No. 4

タイ国国立衛生研究所プロジェクト
最終評価専門家チーム調査報告書

平成6年6月

国際協力事業団
医療協力部

タイ国国立衛生研究所プロジェクト
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国際協力事業団
医 療 協 力 部

序　文

本プロジェクトは、タイ国内に流行する各種の感染症、寄生虫症等の対策を講じるために、これら分野の研究能力の向上及び人材の養成を目的として、昭和60年８月１日から５年間にわたり開始されたものである。

プロジェクトはおおむね順調に進捗、当初協力期間中に基礎的な部分の技術移転についてはほぼ当初の目標を達成したが、研究促進のために２年間にわたり協力期間を延長し、さらに一部の課題の確実な目標達成のため、引続き２年間のフォローアップ協力期間を実施中である。

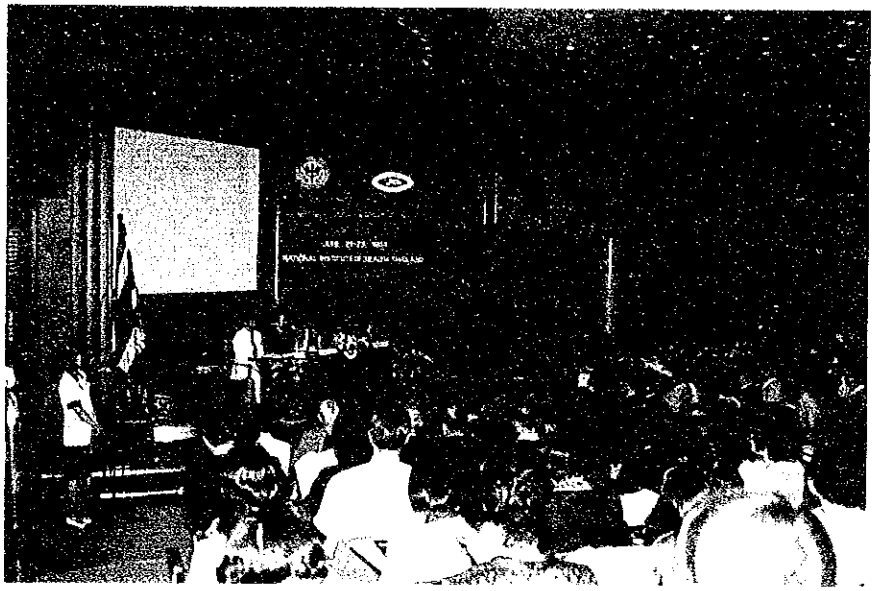
今般、上記フォローアップ期間が平成６年７月末に終了するのを前に、その間のプロジェクトの実績、活動状況をタイ側とともに評価し、あわせて今後の協力のあり方について協議することを目的として、山崎修道国立予防衛生研究所長以下の最終評価専門家チームを派遣した。

本報告書は、上記チームが行った調査、タイ側との協議等の内容及び結果をとりまとめたものである。

ここに、本件調査にご協力いただいた関係各位ならびに今次調査団員、及び本件技術協力のために永年にわたりご支援ご協力を賜った関係各位に深甚なる謝意を表する次第である。

平成６年６月

国際協力事業団
医療協力部長
小早川　隆敏



94. 6. 21
記念セミナー開講式、
山崎評価チーム・リーダー、
プラコーブ前保健省事務次官、
パンヤDMS局長

94. 6. 21
記念セミナー開講式後記念撮影

94. 6. 22
記念セミナー第二日目質疑応答

94. 6. 24
ＮＩＨプロジェクト終了式、
山崎評価チーム・リーダー、
ソンポップＮＩＨ所長、
金井ＮＩＨプロジェクト・
リーダー

94. 6. 24
ＮＩＨプロジェクト終了式、
日本国大使館熊本書記官、
バンヤＤＭＳ局長、
浅野ＪＩＣＡタイ事務所次長

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記念植樹、
村田プロジェクト国内委員長

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1．最終評価専門家チーム派遣の経緯と目的

1.1　派遣の経緯と目的

タイ国政府は、自国内に流行する各種感染症、胃腸疾患、寄生虫症等に対処するための衛生研究活動を行う研究機関の設立について我が国に無償資金協力及び技術協力を要請し、これを受け、我が国は1984、1985両年度にわたり、無償資金協力により建物建設及び機材供与（1984年度24.5億円、1985年度14.6億円）を実施した。これに時期を合わせ、本プロジェクトは、上記分野の研究能力の向上、人材養成のために1985年８月から５年間にわたりプロジェクト方式技術協力を開始したものである。

プロジェクトの目的は、①タイ国内に流行する感染症に係る研究能力の向上、②これら感染症の抑圧に必要な生物製剤の研究開発、③各部門間の共同利用施設の利用体制の強化等である。

当初協力期間終了に先立ち、1989年12月プロジェクトの実績評価のための調査団を派遣し、プロジェクトの活動状況、当初目標の達成状況等についてタイ側との間で協議・検討した結果、「各分野とも基礎レベル技術移転はほぼ終了段階を迎えているが、その応用・展開としての研究は開始されたばかりである（1989年２月タイ国国立衛生研究所プロジェクト評価調査団報告書より引用）」。この評価結果を踏まえて、研究技術の応用、自主的な研究テーマの選定、タイ側スタッフ相互間の研究交流促進等について、1990年８月１日から２年間にわたり協力を延長した。

さらに、延長期間終了前の1992年２月に、評価専門家チームを派遣した結果、以下のような結論に至った。

「全般的に見て、２年間の技術協力の延長に際して取り決められたＲ／Ｄの条項に従い、ＮＩＨにおける研究推進のプロジェクトは順調に進行しつつあり、大部分の目標は期間内に確実に達成できる見通しが得られた。しかしながら、一部の課題については必ずしも延長期間内に達成しうる見通しが得られず、さらに継続支援が必要と認められる（平成４年３月評価専門家チーム調査報告書より引用）」

この評価に基づき、1992年８月１日からさらに２年間、次の４課題についてフォローアップ協力を実施することとなった。

(1)　デング出血熱

(2)　メリオイドーシス（類鼻疽）

(3)　腸内感染

(4)　実験動物

なお、これら４課題は新たに設定されたものではなく、既にそれまでの実績があり、さらに２年間の協力継続によって一層の発展が期待され、技術移転の定着が確実になると判断されたものである。

以上のような背景のもとに、本最終評価専門家チームは、1994年６月フォローアップ期間におけるプロジェクトの実施状況及び実績の評価を目的として派遣されたものである。

本プロジェクトについては、「第三国研修」要請が保健省から技術経済協力局（ＤＴＥＣ）に提出されていることもあり、今後の協力のあり方についても協議することとした。

また、評価の一環として同専門家チームの派遣中にプロジェクト終了記念セミナーを開催することとし、後述のとおり７名のセミナー講師を派遣した。また、プロジェクト終了式まで、本プロジェクト国内委員長である村田良介元国立予防衛生研究所長の同行を得た（ＪＩＣＡ外経費負担による派遣）。

1.2　プロジェクト評価専門家チーム構成

担　当	氏　名	所　属
団長（総　括）	山崎　修道	国立予防衛生研究所長
		ＮＩＨ国内委員
団員（生物製剤）	高橋　理明	大阪大学微生物病研究所名誉教授
		ＮＩＨ国内委員
団員（ウイルス学）	五十嵐　章	長崎大学熱帯医学研究所教授
団員（細　菌　学）	渡辺　治雄	国立予防衛生研究所細菌部長
団員（運営管理）	富田　明子	国際協力事業団医療協力部医療協力第一課職員
団員（協力計画）	慶野知恵子	国際協力事業団医療協力部計画課職員

1.3　調査日程

日　順	月　日	曜	移　動　及　び　業　務
第１日	６／19	日	移動　成田・福岡→バンコク
2	20	月	タイＪＩＣＡ事務所、日本国大使館表敬・打ち合わせ
			ＤＴＥＣ表敬、保健省医科学局長表敬、Ｃ／Ｐと合同評価
3	21	火	プロジェクト終了記念セミナー
4	22	水	〃
5	23	木	〃
6	24	金	Steering Committee
			プロジェクト終了式
7	25	土	Phutawan視察
8	27	日	〃
9	27	月	タイＪＩＣＡ事務所、日本国大使館へ報告
10	28	火	移動　バンコク→成田・大阪

1.4 主な面会者

(1) タイ側

① Dept. of Medical Sciences (DMS)

Dr. Panya Sonkom	Director General
Dr. Panadda Silva	Director, Technical Coordinating Center

② NIH

Dr. Nadhirat Sangkawibha	Honorable Consultant
Dr. Sompop Ahandrik	Director (Deputy Director General, DMS)
Dr. Chuinrudee Jayavasu	Senior Expert
Dr. Paijit Warachit	Principal Medical Scientist
Dr. Mayura Kusum	Director, Div. of Clinical Pathology
Ms. Suranga Sanuanwongse	Director, Virus Research Institute
Mr. Prakong Phan-urai	Director, Div. of Medical Entomology
Dr. Jaroong wongwanich	Director, Div. of Biological Products
Dr. Jakkriss Bhumixawasdi	Director, Health Sciences Research Institute

③ DTEC

Mr. Nipon Sirivat	Chief, Japan Sub-Division

(2) 日本側

在タイ日本国大使館

熊本　宣晴	一等書記官

ＪＩＣＡタイ事務所

表　伸一郎	所長
浅野　寿夫	次長
中島　靖久	所員

ＤＴＥＣ

沼田　道正	ＪＩＣＡ派遣専門家

国立衛生研究所

① 長期専門家

金井　興美	チームリーダー
近藤　瑩子	細菌学専門家
中島　衡平	調整員

② 短期専門家

担当	氏名	所属
細菌学	佐藤　保	国立予防衛生研究所細胞化学部 生体高分子化学室長
クラミジア	萩原　敏旦	国立予防衛生研究所感染症疫学部 リケッチア・クラミジア室長
実験動物	浅野　敏彦	国立予防衛生研究所獣医科学部 実験動物開発室長

2．プロジェクト最終評価の概要

最終評価専門家チームは、6月20日ＮＩＨを訪問、パンヤＤＭＳ局長を表敬した後、山崎、高橋、五十嵐、渡辺各メンバーがそれぞれの担当専門分野の実験室を訪れ、タイ側カウンターパートの活動状況を調査するとともに、彼らとの間で種々の協議を行った。

翌21日から23日までの３日間にわたり、ＮＩＨ講堂においてプロジェクト終了記念セミナーを行った。セミナーにはタイ側カウンターパート並びにタイ国内からの招待講演者及びＪＩＣＡ派遣の最終評価専門家チーム、セミナー講師並びにＮＩＨ長期専門家が参加し、各分野における研究報告がなされ盛んな質疑応答が行われた。ＪＩＣＡ派遣のセミナー講師は以下のとおりであり、セミナーのプログラム及びアブストラクトは附属資料③のとおりである。

担　当	氏　名	所　属
（ＪＩＣＡの感染症対策／セミナー講師団総括）	小早川　隆敏	国際協力事業団医療協力部長
（ＨＩＶの持続感染の機序）	生田和良	北海道大学免疫科学研究所血清学教授
（ロタウィルス）	谷口孝喜	札幌医科大学衛生学助教授
（ヒトヘルペスウィルス）	山西弘一	大阪大学微生物病研究所麻疹部門教授
（細菌感染の分子疫学）	檀原宏文	北里大学薬学部微生物学教室教授
（ウィルス性出血熱）	倉田　毅	国立予防衛生研究所感染病理部長
（インフルエンザウィルス）	根路銘　国昭	国立予防衛生研究所ウィルス第一部呼吸器系ウィルス室長

24日午前、パンヤＤＭＳ局長、ソムポップＮＩＨ所長、ナディラＮＩＨ名誉顧問、他のＮＩＨ首脳及び評価専門家チーム、金井リーダー以下ＮＩＨ長期専門家、浅野ＪＩＣＡタイ事務所次長、中島同所員の出席のもとにステアリング・コミティーを開催し、席上プロジェクト協力期間延長後現在までの活動状況について検討を重ね、プロジェクトの実績についての評価を行った。評価チームの各専門家による評価内容は、後章に記載する。

また、あわせてＮＩＨの今後の方向についてタイ側の考えが明らかにされ、これについても意見が交換された。同コミティーの議事次第は附属資料②のとおりである。

これらの結果に基づいて、合同評価報告書につき双方で議論を交わしつつ意見を調整し、最終的な合意に達した後、同日午後プロジェクト終了式において最終評価専門家チームの山崎団長とパンヤＤＭＳ局長との間で上記報告書の署名・交換を行った（附属資料①）。

双方合意した結論の要点は以下の通りである。

(1)　全般的に見て、1985年４月19日に署名されたＲ／Ｄ、1990年７月31日に署名された延長にか

かるR／D及び1992年6月23日に署名されたフォローアップにかかる覚書きに明記された条項に従い、大部分の目標は確実に達成されてきている。

(2) 9年間にわたる全協力期間は成功裡に遂行されたと評価できる。しかしながら、ＮＩＨのさらなる発展のために、たゆまぬ努力を続けることが望まれる。

(3) エイズを含む感染症に対する国のレファレンス・センターとしてのＮＩＨの役割を強化することを勧める。

(4) 近い将来、「第三国研修」を実施することを強く勧告する。今後、ＮＩＨは、このプロジェクトで得られた技術を東南アジア諸国へ普及する役割を担っていると周知されているものである。

