECEMBER '84

- 1) Makati Medical Center  
Dr. Eriberto Esguerra
- 2) Children's Medical Center  
Dr. Rosa G-Lim
- 3) National Children's Hospital  
Dr. Ana Ma. Cruz (up to Nov. 15/84)

## IV - 7 Abstracts of Completed Researches

### APPENDIX A

#### INTERACTION BETWEEN NORMAL HUMAN MONOCYTES AND SCHISTOSOMULA OF SCHISTOSOMA JAPONICUM: AN ULTRASTRUCTURAL OBSERVATION

Normando C. Gonzaga, M.D.; Remigio M. Olveda, M.D.; Bernadette dL. Libranda, M.Sc.; Marietta C. Baccay, M.D.; and Yosimichi Kozuka, Ph.D.

Recent studies had shown that different effector cells such as eosinophils, neutrophils and mononuclear phagocytes can mediate in vitro damage and killing of schistosomula, the post-penetration larval stage of schistosomes. Ellner and Mahmoud (1), using the schistosomula of Schistosoma mansoni as target organisms demonstrated the schistosomulocidal activity of normal human monocytes independent of specific antibody, complement and macrophage activation. Olveda et al (2), using schistosomula of S. japonicum as target organisms, were able to show the same capacity of normal monocytes to kill schistosomula in vitro. There has been no ultrastructural studies to show changes that occur during the course of interaction of monocytes and schistosomula in culture. The present study describes such changes in both effector cells and target organisms at different time points of incubation.

Schistosomula obtained by the cercarial penetration of isolated mouse skin were suspended in RPMI-1640 supplemented with 10% heat inactivated fetal calf serum and adjusted to a final concentration of 2,000 organisms/ml. Peripheral blood mononuclear cells (PBMC) were isolated by Ficoll-Hypaque centrifugation of heparinized blood from normal donors. PBMC suspensions in RPMI-1640 were adjusted to a final concentration of  $5 \times 10^6$  cells/ml. Adherent mononuclear cells consisting of 90-95% monocytes were prepared by two sequential incubations of the PBMC in 1.6 mm microtiter plate wells for 1 hr at 37°C in 5% carbon dioxide. Non-adherent cells were discarded and the plates washed with sterile Hank's balanced salt solution. Fifty ul of uniformly suspended schistosomula (100 organisms) were added into each tissue culture plate well of adherent mononuclear cells incubated at time intervals of 1, 6, 12 and 24 hours. Samples from quadruplicate wells were pooled and processed for transmission electron microscopy at the end of each time point of incubation. Glutaraldehyde (2.5%) in cacodylate buffer was added to the samples and these were centrifuged at 2,000 rpm for 15 min. The pellets were fixed for 2½ hours at 4°C using the same 2.5% glutaraldehyde-cacodylate buffer solution. Post-fixation was done in buffered 2% osmium tetroxide. Fixed specimens were dehydrated in graded series of ethanol and embedded in Spurr's low viscosity Epoxy resin. Ultra-thin silver sections were obtained using a Sorvall MT-2B ultramicrotome. The sections were then stained with uranyl acetate and lead acetate and examined under the Hitachi H-300 transmission electron microscope. Semi-thin sections of 0.5 u were also obtained, stained in methylene blue and examined with a light microscope. Control schistosomula and control

1. J. Ellner & A. Mahmoud: J. Immunol., 123, 949, (1979).
2. R. Olveda, B. Libranda & L. Acosta: J. Grad. Res., 13, 115, (1983).



monocytes separately incubated in culture media were maintained at the same time point intervals and processed similarly as the experimental groups.

Control monocytes were readily identified by the large bean and U-shaped or irregularly lobed nucleus having cloddy chromatin condensed along the nuclear membrane. Also observed were the irregular finger or tongue-like processes, "short" profiles of ergastoplasm and small electron-dense granules. Sections of control schistosomula showed well-delineated layers of amorphous surface covering, tegument, connective tissue; outer circular and inner longitudinal muscle layers covering the internal structures. The tegumental membrane covered the entire surface of the schistosomula and was observed as pentalaminar although trilaminar structures in several regions still remained. At 1-hour incubation, monocyte orientation towards the schistosomula was noted with some sections showing close apposition of the monocytes with the schistosomula but with no visible damage appreciated. Partial loss of amorphous substance overlaying the tegument of schistosomula was noted. Sections obtained from samples incubated for 6 hours revealed intimate contact of the monocytes (e) with schistosomula (t) and disclosed areas of membrane fusion (x) between the target organisms and effector cells (Fig.1). Vacuole formation and the presence of a number of amorphous and electron-dense ingested particles were observed in the monocytes. Partial to complete damage of the schistosomula tegumental membrane was seen at 12 hour incubation period. Monocytes appeared to be more vacuolated with the presence of enlarged electron-dense bodies. At 24 hour incubation, loss of the entire tegument was noted in several schistosomula. Monocyte pseudopods (p) were seen attached and fused with the basal connective tissue layer of the target organism (Fig.2). In contrast, control schistosomula from 1 to 24 hour incubation showed no appreciable damage in the tegument. Control monocytes likewise did not show any related structural changes during incubation. Our ultrastructural observations revealed a progressive damage to the schistosomula by the monocytes starting at 1 hour to 24 hours of incubation. This study provides ultrastructural evidence of schistosomula damage by monocytes despite the formidable size of the target organisms.



FIGURE 1



FIGURE 2