3．タイ側との協議内容

3.1　ステアリング・コミティーにおける討議内容

ステアリング・コミティーは、２月28日（金)午前９時45分から昼過ぎまでＮＩＨ第Ａ－203会議室において、ソムポップ所長を議長として開催された。

(1) 会議は議事に沿って進められ、まず双方の出席者が紹介された後、金井リーダーが附属資料①のアネックスに基づいてＮＩＨプロジェクトのフォローアップ期間の活動状況について発表、さらに中島調整員が、同期間２年間における日本側の投入実績について発表した。

(2) 続いて山崎最終評価チーム団長から、フォローアップ期間に対する評価として、チームが用意したジョイント・エバリュエーション・レポート案の検討を行った。

まず当該レポートの内容について説明、その後質疑応答に入った。実績等については特に先方からコメントはなかった。双方とも、プロジェクトの活動はフォローアップ期間中においても順調に推移し、目標を達成したと言えるとの認識で一致していた。

レポート案のうち、Conclusionの３．第三国研修の実施に関して、タイ側より積極的に実施したい意向が表明された。タイ側は、ＮＩＨがすでにネパール等からの研修員を受け入れている実績を述べ、アジア地域内の各国からの研修のため、ＮＩＨを利用した第三国研修を実施したいとの意向を示した。我が方は、すでに要請書は保健省からＤＴＥＣに提出されてるが、ＤＴＥＣ内での優先順位の低さにより実現に至らないでいる現状を伝え、また、要請書は毎年提出する必要があることを説明した。タイ側は政府内で調整に努め、準備を進めたいとのことであった。

(3) ＮＩＨ側からさらに、附属資料②に基づいてフォローアップ期間の活動実績発表があった。内容は、(1)の金井リーダーの発表とほぼ同一のものであり、どちらからも特にコメントはなかった。

(4) 最後に、ＮＩＨ側から将来においても今回の「プロジェクト終了記念セミナー」のような、通常よりは大規模なセミナーをＮＩＨが開催する場合に、日本からセミナー講師を派遣することの可能性に関して質問があった。今回のセミナーに対して関心が高く、また評価も高いことを反映した発言であったが、ＪＩＣＡの制度では、ある課題に対する専門家を長期間個別に派遣することは検討可能ではあるが、数名の専門家を短期間、一時期に派遣することは困難であることを説明した。

しかしながら、我が方は何らかの形でＮＩＨに対する支援を続けることを検討していることを明らかにし、プロジェクト終了２年後のアフターケアでの協力もあり得ることを述べた。いずれにしても詳細についてＪＩＣＡタイ事務所に照会するよう伝えた。

(5) レポート案のAccomplishment及びConclusionについて、チーム側の提示した案のとおりに承認された。

3.2　ＤＴＥＣとの協議内容

6月20日（月）午後、ＤＴＥＣ日本課長のMr.Nipon及び同課スタッフとの協議が、ＤＴＥＣ内会議室において行われた。要旨は以下のとおり。

(1) 金井リーダーより、永年にわたる協力期間の活動実績は納得できるものではあるが決して満足とは言えない、なぜならば、ＮＩＨはさらに機能拡大、充実していかなければならないし、またそれを可能にする基礎は確立されていると思われるとの発言があった。ＤＴＥＣ側より、ＮＩＨは既存の活動範囲に留まらず、広い領域・対象に踏み出す必要がある、そのためにはセミナーの開催等が有効であるとの認識が示された。

(2) また、金井リーダーより、ＮＩＨはタイ国の主要疾患の予防治療に関する中央研究機関として広く周知されてはいるが、行政組織上は医科学局に属し、「ＮＩＨ」自体は公的な組織名称ではないことを指摘、公的機関として確立されることを希望する旨、表明があった。

(3) チーム側から、日本としてもＮＩＨへの協力を継続したい意向を有すること、そのためには第三国研修は効果的と思われるので、日本側としてもサポートしたい旨表明した。とはいえ、ＮＩＨの第三国研修がいつ実施できるか、見込みをつけることは困難であるが、ＪＩＣＡタイ事務所と協議しつつ手続きを進めるよう伝えた。

4．各分野の評価

4.1　デング出血熱　　五十嵐　章

デング出血熱はタイ国を含む東南アジアにおいて小児の入院・死亡の最大原因を構成する医学・保健衛生上の重要な課題である。本プロジェクトではその実験室内診断及び媒介蚊の生態学的研究に重点を置いた研究が推進された。

(1)　デング出血熱の実験室内診断には従来血清学的手法、殊に血球凝集抑制反応（ＨＩ）が標準法として用いられてきた。最近ＩｇＭ－ＥＬＩＳＡ法が導入された結果、単一血清でも診断が可能となったが、抗体産生前の発病後初期には診断不能であった。本プロジェクトの目的である「分子生物学的手法の導入による感染症の実験室内診断」の１例として、逆転写酵素ポリメラーゼ連鎖反応（ＲＴ－ＰＣＲ）を用いたデング出血熱の迅速診断法の確立とその応用が実施された。さらに分離ウイルスの分子生物学的解析を目的として、ウイルス遺伝子ＲＮＡの塩基配列解析法が日本国派遣研修生によって実施された。

技術移転項目としては、①ＤＮＡ合成機を用いたプライマー作成、②ＲＴ－ＰＣＲを用いたデング及び日本脳炎ウイルス遺伝子検出法、③その方法のデング患者血清への応用、④デングウイルス感染後のＲＴ－ＰＣＲによるウイルス遺伝子検出とＩｇＭ－ＥＬＩＳＡ抗体産生の経日的変化、⑤デングウイルス遺伝子検出率と臨床的重篤度・初感染あるいは二次感染との関係、⑥ＩｇＭ－ＥＬＩＳＡ抗体測定のための検体採取・保存のための濾紙法の検討、⑦ウイルス遺伝子ＲＮＡからｃＤＮＡの作成、⑧ｃＤＮＡの分子クローニング、⑨塩基配列解析法、が行われた。

上記の技術移転は成功し、研究成果の一部は本プロジェクト記念セミナー、国際学会及び国内学会において発表され、更に学術雑誌に論文として投稿中である。ＤＮＡ合成機、ＰＣＲ関連機器、ＤＮＡ塩基配列解析機などの分子生物学的機器の使用法はタイ側に技術移転され、ＡＩＤＳを含む他のウイルス性疾患の実験室内診断にも応用されるインパクトを与えた。ナコン・パノム県立病院の協力によって、ＲＴ－ＰＣＲ法は発病後５日以内のデング患者の迅速診断には強力な手法であり、地方病院でも検査が可能であることが証明されたが、その実用化には今後検査経費の軽減などの費用効果を考慮する必要がある。血清診断のための検体採取・保存・輸送のための濾紙法の検討結果では、デング初感染例のＩｇＭ－ＥＬＩＳＡ抗体が不活化することが判明し、その使用に関する注意を喚起した。臨床症状の異なるデング症例から分離されたウイルス遺伝子の解析結果から、外被膜糖蛋白質の一次構造は患者の臨床症状とは無関係であることが判明した。

(2)　デング媒介蚊の生態学的研究に関してネッタイシマカ幼虫指数の測定を行った結果、Breteau index(ＢＩ）はタイ国東北部で225.14、東部で189.75、南部で106.44という高い値を示した。観察地域のデング出血熱患者数＋１の対数とＢＩの相関図から、ＢＩが 100以上を示

す地域の 78.75%でデング出血熱患者が発生していることが示された。この結果は媒介蚊対策によってＢＩを 100以下に低下させればデング出血熱の発生を防止できる可能性があること、及びＢＩがデング出血熱の流行を監視するための有効な指標であることを示している。この研究と平行して、日本脳炎媒介蚊の生態学的研究が行われ、患者発生前に媒介蚊数の急激な増加が観察された。媒介蚊数は雨量、気温、発生源である水田面積、殺虫剤散布及び吸血源となる脊椎動物の有無に依存することが示唆さた。

以上の結果を総合的に判断すれば、デング出血熱に関する本研究プロジェクトの目標は成功裡に達成されたと評価できる。

4.2 細菌関連

渡辺 治雄

(1) メリオイドーシス

メリオイドーシスはBurkholderia(Pseudomoas)pseudomallei菌によって起こされる感染症でありタイ全域でみられる風土病の一つである。毎年雨期に患者が発生しており、1993年度までに 2,000例近い患者が報告されている。1987年以来このプロジェクトの研究対象とされており、その研究成果として現在までに菌体成分に対する抗体を用いた免疫蛍光抗体法による菌の検出、間接蛍光抗体法（ＩＦＡ）を用いた患者血清中の菌体成分に対する抗体の検出方法が開発され、迅速診断法として利用されてきている。フォローアップ期間中に、ＩＦＡをもちいた健常者の血清疫学的研究からタイの東北地区においては一般住民の20%以上が不顕性感染を受けていることが明らかにされた。またこの菌の生理学的研究から酸性環境に強い菌であることが明らかにされ、タイ東北地区の土壌が酸性でありそこからのこの菌の分離頻度が高くかつ不顕性感染を受けている頻度も高いという生態学的に興味ある結果が得られている。

また基礎的研究の一つとして当菌の産生する酸性フォスファターゼの生理及び生化学的研究がなされ、糖蛋白で付加された菌体表層にあるProtein tyrosine phosphataseであることが明らかにされた。宿主側に作用していることが推定され、病原性との関わりでも興味ある課題を提供するものと期待される。

これらの研究は日本側からの多くの専門家とタイのやはり多くのカウンターパートの協同研究として行われたものであり、プロジェクト期間中に多数の原著論文が出されており、当プロジェクトの模範的例といえよう。

このような研究および研究体制がこのプロジェクト終了後も、何らかの形でのサポートのもとに継続することこそ、ＪＩＣＡによる国際協同研究の一つのあり方となると思われる。

(2) 腸内細菌

腸内細菌に関しては、病原性大腸菌、サルモネラ菌等の該酸を用いた迅速診断法の技術移転に重点がおかれてきていた。毒素遺伝子や病原性に関与する遺伝子をプローブとして、コロニーＤＮＡ交雑法およびＰＣＲ法によりＬＴ、ＳＴ産生性毒素原性大腸菌、コレラ菌およびサ

ルモネラ菌を糞便から直接検出する試みがなされた。まだ改良の余地はあるもののいくつかのものにおいては検査につかえる段階まできていた。

Ms. Orn-anong Ratchtrachenchaiは日本で研修をすることにより、ＤＮＡの塩基配列の多形性を疫学マーカーとする技術(リボタイピング、およびＦＰＬＦ)及びその応用をS. enteritidisの集団食中毒事例を用いて収得してきた。

これらの技術が定着し、腸内細菌の同定及び疫学に適切に応用されるようになることによりタイＮＩＨによる検査の迅速化及びフィールドをもちいた分子疫学の研究に役立つと期待される。

(3) 提言

9年間のプロジェクト期間内に多くの技術伝達がなされてきたが、それが実をむすんでいくかどうかは、それらが今後どの様に実際に用いられていくかにかかっている。タイ自国内の努力によってなされるべきであることが大前提であるが、今後は実績に基づいたテーマごとの協同研究にたいする財政的および人材的サポートの様な形で続けられていくことが、9年間培われてきた良好なる研究交流を維持していくためにも必要と思われる。

4.3 腸管感染症（ウイルス、細菌）　山崎　修道

(1) 計画内容

2年間のフォローアップ期間（1992年8月－1994年7月）の実施計画として1992年7月に策定された腸管感染症に関する研究とその技術移転の内容は以下の通り。

1) ウイルス性下痢症

－非定型ロタウイルス株の分離と分子遺伝学的解析

－その他の下痢症ウイルス、例えば腸管アデノ40、41型あるいは小型球形ウイルス（ＳＲＶ）等の病原ウイルスに関する研究

2) 細菌性下痢症

－新しいバイオテクノロジーを用いた腸管細菌感染症の研究

(2) 調査結果

1) ウイルス性下痢症に関しては、ロタウイルス感染症の分子疫学的研究が、主として谷口孝喜専門家（札幌医科大学）の指導の下に行われ、以下の技術移転と研究の進展が見られた。

① モノクロナール抗体を用いたＥＬＩＳＡ及びＰＣＲ法の適用によるヒトロタイウルスの検出とG serotyping。

② ＲＮＡ－ＲＮＡハイブリダイゼーション法を用いて、ヒト－動物間のロタウイルス伝播の証明。

③ G10血清型のヒトロタウイルスのＶＰ４、ＶＰ７遺伝子の塩基配列の決定。

以上の技術を用いた疫学調査の結果、タイ国におけるヒト・ロタウイルスのG血清型の分布は毎

年変化するが特に１型の流行が最も多いこと、またＧ３型は1990年以前にはほとんど見られなかったが、1990年以降増加傾向にあることが明らかになった。更に、ウシ・ロタウイルスとして一般に検出されるＧ10血清型がブタとヒトからの分離株にも見出され、ロタウイルスのヒト・動物間の伝播が示唆された。そしてこれらのヒト及びブタのＧ10血清型株のＶＰ４とＶＰ７遺伝子の塩基配列を比較したところ、いずれもタイ国内で分離されたウシのＧ10型株（61Ａ）と極めて類似していることが判明した。ヒト、ブタ、ウシのＧ10型ロタウイルスの近縁性は、更にＲＮＡ－ＲＮＡハイブリダイゼーション法によっても証明された。

(3) 評価

アジアにおけるロタウイルス感染症は、５歳以下の乳幼児下痢症の約30％を占めると言われており、特に途上国においては低栄養と脱水症状による死亡例もみられることから、その疫学的調査研究は極めて重要である。

タイＮＩＨにおける分子疫学的研究は、単にタイ国における流行株の血清型や遺伝型を明らかにしたのみならず、ヒト社会で流行するロタウイルスがウシやブタの間で流行するロタウイルスと極めて似た性質をもっていることを証明して、ロタウイルスのヒト－動物間の交差伝播の可能性を示した。これら研究成果は、1989－1993年の間に７編の英文論文として一流の国際誌に発表されている。これらの一連の研究は、主として札幌医大の谷口孝喜専門家の指導によるものであるが、そのカウンターパートとして活躍したMs. Yaowapa Pongsuwannaの努力と貢献は高く評価される。しかしこれらの研究に必要な高度な技術が、タイＮＩＨのウイルス部全体の能力としてどれだけ生かされているかについては不明である。Ms. Yaowapa自身は、現在この研究によって日本学術振興会の論博研究者となって札幌医科大学と研究交流を続けているが、これらの技術が、一人でも多くのＮＩＨスタッフに伝授されるよう望まれる。

ロタウイルス以外の下痢症ウイルスに関する疫学研究については、この２年間のフォローアップ期間にはほとんど進展はなかったようである。その代わり、腸管系ウイルスに関しては、ＷＨＯの勧告に基づくポリオ根絶のための疫学的調査研究が活発に行われ、ウイルスの分離と血清型別の調査からタイ国内には1993年現在においてもなお多数の野生型ポリオウイルスが分離されることを明らかにしている。

限られた人数の研究者で多くの業務を遂行するのは困難であるから、何に主力を注ぐべきかはタイＮＩＨの指導者の判断によるしかないが、ウイルス性下痢症については今後ＳＲＶなどロタウイルス以外の病因についても研究を発展させていくことが期待される。その基礎的技術として先ず必要なのは、免疫電顕法であるが、その技術と電顕装置はタイＮＩＨに完備している。

なお、細菌性下痢症の調査結果については、細菌関連研究の評価を担当した渡邊治雄団員の調査報告書の中で述べられる。

4.4 生物製剤

高橋　理明

(1) 日本脳炎ワクチン

大阪大学微生物病研究所観音寺研究所より吉田（正道）、高木、大西のスタッフが派遣され、マウス脳由来の日本脳炎ワクチンの試作の指導にあたった。初期には抗原量が少なく、安定性が低いなどの難点があったが、製法の改良の結果、約 3,000doseの抗原性、安定性ともに良好なワクチンがつくられ、野外試験でも良好な結果が得られた。その結果高品質の日本脳炎ワクチンがタイで生産可能となり、1989年以降15,000dose(1989)、128,000dose(1990)、124,000dose(1991)、151,000dose(1992、7月迄)、358,000dose(1993) と生産高は増加し実際に使用されている。

液状ワクチンは2～8℃で保存すれば12ヶ月後でも力価は十分であること、中山株でも北京1型でも副作用、抗体反応の点で同等であり、どちらも日本で作られているワクチンと同等に安全で効果があることもわかった。このように日本脳炎ワクチンの製造技術に関してはほぼ完全に移転されたと思われる。

(2) ニワトリ胚細胞由来狂犬病ワクチン

化血研の坂本研究員が1986年以来3度訪タイし、培養細胞由来の精製狂犬病ワクチンの試験製造について援助したＨＥＰ－flurry株ウイルスを用い培養ニワトリ胚細胞で増殖させ、ウイルスの採取、不活化、精製法が導入された。そして1990年には 180リットルの不活化ウイルス液がつくられた。それを更に濃縮、精製し 4,400doseの6ロットの凍結乾燥ワクチンが試作され、化血研でテストされた結果十分な力価と安全性を有していることが示され、タイＮＩＨのテストでもＷＨＯの規定によるすべての品質試験に合格した。この研究は大規模な精製ニワトリ胚細胞由来狂犬病ワクチン生産に極めて有用である。

(3) 風疹生ワクチン

風疹ワクチンの開発については大阪大学微生物病研究所観音寺研究所の協力の下で、先づ1988年11月にウヅラを病原微生物フリー（ＳＰＦ）の状態で飼育するためのアイソレーターなどの機器が到着しanimal centerに設置された。ＳＰＦの卵計600コも送られ孵化され、新生ウヅラは1989年4月にアイソレーターに移された。

ウヅラ胚細胞の培養にも成功し、風疹ウイルスＶＲＩ株を接種し、得られたウイルスのＲＫ－13、ＢＨＫ21細胞を用いてのプラック法による力価測定も行われた。このようにして生風疹ワクチンのパイロット大量生産の能力は既に得られているが、公式に認められているワクチン株がまだ入手できないので風疹ワクチンの開発研究はこの段階でとまっている。

(4) コンポーネント百日咳ワクチン

タイＮＩＨのテラナート研究員が観音寺研究所に滞在し、技術修得に努めた。彼女のグループは44リットルの培養液を濃縮し塩析、超遠心、庶糖密度勾配などにより精製し、蛋白窒素量の測定、ＰＴ：ＦＨＡ ratioの測定などを行ったが、常に一定の力価をもったワクチンの生産

は困難で且つ生産効率も低く、まだ２ロット（5,400dose)のワクチンが品質規定に合格しているのみである。

本プロンジェクトとは直接関係はないが、日本から導入された耐熱性acellular ＤＰＴワクチンの臨床試験が行われ、その結果ＰＴ及びＦＨＡに對する抗体価は従来のwhole cell ＤＰＴワクチンに比べ有意に高く注目されている。

(5) 結論

ワクチン開発研究プロジェクトとして日本脳炎、狂犬病、風疹、コンポーネント百日咳ワクチンがとり上げられ、それぞれある程度の成果があがり、特に日本脳炎ワクチンは大量生産に進み、実際の接種に利用されるまでに至っている。ワクチンの実用化には技術的問題のみならず、生産効率、株の授受（特に生ワクチンの場合）の問題など多くの要素がからんでおり、ＮＩＨでできる研究には自ら限度がある、しかし少くともこれらのワクチンについての検定技術は修得されており、得られた生産技術とともに今後必要に応じてワクチン生産に活用されることと思われる。

尚ワクチンの技術移転は他の研究の技術移転と異なり、実用化を目指すなら最初からきちんとした契約類を結ぶことも必要なのではないかと感じられた。

4.5 実験動物

浅野　敏彦

実験動物センターは、現在獣医５名（男性１名、女性４名）および学卒の男性職員１名の６名のスタッフのもとに、約15名のワーカーとでなっており、人員的にはセンターの運営には問題はない。あと一名の獣医を採用できる枠を持っているが、公務員の給与の問題で希望者がなかなかいないとのことである。

センターで維持している動物は、マウスがBALB/c, C57BL/6J, C3H/HeJ の近交系とＩＣＲ，ＤＤＹのクローズドコロニー、モルモットはハートレイ系である。近交系マウスとモルモットに関してはタイ国内で入手が困難であるため、どうしても維持をする必要があり、クローズドコロニーのＩＣＲに関しては離乳後のマウスはマヒドン大学サラヤ校より購入しているが、新生仔マウスを使用する場合があり、それに自家生産マウスを用いている。

ラット：自家生産をしているラットは高血圧モデルのＳＨＲであり、他のラットはサラヤ校より購入している。ＳＨＲは薬用植物部が使用する為に日本より導入したが（この導入に伴いラットの血圧計も供与）、現在繁殖不良になり再導入を要請された。日本の施設でも、おうおうに繁殖不良になることはあるので、これをもって施設の運営が悪いとは一概にはいえない。

ウサギは全てサラヤ校より購入しているニュージーランドホワイト系を用いている。施設に導入されたウサギは検疫室で検疫を受けた後、実験に供されている。

実験者に払い出した数等を表１に示す。このように動物の生産に関しては今まで通りに行っていって、今後不都合は出てこないと思われる。しかしながら、研究の進展に伴い新たな系統やモデ

ル動物の導入を要請される事は今後必ず起こるであろう。かなり厳密な環境で維持しなければならないような動物の場合に、今の環境では問題は出てくるであろう。例えば、現在単クローン抗体作成にはＳＰＦのBALB/cを使用しているが、ＳＰＦ動物を生産する室はあるがＳＰＦ動物を用いて実験する為の部屋はない。そのために感染実験施設にＳＰＦ動物を持ち込んで動物実験を行っている。（抗原には感染性全くない）。しかしながら、タイ側も現在モルモットとマウスの生産用の建物（鉄筋二階の建物）を建設中であり、また私が滞在中にもモルモットをＳＬＣ（日本の実験動物生産業者）にタイ側の予算で発注している（約50万円）。また昨年度にはなかったケージワッシャーが洗浄室に導入されていた。これらのことを考慮すると、私の今までの東南アジアでの経験（ミャンマー：当時ビルマ、インドネシア、フィリピンとタイ）のなかで最も自助努力をしている国であるし、経済的な裏付けがかなりの程度に為される国であるように思われる。これらのことから、タイは一時的には多少の混乱はあるかも知れないが、自分たちの力で発展していく力は充分にあると思われる。

以上のことから、研究所のサポートセンターとしての実験動物部門は現在も充分にその責任を果たしており、今後も幾つかの小さいトラブルは発生するであろうが、それを克服してその責を果していくと思われる。

今後実験動物部門に必要なことは、実験動物部門の研究、開発である。我々は意識して研究に関することは今回の技術協力から除いていた。もし、最初の段階から研究に関しても指導すると、タイ側の職員は研究にその精力を使い、サポーティングセンターとしての運営等がおろそかになると考えたからである。現在の運営のレベルを落とさないで研究を行うことは研究者の数等から可能である。また他部門の研究者の動物実験を全面的にバックアップしていく力を付けるためにも、実験動物に関する研究を開始する時期に来ていると思われる。タイ（或いは熱帯地方）独自の研究分野は実験動物の世界にもあり、タイ側とは今後もコミュニケーションを絶やさずに協力して行くことを話し合っておいた。

表１．実験動物総数表

Activities	1987	1988	1989	1990	1991	1992	1993
1. Production (heads)							
1.1 Mice							
- ICR strain	42,380	42,190	38,570	40,150	42,808	41,439	50,677
- SPF strain				4,227	5,364	2,236	2,804
- Inbred strain						1,292	17,179
1.2 Hypertensive rat				365	483	479	596
1.3 Guinea pig (hart Ley)				1,973	1,095	1,623	1,855
1.4 SPF Japanese Quail's (eggs)				13,907	6,101	5,304	5,081
2. Procurement (heads)							
2.1 Mice	6,010	13,270	32,550		46,900	45,800	49,700
2.2 Rat	509	1,658	3,132	1,395	961	1,197	
2.3 Guinea pig	239	376	1,013		271	56	
2.4 Rabbit	74	275	308		211	368	359
2.5 Goat		6			3	10	
2.6 Sheep		30	5		10		
2.7 Others	20	32	21		5		2
3. Purchasing (heads)							
3.1 Rat				2,141	1,414	967	1,247
3.2 Suckling mice (Litters)	240	206	240	545	632	371	416
3.3 Weaning mice	20,654	34,382	44,187	50,718	61,616	46,700	66,244
3.4 Guinea pig	238	328	809	1,022	1,369	1,861	1,214
3.5 Rabbit	74	281	308	202	211	350	486
3.6 SPF BALB/c mice	71		144	296	480		
3.7 SPF DDY mice			1,612	1,523	1,148	2,454	
3.8 SPF mice				23	78		
3.9 SPF Japanese Quail's (eggs)			2,500	2,750	680	250	
3.10 Goat		6		4			
3.11 Sheep		30	5	4			
3.12 Others	20		32	21	2		

Activities	1987	1988	1989	1990	1991	1992	1993
3.13 Horse Blood (ml)				5,000		20,000	37,500
3.14 Sheep Blood (ml)			14,400	16,170	20,900	20,100	20,620
3.15 Other Animal Blood (ml)					27,625	11,222	3,540
4. Lab Animal Monitoring (samples)							
4.1 Quarantining						65	313
4.2 Microbiological Control			120	200	174	40	220
4.3 Autopsy			525	308	189		
4.4 Haematology Control							50
Scientific Equipment Center							
1. Analytical Research & Diagnosis							
1.1 Specification & Installation (pcs.)	236	243	175	416			
1.2 Repairing (pcs.)	222	214	218	177			
1.3 Special Maintenance (times)	180		32				
1.4 Maintenance for Medical Science Center (pcs.)		335	309	228			
1.5 Central Equipment Service (hrs.)	7,128	6,963	6,412	6,766			
2. Supportive for Research (Water system, Electrical system, waste water Treatment, Air Conditioning System)							
2.1 Service (hrs.)	18,218		26,430	30,810			
2.2 Repairing (hrs.)	5,657		1,306	1,746			

附 属 資 料

① 合同評価レポート

Mutually attested and submitted

to all concerned

Bangkok
The Kingdom of Thailand
June 24, 1994

山崎修道

Dr. Shudo Yamazaki
Leader,
Japanese Evaluation Team,
Japan International Cooperation Agency,
Japan

Panya Sonkom

Dr. Panya Sonkom
Director General,
Department of Medical Sciences
Ministry of Public Health
The Kingdom of Thailand

JOINT EVALUATION REPORT

ON

JAPANESE TECHNICAL COOPERATION

FOR

THE RESEARCH PROMOTION PROJECT IN THE NATIONAL INSTITUTE OF HEALTH

IN

THE KINGDOM OF THAILAND

June 24, 1994
Bangkok
The Kingdom of Thailand

Discussion meeting between the Evaluation Team of the Japan International Cooperation Agency (JICA) and the National Institute of Health, Department of Medical Sciences, for evaluation of Japanese Technical Cooperation for the Research Promotion Project in the National Institute of Health

Date : June 20 - 27, 1992

Place : National Institute of Health, Department of Medical Sciences, Nonthaburi, The Kingdom of Thailand

Attendants : JAPANESE PANEL

JAPANESE EVALUATION TEAM

Dr. Shudo Yamazaki	Leader
Dr. Michiaki Takahashi	Member
Dr. Akira Igarashi	Member
Dr. Haruo Watanabe	Member
Dr. Takatoshi Kobayakawa	Member
Miss Akiko Tomita	Member

JICA Thailand Office

Mr. Toshio Asano

Mr. Yasuhisa Nakajima

Japanese Expert Team

Dr. Komi Kanai

Dr. Eiko Kondo

Mr. Kohei Nakajima

THAI PANEL

Dr. Panya Sonkom

Dr. Nadhirat Sangkawibha

Dr. Sompop Ahandrik

Dr. Chuinrudee Jayavasu

Mrs. Pratummal Xumsaeng

Mrs. Pranee Srisomboon

Dr. Somphot Montienart

Dr. M.L. Ratanasuda Phan-urai

Dr. Paijit Warachit

Dr. Vinita Boriraj

Mr. Kamol Sawadimongkol

Dr. Chongdee Wongpinairat

Dr. Mayura Kusum

Mrs. Suranga Saguanwongse

Mr. Prakong Phan-urai

Dr. Daroon Petchplai

Dr. Jaroong Wongwanich

Dr. Jakkriss Bhumisawasdi

Dr. Panadda Silva

Mrs. Siripan Wongwanich

I. INTRODUCTION

The Japanese Evaluation Team (hereinafter referred to as "the Team") organized by the Japan International Cooperation Agency (hereinafter referred to as "JICA") and headed by Dr. Shudo Yamazaki, visited the Kingdom of Thailand from June 20 to 27, 1994 in order to jointly evaluate with the Thai authorities concerned the past achievements and future prospects of Japanese Technical Cooperation for the Research Promotion Project in the National Institute of Health (hereinafter referred to as "the Project") on the basis of the Minutes of Discussions concerning the Follow-up Program on Technical Cooperation signed on June 23, 1992.

During its stay in the Kingdom of Thailand, the Team discussed and studied together with the Thai counterpart personnel concerned a number of aspects regarding the progress and achievements of the Project, as well as fulfillment of commitments.

Through careful studies and discussions, both sides summarized their findings and observations as described in the following chapters.

II. METHOD OF EVALUATION

1. Materials used as reference

In order to evaluate the past performance and achievements both quantitatively and qualitatively, the following materials were used as references:

(1) The Minutes of Discussions concerning the Follow-up Program on Technical Cooperation
(2) The Tentative Schedule of Implementation of the follow-up Program
(3) The official requests made by the Government of the Kingdom of Thailand with respect to dispatch of Japanese experts, Thai counterpart personnel training in Japan and provision of equipment by means of Technical Cooperation Forms A-1, A-2, A-3, and A-4, respectively.
(4) Other publications concerning the Project

2. Discussions and Observations

The Team discussed various aspects of the Project and observed the buildings, machinery, equipment, facilities and utilities made available for the Project.

To recognize the impact and efficiency of the training, discussions were held with counterparts trained in Japan.

Ⅲ. OBJECTIVE AND ACTIVITIES OF TECHNICAL COOPERATION FOR THE PROJECT

1. Objective

According to the Minutes of Discussions signed on June 23, 1992, the objective of the follow-up period is to bring the Project a successful end by further technological cooperation in the selected subjects for which further support is needed.

2. Activities of Technical Cooperation

In order to accomplish the above-mentioned objective, both sides agreed that technical cooperation should be implemented for the following activities through dispatch of Japanese experts, acceptance of Thai counterpart personnel for technical training in Japan and provision of equipment.

(1) Dengue Hemorrhagic Fever

① Study on the molecular epidemiology of dengue hemorrhagic fever

② Study on the vector mosquito ecology

(2) Melioidosis

① Production of monoclonal antibody

② Gene cloning

③ Immunohistochemistry

(3) Intestinal Infection (viral and bacterial)

① Viral diarrhea

- Molecular study of unusual strains, and cultivation of non-serotypable rotavirus
- Study on other causative agents of viral diarrhea such as enteric adenovirus type 40, 41 and other small round viruses

② Bacterial diarrhea

- Study on intestinal bacterial infection by biotechnological methods

(4) Monitoring of Laboratory Animals

① Genetic monitoring of laboratory animals, together with microbial monitoring of Sendai virus and mouse hepatitis

Ⅳ. PERFORMANCE OF THE PROJECT

1. Facilities

Construction of the Institute facilities and installation of equipment directly related to the activities of the Project were completed at the end of October 1986 under the Japanese Grant Aid Program. Other facilities (including electricity, gas, water supply systems, sewage system, telephone and furniture) necessary for implementation of the Project were provided by the Thai side.

The efforts made by the Government of the Kingdom of Thailand for provision of equipment, offices, laboratories, etc. are highly appreciated.

Since the completion of NIH building in 1986, the general conditions and the functions of the facilities have been satisfactorily maintained or even improved up to this time. There has occurred no serious problem except the dew-foaming at one time in some parts of the duct system for air-conditioning.

During the follow-up period from August 1992 to the present time, the facilities has been maintained in good condition and also cleaned up daily through the contract between NIH and the private cleaning company.

2. STAFFING

At present, a total of eleven (11) Thai counterpart personnel have been assigned to the Project for effective implementation and successful transfer of technology. The list of the Thai counterpart personnel is presented in ANNEX 1.

3. MANAGEMENT AND ADMINISTRATION

All administrative and managerial services has been provided by the Thai counterpart personnel.

(1) Thai side:

a. Director-General, DMS
b. Senior Experts, DMS
c. Principal Medical Scientists, DMS
d. Directors of divisions concerned, DMS
e. Staff concerned, Japan Sub-Division, DTEC

(2) Japanese side:

a. Team Leader
b. Coordinator
c. Other experts and personnel concerned dispatched by JICA
d. Staff concerned of JICA Thailand Office

4. JAPANESE EXPERTS

JICA has dispatched three (3) long-term experts and ten (10) short-term experts during the follow-up period of the Project, whose names and fields are listed in ANNEX 2.

5. THAI COUNTERPART PERSONNEL TRAINING IN JAPAN

Thus far, five (5) Thai counterpart personnel have been sent to Japan for either observation or technical training. Their names are listed in ANNEX 3.

JICA accepted the Thai counterpart personnel in the fields agreed in the Minutes of Discussions. Their technical training was very effective for obtaining research ability, new technology and information.

6. EQUIPMENT

Between 1992 and 1994, equipment worth about 33 million yen was donated by the Government of Japan. The main equipment items and supplies are listed in ANNEX 4.

Equipment for the Project provided by the Government of Japan has been used efficiently in the activities of the Project.

7. BUDGET

Both sides made the best effort to secure the budget necessary for implementation of the Project.

8. ACCOMPLISHMENT OF TECHNICAL COOPERATION

Through careful evaluation and discussions, the both sides agreed that the technical cooperation implemented during the follow-up period has accomplished the afore-mentioned objectives. The following four subjects were taken up as our main items of cooperation;

(1) Dengue hemorrhagic fever
(2) Melioidosis
(3) Enteric infection
(4) Monitoring of laboratory animals

The subjects (1) and (2) are each an important endemic disease in Thailand and the subject (3) is the universal health problem in tropical countries. The (4) is an essential technology to maintain and promote the laboratory functions of NIH.

Through the cooperative research activities between experts and counterparts in these subjects, the introduction of new technology and the extended application of preacquired methodology were made possible with successful results. The contents of cooperation are listed in ANNEX 5.

The fellows to Japan during this period were excellent in getting the new laboratory experiences and in developing their potential. Their achievements were introduced by their own presentation in "the Memorial Seminar of NIH Project" held from June 21 to 23, 1994.

As a whole, the follow-up cooperation of two years is evaluated to be well rewarded by the success as above.

IV. CONCLUSION

As the results of the joint evaluation and discussions, both sides reached the following conclusions:

1. In general, the goals of most activities of the Project, as stipulated in the Record of Discussions signed on April 18, 1985, the Record of Discussions concerning Extension of the Period signed on July 31, 1990 and the Minutes of Discussions concerning Follow-up Program signed on June 23, 1992 have been realized.

2. The total cooperation period of nine years is evaluated to have been successfully accomplished. However, it is greatly desired that unyielding efforts be further made to create future development of NIH.

3. Moreover, it is advisable to further strengthen the role of NIH as the national reference center for infectious diseases including AIDS.

4. It is strongly recommended that "the third country training program" be implemented in the near future. Hereafter NIH is acknowledged to have a mission to disseminate the acquired technology to South-East Asian countries.

ANNEX 1

LIST OF THAI COUNTERPART PERSONNEL
(STAFF OF EACH DIVISION)

DIVISION	NAME	POSITION
1. Clinical Pathology Division	Mrs. Pimjai Naigowit	Scientist
	Miss Paradee Mamechai	-ditto-
	Mr. Preecha Panyarraggit	-ditto-
	Mr. Wattanapong Vutta	-ditto-
	Mrs. Siripan Wongwanich	-ditto-
2. Health Science Research Institute	Mr. Wattana Awanit	Scientist
	Miss Panasda Isarangkul Na Ayuthaya	-ditto-
	Dr. Tanawat Nantamingcharoen	-ditto-
3. Virus Research Institute	Miss Suntharee Rajanasuphot	Scientist
	Miss Sumlee Pothipunya	-ditto-
4. Medical Entomology Division	Mrs. Usawadee Thavara	Scientist

ANNEX 2

LIST OF JAPANESE EXPERTS DISPATCHED BY JICA

NO. JAPANESE FISCAL YEAR	NAME	PERIOD	FIELD
(LONG TERM EXPERT)			
1. 1985-1994	Mr. Kohei Nakajima	85. 8. 1～94. 7.31	Coordinator
2. 1987-1994	Dr. Komi Kanai	87. 6.15～94. 7.31	Team Leader
3. 1990-1994	Dr. Eiko Kondo	90.11. 1～94. 7.31	Bacteriology
(SHORT TERM EXPERT)			
1. 1992-1993	Dr. Toshikatsu Hagiwara	92.11. 3～93. 1.22	Chlamydia trachomatis
2.	Dr. Takeshi Kurata	92.12.14～92.12.28	Histopathological diagnosis of infectious diseases
3.	Dr. Toshihiko Asano	93. 3.22～93. 4.18	Genetic monitoring of experimental animals
4. 1993-1994	Dr. Tsutomu Koyama	93. 7.26～93. 8.21	Laboratory diagnosis of Cryptosporodium, Giardia lamblia, Entamoeba histolytica in diarrheal disease
5.	Dr. Mitsuyoshi Kumada	93. 7.26～93. 8.21	-ditto-
6.	Dr. Koichi Morita	93. 8.18～93. 9.15	Dengue fever virus
7.	Prof. Yoshito Wada	93.12. 1～93.12.21	Medical entomology
8. 1994-1995	Dr. Tamotsu Sato	94. 4.18～94. 7.15	Bacteriology
9.	Dr. Toshikatsu Hagiwara	94. 6.15～94. 6.28	Laboratory diagnosis of chlamydia apneumoniae Infection
10.	Dr. Toshihiko Asano	94. 6.19～94. 7.15	Experiment of laboratory animals

ANNEX 3

LIST OF FELLOWSHIP

NO. JAPANESE FISCAL YEAR	NAME	PERIOD	FIELD
1. 1992-1993	Mrs. Sukhjai Pholumpaisathit	92. 9. 7-93. 8.31	Papilloma virus
2.	Miss Orn-Anong Ratchtrachenchai	93. 3. 9-94. 3. 8	Enteropathogenic bacteria
3. 1993-1994	Miss Prukswan Chetanachan	93.10. 5-94. 9.16	Instrument quality assurance
4.	Dr. Jaroong Wongwanich	93.10.26-94. 1.11	Production and quality control of vaccine
5. 1994-1995	Dr. Panya Sonkom	94. 5. 17-94. 5.26	Administration and management

ANNEX 4

PROVISION OF EQUIPMENT

JAPANESE FISCAL YEAR	ITEMS OF MAIN EQUIPMENT	AMOUNT(YEN)
1992-1993	Automatic dispenser for liquid medium	¥20,000,000
	Chromatography chamber	
	ST 60 Incubator	
	Electrophoresis system	
	Blood pressure monitor for mice	
	High temperature incubator	
	Microrefrigerated ultra centrifuge	
	Regregerated centrifuge	
1993-1994	Animal cage washing machine	¥13,000,000
	P.H.meter and controlling system	
	Separator in sewerage facility	
	Air blower	
	Power supply for electrophoresis	
	Dry ice maker	
	Low speed centrifuge	

ANNEX 5

ITEMS IN COOPERATION SUBJECTS

(1) Dengue hemorrhagic fever

Technology transfer

---------- Detection of dengue virus, virus genom and serotypes by PCR from culture fluid, sera, clinical specimens

---------- DNA synthesis

---------- Detection of anti NS 1 antibodies in patient sera by antigen capture ELISA

---------- Data analysis

Cooperative research

---------- Development of early diagnosis

Relation between onset of disease and the detectable days of of IgM and IgG

---------- Comparison of the efficiency for the dengue diagnosis between PCR method and ELISA

---------- Relation between the severity of disease and PCR-positivity

---------- Distribution of Ns 1 antibodies in dengue patients

---------- Laboratory technologies necessary for molecular epidemiologies of dengue hemorrhagic fever

(2) Melioidosis

Technology fransfer

---------- Isolation of B.pseudomallei from soil samples

---------- Identification of B.pseudomallei colonies by immunofluorescent staining

---------- Fractionation of bacterial components from the culture

filtrates and cells of B.pseudomallei

---------- Techniques in enzymology

---------- Receptor-ligand experiments

Cooperative research

---------- Evaluation and franslocation of acid phosphatase in B.Pseudomallei and their association with pathogenicity

---------- Seroepidemiology of melioidosis

(3) Enteric infection

Technology transfer

---------- DNA hybridization, PCR for laboratory diagnosis of enteric infections,such as rota virus,pathogenic E.coli,Salmonella.

---------- Laboratory diagnosis of diarrhogenic anaerobic bacteria, especially clostridium difficille

---------- Pulsed-field gel electrophoresis and ribotyping

---------- Heidenhain staining and modified Kohn staining for detection diarrhogenic protozoa

---------- Culture method for dysentery amoeba

---------- PVA method for preservation of protozoa-contaminated clinical specimens

---------- Formaline-ether method for collection of cysts

Cooperative research

---------- Molecular and antigenic analysis of human and bovine rotaviruses in Thailand

---------- The complete nucleotide sequencing of a variant of coxachievirus A24

---------- Rapid and sensitive detection of Salmonella by 16S ribosomal RNA gene as probe

---------- Molecular epidemiology of Salmonella enteritidis

(4) Monitoring of laboratory animals

Technology transfer (Genetic monitoring)

---------- Ditection of marker genes by electrophoresis

---------- Skin transplantation method

---------- Advices for the maintenance of laboratory animals

(5) Others

Entomology

---------- Ecological survey of JE vector mosquitos in several provinces

---------- Data analysis and advices for future direction

Papilloma virus

---------- Molecular method for laboratory diagnosis of nasopharyngeal papilloma virus

---------- Cooperative research

Clamydia trachomatis

---------- Tissue culture and infection

---------- Immunofluorescent microscopy for detection of clamydia

Electronmicroscopical technology

---------- Training in NIH-Tokyo

② Steering Committee資料

The 41-1/1994 Steering Committee Meeting

On Friday, June 24, 1994 at 9.30 am

Room no. A-203, National Institute of Health, Nonthaburi

Agenda

1. Information from Chairman
2. Matter for Discussions :
   - 2.1 Progress report of follow-up period by Japanese project team leader,
   - 2.2 Supplement report of follow-up period by Japanese project team coordinator,
   - 2.3 Evaluation of follow-up period :
     - by Japanese evaluation team (Dr.S.Yamazaki and other members of the team)
     - by Representative from Thai side,
   - 2.4 Discussion of Tentative Minutes of Evaluation.
3. Others

Steering Committee

1.	Dr. Panya Sonkom	Director-General
2.	Dr. Nadhirat Sangkawibha	Honorable Consultant
3.	Dr. Sompop Ahandrik	Senior Expert
4.	Dr. Chuinrudee Jayavasu	Senior Expert
5.	Mrs. Pratummal Xumsaeng	Deputy Director General
6.	Mrs. Pranee Srisomboon	"
7.	Dr. Somphot Montienart	"
8.	Dr. M.L. Ratanasuda Phan-urai	Principal Medical Scientist
9.	Dr. Paijit Warachit	"
10.	Dr. Vinita Boriraj	"
11.	Mr. Kamol Sawadimongkol	"
12.	Dr. Chongdee Wongpinairat	Director, Drug Analysis Division
13.	Dr. Mayura Kusum	Director, Clinical Pathology Division
14.	Mrs. Suranga Saguanwongse	Director, Virus Research Institute
15.	Mr. Prakong Phan-urai	Director, Medical Entomology Division
16.	Mr. Daroon Petchplai	Director, Research and Development of Medicinal Plant
17.	Dr. Jaroong Wongwanich	Director, Biological Products
18.	Dr. Jakkriss Bhumisawasdi	Director, Health Science Research Institute
19.	Dr. Panadda Zilva	Director, Technical Coordinating Center
20.	Mrs. Siripan Wongwanich	

Japanese-side

1. Dr. Shudo Yamazaki
2. Prof. Michiaki Takahashi
3. Dr. Takatoshi Kobayakawa
4. Dr. Haruo Watanabe
5. Prof. Akira Igarashi
6. Mr. Shinichiro Omote
7. Dr. Komi Kanai
8. Dr. Eiko Kondo
9. Mr. Kohei Nakajima
10. Miss Akiko Tomita

Achievement of Technical Transfer during the Follow-up Period
(August 1992 - July 1994)

Activity	Achievement
I. Dengue Hemorrhagic Fever	
Two research projects have been carried out:	
(1) Synthesis of Dengue and JE primers	- Synthesizing technique for Dengue and JE primers was established in NIH - 6 JE primers, 4 universal primers and 2 dengue primers were produced.
(2) Comparative study on nucleotide and deduced amino acid sequence of the envelope glycoprotein gene among three dengue virus type 2 strains isolated from patients with different severities in Maha Sarakham, Northeast Thailand	- We found that the primary structure of dengue - 2 virus is not related with clinical severity of infected patient.
Training Miss Sumlee was trained in laboratory technologies necessary for molecular epidemiologies of dengue hemorrhagic fever.	
II. Melioidosis	
- Development of immunodiagnosis of melioidosis.	- Polyclonal antibody to LPS of Pseudomonas pseudomallei are produced. - ELISA test kit is developed for detection of IgG antibody against P.pseudomallei - The study at molecular level could not be accomplished in the Follow-up program.
III. Intestinal Infection	
1. Viral Diarrhea	
- Molecular epidemiology of rotavirus infections in Thailand	- Evidence of interspecies transmission between human and animal rotaviruses was found. - The serotype distribution of rotavirus varies by time and place.
2. Bacterial Diarrhea	
(1) Purification and characterization of toxins from Clostridium difficile and Clostridium perfringens.	- Techniques for toxin purification and characterization have been transfered to Thai counterpart. - Enterotoxin and cytotoxin from C.difficile were purified.

Activity	Achievement
(2) Development of laboratory diagnosis of C.difficile associated diarrhoea.	- Alpha-toxin from C.perfringens was also purified. - The use of PCR technique for detection of toxigenic C.difficile was established in NIH.
Training Ms. Orn-Anong was trained in Japan on Enteropathogenic bacteria	Pulsed-field gel electrophoresis and ribotyping techniques were transfered to the NIH personnel.
IV. Parasitic Infections Laboratory diagnosis of intestinal protozoa (Cryptosporidium, Giardia lamblia and Entamoeba histolytica)	- Better staining procedures for detection of diarrhogenic protozoa were established.
V. Vaccine Clinical trial of Thermostable DTaP (Acellular Pertussis)	- DTaP can induce higher immunity than Pertussis toxin (PT) and Filamentous Haemagglutinin (FHA)
VI. AIDS Development of nested PCR for the detection of HIV-1 Proviral DNA in clinical specimens	- Nested PCR technique was established in NIH.
VII. Laboratory Animal Center Establishment of Laboratory for genetic monitoring of laboratory animal.	- Biochemical marker method and skin grafting method were established in NIH. - Two couple of BALB/cByJ strain mice are donated to NIH.
VIII. Medical Entomology (1) Ecological Aspects on Mosquito Vectors in Relation to Epidemiology of Japanese Encephalitis in Thailand	- There were sharp increases of the vector mosquitoes and the infection of JE virus in wild-caught mosquitoes before the occurrence of human cases - Abundance of mosquito vectors was most consistently correlated with rainfall, temperature, area of rice field, the irrigation system insecticides and the number of pigs (amplifying animal)

Activity	Achievement
(2) Distribution of Dengue Vector, Aedes aegypti in the Rural Area of Thailand	- The average BI in the northeastern, eastern and southern regions were 225.14, 189.75 and 106.44 respectively. Scatter plots between log 10 (DHF cases+1) and the average BI in surveyed provinces showed that 78.75% of the areas where DHF occurred had the average BI higher than 100.

③ Memorial Seminarプログラム及びアブストラクト

MEMORIAL SEMINAR

RESEARCH PROMOTION PROJECT

ABSTRACT

National Institute of Health

Nonthaburi, Thailand

June 21-23, 1994

Schedule for the Memorial Seminar Research Promotion Project
National Institute of Health, Nonthaburi, Thailand
June 21 - 23, 1994

Tuesday, June 21, 1994

09.00 - 09.30	**Opening ceremony** **- Reporting Address by Dr. Panya Sonkom** **Director-General, Department of Medical Sciences** **- Opening Speech by Prof. Prakorb Tuchinda** **Ex-Permanent Secretary, Ministry of Public Health** **- Remark by Dr. Shudo Yamazaki** **Director-General, National Institute of Health, Tokyo**
09.30 - 09.45	Coffee break
Session I	**Chairman : Dr. Komi Kanai** **Co-chairman : Dr. Mayura Kusum**
09.45 - 10.10	Future plan for NIH, Thailand Dr. Panya Sonkom
10.10 - 10.35	How JICA is challenging infectious diseases in the world Dr. Takatoshi Kobayakawa
10.35 - 11.00	Food sanitation in Thailand Mrs.Pranee Srisomboon
11.00 - 11.25	Detection of enterotoxigenic *E.coli, V.cholerae and Salmonella* by plasmid-profile analysis, DNA-DNA hybridization and polymerase chain reaction Prof. Hirofumi Danbara
11.25 - 11.50	Molecular dissection of *Shigella sonnei* cell invasion and its regulation Dr. Haruo Watanabe
11.50 - 13.45	Lunch
Session II	**Chairman : Dr. Suchitra Nimmannitya** **Co-chairman : Dr. Koki Taniguchi**
13.45 - 14.10	Studies on dengue virus infections in Nakhorn Phanom, Northeast Thailand Prof. Akira Igarashi

14.10 - 14.35	Viral hemorrhagic fevers (VHF) Dr.Takeshi Kurata
14.35 - 14.50	Comparative nucleotide and deduced amino acid sequence of the envelope glycoprotein gene among three dengue virus type 2 strains isolated from patients with different severities in Maha Sarakam, Northeast Thailand. Ms.Samlee Duangchanda
14.50 - 15.15	Coffee break

Session III **Chairman : Prof. Akira Igarashi**
Co-chairman : Mrs. Suranga Saguanwongse

15.15 - 15.40	Epidemiology and vaccination control of Japanese encephalitis in Thailand Dr. Nadhirat Sangkawibha
15.40 - 15.55	Study on the stability of JE vaccine produced in Thailand Mrs.Teeranart Jivapaisarnpong
15.55 - 16.10	Molecular biology study of hepatitis B virus (HBV) in Thailand Mrs.Kruavon Balachandra
16.10 - 16.25	Juvenile Laryngeal Papillomatosis in Thailand: detection of antibodies to HPV-11 E6 and L2 recombinant proteins Mrs. Sukjai Pholampaisathit
16.25 - 17.00	General discussion
17.00 - 18.00	Reception party by Dr. Komi Kanai (Cafeteria, NIH) Greeting by Dr. Ryosuke Murata Greeting by Dr. Nadhirat Sangkawibha

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Wednesday, June 22, 1994

Session IV	**Chairman : Prof. Michiaki Takahashi**
	Co-chairman : Dr. Vinita Boriraj
09.00 - 09.25	Elimination of Leprosy in Thailand
	Prof. Theera Ramsoota
09.25 - 09.50	New trend in vaccine development
	Prof. Pornchai Matanghasombut
09.50 - 10.05	Coffee break
Session V	**Chairman : Dr.Takashi Kurata**
	Co-chairman : Mr. Daroon Pecharaply
10.05 - 10.30	A clinical trial of thermostable DTP vaccine in Thailand
	Dr. Suchitra Nimmannitya
10.30 - 10.55	Hemorrhagic principles and anti-hemorrhagic principle in Habu snake
	Dr. Tamotsu Sato
10.55 - 11.20	Model animals: their production and application
	Dr. Toshihiko Asano
11.20 - 11.45	At the crossroads: challenges for Thailand's Health development
	Dr. Somsak Chunharas
11.45 - 13.30	Lunch
Session VI	**Chairman : Prof. Koichi Yamanishi**
	Co-chairman : Dr. Paijit Warachit
13.30 - 13.55	Persistently infecting forms of HIV type 1 are highly correlated with mutations at *vif* and *vpr*, but not *nef* genes
	Prof. Kazuyoshi Ikuta
13.55-14.20	The model study for molecular design of future HIV vaccines using of influenza-HIV chimera DNAs
	Dr. Kuniaki Nerome
14.20-14.45	Molecular epidemiology of HIV-I in Thailand
	Dr. Timothy Mastro
14.45-15.00	Coffee break

Session VII	**Chairman : Dr. Sompop Ahandrik**	
	Co-chairman : Prof. Kazuyoshi Ikuta	
15.00-15.15	Quality control of HIV diagnosis	
	Mr.Wattana Uwanich	
15.15-15.30	Early detection of vertical HIV-I infection using Nested PCR	
	Mr.Suthon Wongcheeree	
15.30-15.45	Investigation on the bioactive Thai medicinal plants to Yellow Head Baculovirus (YBV) in Black Tiger Prawns	
	Dr. Angkana Heransalee	
15.45-16.00	General discussion	

Thursday, June 23, 1994

Session VIII	**Chairman : Dr. Haruo Watanabe** **Co-chairman : Dr. Eiko Kondo**
09.00 - 09.25	Evolution and translocation of acid phosphatase (presumably protein tyrosine phosphatase) in *Burkholderia pseudomallei* and their biological significance Dr. Komi Kanai
09.25-09.40	Immunodiagnosis of *Pseudomonas pseudomallei* Mrs. Pimjai Naigowit
09.40-10.05	*Chlamydia trachomatis* infection in Thailand Dr. Toshikatsu Hagiwara
10.05-10.20	Coffee break
Session IX	**Chairman : Dr.Chuinrudee Jayavasu** **Co-chairman : Dr.Kuniaki Nerome**
10.20-10.45	Human herpesvirus 6 (HHV-6) and 7 (HHV-7) infections Prof. Koichi Yamanishi
10.45-11.10	Species specificity and interspecies relatedness in human and animal rotaviruses as determined by sequence analysis and hybridization assay. Dr. Koki Taniguchi
11.10-11.25	Polio eradication programme in Thailand Dr. Supamit Chunsuttiwat
11.25-11.40	Laboratory supporting on polio eradication programme Dr. Yaowapa Pongsuwanna
11.40-13.30	Lunch
Session X	**Chairman : Prof.Hirofumi Danbara** **Co-chairman : Dr.M.L.Rattanasuda Phanurai**
13.30-13.45	A national collaborative study of resistance to antimicrobial agents in *Haemophilus influenzae* and *Streptococcus pneumoniae* Mrs. Surang Dejsirilert
13.45-14.00	Laboratory diagnosis of *C. difficille* associated diarrhoea Mrs. Siripan Wongwanich

14.00-14.15	Molecular epidemiology of *Salmonella Enteritidis* by Pulsed-Field Gel Electrophoresis and Ribotyping Ms. Orn-anong Ratchtrachenchai
14.15-14.30	Coffee break
Session XI	**Chairman : Dr.Shudo Yamazaki** **Co-chairman : Dr.Jakkris Bhumisawasdi**
14.30-14.55	Environmental impact assessment on pesticides and lead for agricultural and industrial workers in the upper northeastern area Ms. Lugsana Leuprasert
14.55-15.10	A pilot programme for neonatal screening in Thailand Ms. Wiyada Charoensiriwatana
15.10-15.50	General discussion
15.50-16.00	Closing speech by Dr. Komi Kanai Leader of Research Promotion Project of NIH, Thailand

REPORTING SPEECH

BY

DR. PANYA SONKOM

DIRECTOR-GENERAL, DEPARTMENT OF MEDICAL SCIENCES

AT THE NATIONAL INSTITUTE OF HEALTH, NONTHABURI

JUNE 21, 1994

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EXCELLENCY

On behalf of the Organizing Committee, I am greatly honoured to have the presence of Your Excellency in this Opening Ceremony of the Memorial Seminar of the Research Promotion Project in the National Institute of Health.

The Research Promotion Project of the National Institute of Health is a 5-year project, which has been successfully established since 1985 with the cooperation between the Department of Medical Sciences and the Japan International Cooperation Agency. During the period of the Project, many sophisticated technologies in medical sciences have been developed and transferred from many Japanese experts to Thai scientists. Meanwhile, the Department of Medical Sciences has also fully supported its personnel in various aspects in order to broaden and strengthen their knowledge. So far many research achievements have been obtained, such as the development of JE vaccine, which are very beneficial to the health of Thai people. There are also other research projects currently applied in the regional areas throughout the country. The National Institute of Health could provide a lot of successful training courses and workshops transferring the technical know-how to the health personnel and has cooperated with other organizations in different research projects. Many speakers of the Institute were well accepted in international seminars.

The first 5 years of the Research Promotion Project was ended in1990 but some research activities and technical transfer were not completed. Therefore the Project has been extended for two years and followed by a two-year Follow-Up Period, which is to end in this coming July. As a celebration of the successful completion of the project, the Department of Medical Sciences with the cooperation of the Japan International Cooperation Agency has organized this Memorial Seminar, which will last for three days from June 21 to 23 with the financial support from the Japanese Government. The objectives of this seminar are to strengthen the close relationship between Thai and Japanese scientists, as well as

to provide the technical know-how and research achievements arising from this project. The participants will have a good chance in obtaining knowledge in advanced technologies developed in Thailand and Japan. This will also enable them to exchange their experience on the same interest. Nine Thai and twelve Japanese experts are invited as our lecturers. Fifteen Thai counterparts will also present their research achievements which will be useful for all interested persons.

I am now have the honour to invite Your Excellency to give us an address and to open the seminar.

OPENING ADDRESS
BY
H.E. DR. ARTHIT OURAIRAT
MINISTER, MININSTRY OF PUBLIC HEALTH
AT NATIONAL INSTITUTE OF HEALTH, NONTHABURI
JUNE 21, 1994

Director-General, Dr. Yamazaki, Ladies and Gentlemen

It is, indeed, a great pleasure and honour to have this opportunity today to preside over the Opening Ceremony of the Memorial Seminar of the Research Promotion Project in the National Institute of Health.

The laboratory research in medical sciences is one of the essential activities which is very helpful in solving the national health problem. The Research Promotion Project in the National Institute of Health is one of the most successful cooperative research projects in Thailand, a project in which Thai and Japanese scientists have devoted their endeavour together all through almost a decade, and finally resulted in the better health of the people. I regard the achievement as being less of a proud to the Institute individually than to the Thai and Japanese Governments as a whole, and would like to take this opportunity to express my sincere gratitude to the Japan International Cooperation Agency, the various health institutes and universities in Thailand for all their kind cooperation and assistance, as well as to all persons concerned who have contributed to this success.

I trust that all participants of this seminar will gain a substantial advantages from the invaluable knowledge and long experience of the Thai and Japanese lecturers, and from the successful researchers of the National Institute of Health. I fully hope that this seminar will lead to the new domestic and international understanding and cooperation, and strengthening the existing relationship. Hereby I would like to convey my sincere thanks to all the speakers who will give us the knoweledge, and to the Japanese Government who has provided the financial support for this seminar.

I now have the honour and pleasure to declare the Memorial Seminar of the Research Promotion Project in the National Institute of Health open. I wish this seminar a success and wish all of you here happiness and good luck.

REMARK

BY

SHUDO YAMAZAKI M.D., Ph.D.
DIRECTOR-GENERAL
NATIONAL INSTITUTE OF HEALTH OF JAPAN

JUNE 21, 1994

On behalf of the Joint Evaluation Team dispatched from JICA, I would like to extend to all the participants my warmest congratulations on the opening of the NIH-Project Memorial Seminar. I say congratulations because this seminar has been planned to mark the achievement of the Research Promotion Project of the National Institute of Health, Thailand (RPP-NIH) in accordance with its final evaluation. The project was initiated in August 1985 by a *Record of Discussion* signed by Dr. Ryosuke Murata, Chairman of Advisory Committee, JICA and Dr. Nadhirat Sangkawibha, former Director-General of the Department of Medical Sciences (DMS), Thailand, and it will endproving great success at the end of July 1994.

Recently, DMS and JICA have published a final summary of RPP-NIH. This extensive report was prepared by Dr. Komi Kanai, Leader of the Japanese Technical Experts; he has been staying in Bangkok since 1987 and during these last seven years devoted himself to the accomplishment of this project. The book describes the successful history of the project and reviews all the research activities and achievements during the period from 1985 to1994. According to the report, more than 100 Japanese experts have visited the Thai NIH to work in close cooperation in order to transfer technology useful for the diagnosis, prevention, and control of infectious diseases. In addition as many as 50 Thai research fellows and administrators have been sent to Japan to upgrade relevant techniques as well as to deepen mutual understanding and to promote friendship between Thailand and Japan. I was particularly delighted to learn from this report that more than 130 scientific papers have been published in international journals, and 128 presentations have been made at either international or domestic meetings is connection with this project.

This Memorial Seminar is being attended by both Thai and Japanese scientists, and I am so pleased to be able to participate. Although this seminar marks the close of one cooperative medical effort between Japan and Thailand,

I wish it to be the begining of a joint endeavor towards establishing NIH Thailand as a center of excellence in Asia

Finally, I sincerely hope a relationship between two countries will continue to deepen and grow stronger as we pursue common interests towards a universal goal.

GREETING NOTE
FROM
TAKATOSHI KOBAYAKAWA M.D., PH.D.
MEDICAL COOPERATION DEPARTMENT
JAPAN INTERNATIONAL COOPERATION AGENCY

The Research Promotion Project of the National Institute of Health (NIH) was initiated in 1985 as technical cooperation through Japan International Cooperation Agency (JICA), taking advantage of the occasion of the establishment of the NIH by Japanese grant aid cooperation.

During the total project period of nine years including two years of extension followed by another two years of follow-up, the project proceeded smoothly and successfully, by the mutual understanding and cooperation of participants of both countries, with magnificent achievements some of which will be presented in this memorial symposium.

Although the project itself draws to a close, I sincerely hope that the cooperation between Thai and Japanese governments be more extensive and ever-lasting. It goes without saying that the NIH will contribute to the health-blessed prosperity and welfare of not only Thai but also everybody in Asian countries as one of the most appreciated international medical research and reference center.

HOW JICA IS CHALLENGING INFECTIOUS DISEASES IN THE WORLD

Takatoshi Kobayakawa
Medical Cooperation Department, Japan International Cooperation Agency

The Japan International Cooperation Agency (JICA) is a governmental agency responsible for contributing to the economic and social development of developing countries and to promote international cooperation. As a main and comprehensive approach to promote technology transfer, JICA implements project-type technical cooperation programmes. This programme provides integrated assistance from planning and implementation to evaluation through combination of the three types of cooperation including training programme in Japan, dispatch of experts and provision of equipment which initially lasts for five years with or without extension or follow-up.

In the infectious diseases related fields, various types of cooperation are being implemented. They are medical research and health laboratory services, infectious disease control and vaccine production and its quality control projects.

In addition, JICA has a unique programme for anti-infectious diseases with the main emphasis upon EPI activity which is, in part, a cooperative programme with UNICEF.

Thirdly, JICA has a training programmes which consists of two classifications :

(1) Training conducted in Japan,

(2) Third-country training held in the host countries outside Japan.

Details of those cooperation will be presented.

FOOD SANITATION IN THAILAND

Pranee Srisomboon
Department of Medical sciences, Ministry of Public Health

Epidemiological information from the Ministry of Public Health shows that foodborne diseases have been one of the major health problems in Thailand. Cases of acute diarrhoea, dysentery, enteric fever, food poisonig due to miorobial toxins, parasitic and viral diseases are relatively high among Thai people of all ages. These illness and diseases cause by micobiological agents contaminating the food and water. They can be eliminated or reduced by sanitary practices in handling of food and proper protection of water reservoirs. Food for humans must be protected from gross contamination of pathogenic microorganisms. In addition, perishable foods be handled properly in order to prevent growth of microorganisms which cause them unsafe for consumption and /or spoilage. Now-a-days people demand not only enough food but also safe and nutritious food for better quality of life.

One of the ultimate goals of health education is to make people realizing the importance of sanitary food handling, preparation and processing which keep them
and their families healthy and wealthy. Food handlers must be aware of the impacts of insanitation condition to food safety and economic loss.

The problems concerning unsafe food and foodborne diseases relate to a wide range of complicated elements such as food habit, traditional practices, shortage of clean water supply especially in rural areas, uneducated refugees, movement of population due to work opportunities, pilgrimage and expansion of tourism.

Health Sector of the Goverment of Thailand take responsibilities in this issue by laws and regulations. Central health authorities in the Ministry of Public Health and local health authorities in provincial, district and rural administrations cooperate with community leaders in combating against foodborne illness through various activities. Upon improvement of sanitary practices, health authorities are focusing on risks of vulnerable groups, mother and child health care, health education in primary and secondary schools, environmental sanitary improvement. in villages, incorperation of food sanitation as a key element in primary health care programmes, introduction of Good Manufacturing Practices in food service

establishments promotion of sanitation for street vended foods, emphasis on the application of HACCP to every steps of food handling in food processing, storage and distribution. Enormous effort and resources have been put through a great number of programmes and activities planned and implemented by various agencies in order to create public awareness in food sanitation improvement and to reduce economic impact due to unsafe food.

DETECTION OF ENTEROTOXIGENIC *E. COLI, V. CHOLERAE,* AND *SALMONELLA* BY PLASMID-PROFILE ANALYSIS, DNA-DNA HYBRIDIZATION AND POLYMERASE CHAIN REACTION

Bangtrakulnonth A.,* Bangtrakulnonth S.,* Pornruengwong S.*
Ratchtrachenchai O.,* Abe A.**, Danbara H.***
*National Institute of Health, Department of Medical Sciences, Ministry of Public Health,Thailand
**Department of Bacteriology, The Kitasato Institute, Japan
***Department of Microbiology, School of Pharaceutical Sciences, Kitasato University, 5-9-1 Shirokane, Minato-ku, Tokyo 108, Japan

Plasmid-profile analysis, DNA-DNA hybridization, and polymerase chain reaction were applied for the detection of enterotoxigenic *Escherichia coli* (ETEC), *Vibrio cholerae*, and*Salmonella.*

1) An agarose gel electrophoresis was applied for the analysis of plasmid profile of salmonellae. This method was simple and rapid, and able to detect the 50-90 kb virulence plasmid which is an indicator plasmid for systemic infection in humans and animals by many serovars of *Salmonella* (*S. Typhimurium , S. Enteritidis, S. Gallinarum, S. Choleraesuis* etc.).

2) A cassette-probe plasmid containing a 1,268 bp trivalent LTH-STIa-STIb probe was constructed. The trivalent probe conjugated with horseradish peroxidase was able to detect ETEC and *V. cholerae* colonies by DNA-DNA hybridization.

3) A polymerase chain reaction (PCR) method using LTh, STIa, and STIb primer pairs was developed. Five types of ETEC strain with LTh, STIa, STIb, LTh-STIa, and LTh-STIb genotypes were distinguished by the single PCR procedure using the mixture of the three set of primers . ETEC and *V. cholerae* with LTh and CT genes, respectively, were also distinguishable.

4) Genus-specific probe was developed for the detection of *Salmonella* in foods. The target fragment of 16S rRNA gene amplified and biotin-labeled by PCR was hybridized the membrane-immobilized *Salmonella* probe, and the hybidized was detected by chemiluminescence. All the 24 different serovars of *Salmonella* tested specifically hybridized with the probe. It was possible to detect in the order of 10^4 bacteria in fish meat homogenate in 10 h.

MOLECULAR DISSECTION OF *SHIGELLA SONNEI* CELL INVASION AND ITS REGULATION

Haruo WATANABE, Shyu-ichi NAKAYMA, Eiji ARAKA and Jun TERAJIMA
Department of Bacteriology, National Institute of Health Tokyo, Japan

Essential pathogenesis of *Shigella* is the invasiveness of epithelial cells. Molecular events of *Shigella* cell invasion are divided into four processes; cell entry, escape from phago-vacuole, intracellular multiplication, and intercellular spreading. These processes are controlled by plasmid and chromosome-encoded gene products. Many genes spanning about 27-kb region of *Shigella sonnei* invasion plasmid are involved in bacterial cell entry: ipaBCD gene products are secreted into the surface of bacterial outer membrane and thought to act as an invasin, which interacts with host cells and induces phagocytosis-like movemnt to uptake bacteria. Expression of these gene products is tightly regulated by dual positive regulators virF and invE. virF is a key factor for the regulation. Invasiveness of *Shigella* is regulated by environmental conditions, temperature, osmolarity and external pH. One of environmental conditions, external pH, is sensed by CpxA-CpxR two components-system of bacteria and its signal is transmitted to the expression of VirF gene. We will describe the molecular mechanism how *Shigella* senses the change or environmental conditions works efficiently the machinery of cell invasiveness

STUDIES ON DENGUE VIRUS INFECTION IN NAKHORN PHANOM, NORTHEAST THAILAND

Akira IGARASHI
Department of Virology, Institute for Tropical Medicine, Nagasaki University, 12-4 Sakamoto-1-chome, Nagaski, Japan 852

Studies on hospidtalized dengue fever (DF) and dengue hemorrhagic fever (DHF) patients as well as outpatients of fever of unknown origin (FUO) were carried out at Nakorn Phanom Provincial Hospital during the epidemic seasons in 1992 and 1993. Inoculation of patientsû sera into C6/36 cells isolated 31 dengue virus strains (19 type 2, 8 type 4, 4 type 1) in 1993. Prevalence of type 4 dengue virus followed that of type 2, which had been predominant in 1992 and 1993. The virus isolation results generally agreed with viral genome detection by reverse transcriptase-polymerase chain reaction (RT-PCR), which was applied directly on serum specimens. RNA extraction prior to the RT-PCR did not significantly improve the efficiency to detect viral genome. Cytokine levels (II-1, II-6, TNF) in patientûs sera did not correlate with clinical severity of the disease, with normal level of TNF. The viral genome detection rate by RT-PCR was highest on the 2nd day and quickly decreased to undetectable level on the 6th day. While IgM anti-dengue antibody detection rate increased along with the day of the disease, reaching 100% on the 5th day of the disease. Combined results of RT-PCR and IgM-ELISA provided over 80% sensitivity of dengue laboratory diagnosis regardless of the day of the disease when serum specimens were collected. Sequential ELISA on blood or serum specimens dried on filter paper strips showed stability of anti-dengue IgG antibodies. While, anti-dengue IgM antibodies was unstable on storage, especially for serum from primary dengue cases. These studies were conducted in collaboration with NIH, Mahidol University, and Nakorn Phanom Hospital, Thailand, and supported by the Grant-in-Aid for Scientific Research, International Scientific research Program, from the Ministry of Education, Science and Culture of Japan.

VIRAL HEMORRHAGIC FEVERS (VHF)

Takeshi KURATA
Department of Pathology, National Institute of Health, Tokyo 162

The diseases (VHF) are characterized by fever and in the most cases, shock and hemorrhage. The four agents, Lassa, Marburg, Ebola and Crimean-Congo hemorrhagic fevers (CCHF) are known to have caused significant outbreaks of disease with person-to-person transmission. The increased travelling in the tropical areas provides opportunity for importation of these diseases into non-endemic countries. Except for CCHF, other three diseases are restricted to sub-Saharan Africa. Travelling in the areas will be one of differential diagnostic point. Virology, epidemiology, clinical signs, diagnosis, and pathology will be discussed comparatively. There are many other viral diseases causing hemorrhages as one of important clinical signs without human-to-human transmission. The new disease, ARDS (acute respiratory distress syndrome) or HPS (hantavirus pulmonary syndrome), suddenly appeared in USA in 1993 to 1994, with high mortality rate. The causative agent has been determined as one of hantavirus family, etiology of classical HFRS, which are popular disease in Asian countries. The illness also will be introduced.

COMPARATIVE NUCLEOTIDE AND DEDUCED AMINO ACID SEQUENCE OF THE ENVELOPE GLYCOPROTEIN GENE AMONG THREE DENGUE VITUS TYPE 2 STRAINS ISOLATED FROM PATIENTS WITH DIFFERENT SEVERITIES IN MAHA SARAKHAM, NORTHEAST THAILAND

S. Duangchanmda*, Tanaka M.**, Morita K.**, Rojanasuphot S.*, Igarashi A.**

*Virus Research Institute, Department of Medical Sciences and
**Department of Virology, Institute of Tropical Medicine, Nagasaki University, Nagasaki 852, Japan

Nucleotide (nt) sequence of the envelope glycoprotein (E) gene was determined by the primer-extension dideoxy chain termination method for 3 dengue virus type 2 (D2) strains which had been isolated from patients with dengue fever (DF), degue hemorrhagic fever (DHF), and dengue shock syndrome (DSS), in Maha Sarakham, Northeast Thailand, in 1986-1987. Their nt sequences were essentially the same except a single silent nt replacement in each DHF and DSS strain compared with DF strain. Therefore, these 3 strains possessed identical deduced amino acid (AA) sequences in their, E protein. The result indicated that the primary structure of the E protein of D2 virus is not related with the clinical severity of the infected patients. Eleven nt replacements which resulted in 4 AA replacements were found unique to these 3 Northeast Thai strains. Sequence similarity showed that the d3 Northeast Thai strains were closest to the DSS isolate (H) followed by the DHF isolate (D) in Bangkok 1980 and Jamica strain.

EPIDEMIOLOGY AND VACCINATION CONTROL OF JAPANESE ENCEPHALITIS IN THAILAND

N. Sangkawibha*, Chunsuttiwat S.**, Rojansuphot S.*
*Department of Medical Sciences
**Department of Communicable Diseases Control

Japanese encephalitis (JE) has been a serious health problem in Thailand since 1969. The pattern of the disease is endemic and distributed all over the country with yearly outbreaks in the north and northeast during rainy season. More than 80% of patients are under 15 years old. After 1986, a gradual decreasing trend of encephalitis cases was observed in all regions and in every age group.

Several studies showed the efficacy, safety and immunogenicity as well as the possibility to integrate JE vaccine into the routine immunization programme. Imported JE vaccine has been registered and widely used in Thailand since 1986. The local production of Nakayama vaccine was successful in 1988. Even the implementation of the national programme was launched in 1990, extensive JE vaccination had been carried out by the community participation. From 1986 up to the end of 1993, a total of about 5,200,000 doses of Nakayama and Beijing vaccines has been used in this country. A 14% of the total amount was used in the national programme. The vaccine used in the national programme is preferably the Nakayama strain for particular reasons.

The possible influenzing factors for the decreasing trend of JE may be vaccination and/or the environment changes that do not favour the virus transmission. The future research and surveillance to support JE control programme were commented.

STUDY ON THE STABILITY OF THE JAPANESE ENCEPHALITIS VACCINE PRODUCED IN THAILAND

T.Jivapaisarnpong*, Leelasiri K.*, Tapjula A.*, Subhachaturus s.**
*Department of Medical Sciences
**Government Pharmaceutical Organization

The stability of the first 5 lots of liquid Japanese encephalitis (JE) vaccine locally produced by the Government Pharmaceutical Organization was studied. The potency of the vaccine was determined by plaque reduction neutralization test (PRNT) in chick embryo cell culture and kept at different degrees of temperature, at different time intervals. It was found that, at 2-8°C, all 5 lots passed the potency test when kept for 12 months and 4, 3, and 1 lots of the 5 lots passed the standard after 1-, 2- and 6-month storage respectively. However,the potency of all lots of the vaccine was below standar when they were kept at 37°C and 40°C for 1 month.

MOLECULAR BIOLOGICAL STUDY OF HEPATITIS B VIRUS (HBV) IN THAILAND

Balachandra K.*, Thawaranantha D.*, Pitaksutheepong C.*, Wattaanaseree J.**, Boonchird C.***, Bhumisawasdi J.*, Warachit P.* and Pantuwatana s.***
*National Institute of Health
** Government Pharmaceutical Organization
*** Faculty of Sciences, Mahidol University

Hepatitis B viral genome was mostly concerned in this molecular biological study. HBV genomes from active chronic HBV carriers were firstly identified their subtypes by using polymerase chain reaction (PCR) and secondly analyzed their heterogeneities by gene cloning and restriction endonuclease analysis. By using PCR, it revealed that thai HBV carriers could be devided into two subtypes (adr 81% and adw 19%). Fro gene cloning, HBV genome, isolated from Dane particles of donated blood of active chronic HBV carrier was incomplete double strand circular DNA. Using the endogenous DNA polymerase, HBV genome could be converted to a complete double strand circular form. The double strand HBV-DNA was then cloned into *Escherichia coli* strain HD-5-alpha, using the unique BamHI cleavage site within the tetracycline (Tet) resistance gene of the PBR322 plasmid vector. Four clones from different HBV carriers were further analyzed and compared the heterogeneities among these clones and standard clones from other countries, by restriction endonuclease enzymes. It was found that there were much more homogeneity in endonuclease cleavage patterns among clones from Thai isolates than from other countries. The result of this study gave preliminary data of the genome structures and the ability of clones in production of substantial quantities of HBV-DNA for further studies such as gene sequencing and gene expression.

JUVENIL LARYNGEAL PAPILLOMATOSIS IN THAILAND; DETECTION OF ANTIBODIES TO HPV-11 E6 AND L2 RECOMBINANT PROTEINS

S. Pholampaisathit *, Sameshima A.**, Kohno Ml.**, Fujiyoshi T.†, Sonoda S.†, Ohyama M.**

* Virus Research Institute, Department of Medical Sciences

** Departmment of Otolaryngology, Faculty of Medicine, Kagoshima University, Kagoshima, Japan

† Department of Virology, Faculty of Medicine, Kagoshima University, Kagoshima, Japan

Juvenile Laryngeal Papillomatosis (JLP) is a histologically benign tumor, but causes a serious problem of recurrent airway obstruction. The prevalence of JLP in Thailand is 2.8 (per 100,000 chidren aged at 0-14 years) that is 5-10 times more than those in other countries. We demonstrated the HPV-11 in tumor tissues from JLP patients of Thai children. In this report, we present serological detection of antibodies against HPV-11 E6 and L2 recombinant proteins.

Sera and biopsy specimens were obtained from 20 JLP patients admitted to 3 major hospitals in Thailand. HPV-11 DNDwas detected in the biopsy specimens by PCR and dot blot hybridization test. The HPV-11 genomic DNA was cloned using EMBL3 as a vector. E6 and L2 regions of the HPV-11 DNA were subcloned with expression vector pEXL and pEX3, respectively and the recomvinant E6-alpha-gal and L2-alpha-gal fusion proteins were expressed in the *E. coli* pop 2136. The bacterial extracts of *E. coli* pop2136 harboring either pEX1-E6 or PEX3-L2 plasmids were subjected to 6% SDS-PAGE, then transferred to Immobilon-P transfer membrane to test the positivity of antibodies against HPV-11 E6 or L2 recombinant proteins.

We examined 20 serum samples of JLP patients who were positive for HPV-11. Western blot analysis revealed that anti-E6 seropositive were 5% (1/20) , anti-L2 seropositive were 10% (2/20), respectively. It is thus indicated that HPV-11 viral antigens are recognized by host immune system even though the lesion of laryngeal papilloma as limited on the surface of laryngeal mucosa.

ELIMINATION OF LEPROSY IN THAILAND

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Modern Leprosy Control Programme, based on active case finding and domicilary treatment of Dapsone Monotherapy was started in Thailand in 1955 as a specialized programme. It was the integrated into basic health services in 1971 covering 67 of total 73 provinces. This successful efforts had resulted in good impact that leprosy was undercontrol (prevalence below 10 per 10,000 population) in 1974. Due to emergence of Dapsone resistance, W.H.O. Recommended Multidrug Therapy (MDT) programme was implemented in 1984 and gradually expanded to cover total 73 provinces in 1989, 83 and 98% of total registered cases of leprosy in 1989 and 1991, respectively. The more rapid and effective technology of MDT has drastic impact on reduction of prevalences and detection rate of new cases of leprosy from 1989-1993 at the reduction rate of 13.4 and 6 percent per year, respectively. These changes lead to natural decline of leprosy in Thailand as measured by some epidemiological indicators.

The Leprosy Eliminationa Progamme has been formulated in 1993 with the goal to illminate leprosy as a public health problem by the year 2000. This elimination was defined as attaining a level of prevalence and detection-rate of new case below 1 per 10,000 and 1 per 100,000 population, respectively in three consecutive years.

Up to the end of 1993 out of total 73 provinces, 47 already met with prevalence lower than 1 per 10,000 population meanwhile 27 showed detection rate less than 1 per 100,000 population in addition, out of total 376 districts, there were 376 (51%), 199 (27%) and 179 (24%) districts where no newly detected case of leprosy have been found for one, two and three consecutive years, respectively.

With these encouraging trend and strongly political committment, it is hoped that Thailand can achieve the Leprosy Eimination Target by the Year 2000 as set by The World Health Assembly in May 1991.

A CLINICAL TRIAL OF THERMOSTABLE DTP VACCINE IN THAILAND

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Since the introduction of Expanded Programme on Immunization in 1978, immunization has been the greatest public health success story of the last decade. However the cold chain remains the major problem in vaccine management in most tropical countries. In 1988, the Research Foundation for Microbial Diseases of Osaka University, Biken has successfully produced the thermostable DTP-A (acellular) vaccine. Expecting its potential benefit, a joint Thai and Japanese cooperative clinical trial had been designed in 1991-1992. The aim of the study was to evaluate this new thermostable DTP-A vaccine regarding the frequency of adverse reactions and immune response in Thai infants by comparing with regular DTP used in EPI.

There were 2215 DTP and 2483 thermostable DTP-A immunizations given to infants 2-6 months of age. The prospective study for local and systemic reactions during the 7 day-period following series of 3-dose primary immunizations
revealed that the local reactions were much lower in frequency in the thermostable DTP-A vaccine group than in the DTP group. The increase in frequency of local reactions with the increasing immunization series number was observed in both groups. Except for vomiting and drowsy, systemic reactions were also less frequent in the group of DTP-A vaccines. Convulsion was the only serious systemic reaction observed in 0.27% in the DTP group and in 0.04% in the DTP-A
group. The thermostable DTP-A vaccine is considerably as safe as DTP. Its acellular pertussis component contributed to lesser local and systemic reactions.

The immunogenicity of the DTP-A vaccine as measured by antibody response to its components was comparable to the DTP vaccine. The better responses to PT and FHA components of pertussis antigens were observed in DTP-A vaccine recipients while the response to diphtheria and tetanus are similar.

HEMORRHAGIC PRINCIPLES AND ANTI-HEMORRHAGIC PRINCIPLE IN HABU SNAKE

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Hemorrhage is one of the most striking manifestations evoked by the parenteral injection of crotalid and viperid snakes. We purified two principles, HR 1 and HR 2, responsible for the hemorrhagic reaction from the venom of Habu snake *(Trimeresurus flavoviridis)*, a crotalid. HR 1 possesses the strongest hemorrhagic activity among snake venom hemorrhagic principles hitherto obtained. HR 1 and HR 2 are immunologically distinct and proteinases having molecular weights of 55 kD and 25 kD , respectively. Their primary structures indicated that they have a common structure including the putative active site for metalloproteinases. On the other hand, we isolated an anti-hemorrhagic principle from the Habu snake serum and investigated its biological and physicochemical properties. It is an alpha 2-HS glycoprotein like protein with the cystatin superfamily related structure. The role of such a natural anti-toxic substance in venomous animals will be discussed.

MODEL ANIMALS: THEIR PRODUCTION AND APPLICATION

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It is true that laboratory animals take very important position for basic study
of bio-medical sciences. Most of them have been used as model animals. There are two types of model animals. One is experimentally induced disease animal models and the other one is spontaneously occurring pathological animal models. We will introduce you the activities in our laboratory with respect to establishment of model animals especially hereditary disease models. We shall be happy if this will be able to contribute to the progress of bio-medical science and laboratory animal science in Thailand.

1. ICGN mouse: this mouse is hereditary nephrose model mouse. We found this mutation from our ICR mouse and established new strain. MCC and MST strains of Mastomys: These two strains of the mastomys are hereditary storage disease model animals. We found these character from our mastomys colony.
2. SCID bg and Nude-bg-Xid mouse: It is easy to introduce some mutant gene to hereditary model animal by mating. We have established those severe combined immunodeficient mice and now are going to use them for HIV study.
3. Transgenic and knock out mouse: It is well known that transgenic and knock out animals are produced by gene manipulation.

AT THE CROSSROADS : CHALLENGES FOR THAILANDûS HEALTH DEVELOPMENT

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Over the past twenty years, Thailand has undergone rapid economic and health (demographic, epidemiological) transitions. While on the one hand the economic outlook is bright, even to the extent of Thailandûs emerging status as a Newly Industrialized Country, persisting health development challenges remain as targets for future research and international support. This paper documents Thailandûs current economic and health development situations, their transitions and challenges. Special reference is made towards emerging post-transitional health/epidemiological problems, reorientation of health services and the referral system, community participation, health care financing, public-private health care partnerships, decentralization of the health service system and essential national health research.

THE MODEL STUDY FOR MOLECULAR DESIGN OF FUTURE HIV VACCINES USING INFLUENZA-HIV CHIMERA DNAS

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Although a number of efforts have been made to develop HIV vaccines, prevention or modification of HIV-induced disease is still crucial to stemming the AIDS epidemic. This study was initiated to design a successful HIV vaccine that will elicit neutralizing antibodies as well as cell-mediated cytotoxicity using influenza-HIV chimera DNAs. We inserted DNA segments coding for 7 to 15 amino acids of the V 3 region if gp 120 of HIV-1 into the loop region of the influenza A/SW/ Ehime/1/80 virus hemagglutinin gene. The resultant influenza-HIV chinera DNA was inserted into the genome of vaccinia virus under the control of a hybrid promoter. Expression of influenza virus hemagglutinin-HIV proteins was demonstrated in the infected cells by immunofluorescent labeling with antibodies to influenza virus hemmagglutinin and HIV peptide, coinciding with the evidence obtained from immunoprecipitation after metabolic labeling with 35 S-methionin with antibody to H 1 hemagglutinin. It was of particular interest to observe that infection in mice with a recombinant bearing influenza virus hemagglutinin containing a HIV15-amino acid peptide corresponding to the V 3 region of gp 120 at positions 308 to 322, induced, in addition to humoral immune responses, in generation of marked cytotoxic T lymphocytes specific for either influenza virus or the AIDS (HIV-1) virus. This suggests that molecular design using influenza virus hemagglutinin gene may be useful for development of a potential HIV vaccine.

PERSISTENTLY INFECTING FORMS OF HUMAN IMMUNO-DEFICIENCY VIRUS TYPE 1 ARE HIGHLY CORRELATED WITH MUTATIONS AT *vif* and *vpe*, BUT NOT *net* GENES

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The mechanism that regulate either cell death or latent/persistent infection in human immudeficiency virus type 1 (HIV-1) infected cells is essential to our understanding of the pathogenesis of acquired immune deficiency syndrome (AIDS). Here, we examined the correlation between the mutant HIV-1 and generation of persistent infection in MT-4 derived subclone M10. The result showed that the cells survived the infection with *vif*, *vpr*, or *vpu* mutant HIV-1 after transient cytopathicity. Most of the survivors producing infectious, but non-cytopathic, HIV-1 were found to carry heterogeneous HIV-1 genomes containing naturally occurring additional mutations containing marked internal deletions in the region overlapping *vif* and *vpr* or nucleotide substitutions in *vif* and/or *vpr* region. On the other hand, no survivor cells were obtained by infection with wild-type or *nef* mutant HIV-1. Then, we examined the possible generation of less of or non-cytopathic HIV-1 leading to persistent infection be in vitro serial passage. Peristent infection could be induced by only 4 passages of wild-type HIV-1 and increasing persistent infection was observed by the serial passage, but not be *nef* mutant even after 50 passages. The DNA sequencing showed that all viral genomes derived from persistently infected cells contained termination codon in *vpr* was also identified. These structures were identified in the cells acutely infected with serial passages of wild-type, but not of *nef* mutant HIV-1. Thus, the *vif* and *vpr* gene mutations seem to be essential for persistent infection and these mutations were naturally progressively induced by serial passage of wild-type HIV-1, while not be serial passage of *nef* mutan HIV-1, indicating that *nef* gene

or Nef protein might be important for such mutations induced during the serial passage.

Similar mutated structures were also observed in peripheral blood mononuclear cells (PBMC) sequentially (every year for 3 years) obtained from two asymptomatic carriers. In addition, analysis by polymerase chain reaction of serially diluted PBMC-DNAs from 93 HIV-1 carriers showed that only 33% in the gag-positive DNAs was positive for the region overlapping *vif* and *vpr*.

Recently, the importance of HIV-1 *nef* expression for the development of AIDS has been suggested by experiments in rhesus monkeys infected with simian immunodeficiency virus *nef* mutants. Since we showed here that the *nef* geneproduct might play an essential role for HIV-1 persistent infection, we next focused on the immunological function of the Nef protein, and revealed the evidence that the protein reduced the CD4/CD8 ratio in Il-2-dependent cultures of PBMC from healthy donors. In addition, it was shown that the carboxy-terminal region of Nef protein was expressed, at least in part, on the surface of the persistently infected cells. Thus, the Nef protein expressed on the surface of persistently infected cells might be responsible for the induction of CD4-specific immunodysfunction.

MOLECULAR EPIDEMIOLOGY OF HIV-1 IN THAILAND

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A joint activity of the Thai Ministry of Public Health and the U.S. Centers for Disease Control and Prevention (CDC)

Although the first case of AIDS in Thailand was reported in 1984, low rates of HIV-1 infection were detected in multiple surveys of various high-risk groups until 1988 when a dramatic increase was documented among injecting drug users (IDUs) in Bangkok. HIV-1 rates among Bangkok IDUs increased to 31.44% in 1988 and by 1989, similar rates were observed among IDUs in all regions of Thailand.

An explosive epidemic of heterosexually transmitted HIV-1 began in 1989.

By 1993, national rates of HIV-1 seroprevalence were: female brothel prostitutes, 27%; men attending sexually transmitted disease (STD) clinics, 8%; 21-year-old male military conscripts, 4%; and pregnant women, 1.4%. The highest rates among these groups have been documented in northern Thailand.

Studies of the genetic character of HIV-1 strains in Thailand have identified two distinct envelope subtypes, B and E. When characterized be *ene* nucleotide sequence, isolates within the two subtypes display limited divergence, indicating recent and separate introduction into Thailand. A 1991 study found these two subtypes to segregate by patient risk behavior. Subtype B (Thai genotype B) predominated (76%) among IDUs while most persons (86%) with sexual risk factors had subtype E (Thai genotype A) [Ou C-Y, et al. *Lancet.*. 1993; 341:1171-74]. Subtype B accounts for most HIV-1 infections in North america and Europe; subtype E strains have subsequently been found in the Central African Republic.

Molecular epidemiologic studies in Thailand have been aided greatly by the development of serologic methods for determining the infecting HIV-1 subtype. In Thailand, enzyme immunoassays based on14-amino acid peptides from the gp120 V3 loop of subtypes B and E (Thai genotypes Band A) are highly specific and quite sensitive [Pau C- P, et al. *AIDS*. 1993;7:337-40]. Serotyping of more than 1,500 specimens in Thailand has confirmed that subtype E predominates (>90%) among persons with sexual risk factors in all regions of the country while

subtype B predominates among the smaller population of IDUs, particularly in Bangkok and the South.

Understanding the evolving molecular epidemiology of HIV-1 in Thailand is important in preparing for possible HIV-1 vaccine trails. Also, further study of Thailandûs unique molecular epidemiology may lead to new insights into HIV-1 transmission, immunity, and pathogenesis.

EARLY DETECTION OF VERTICAL HIV-1 INFECTION USING NESTED PCR

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A simple, sensitive, specific and inexpensive Nested PCR was developed for detection of HIV-1 provirus in clinical specimens. The test showed 100% coincided with reference serological methods when the test was evaluated in 295 IVDU. An open cohort study of 100 pairs of HIV-1 seropositive mothers and infants was set up at Chiang Rai Prachanukrow Hospital. Up to date, 55 pairs of the blood samples were tested by Nested PCR using primers at pol region. HIV-1 provirus was identified 9/55 (16.4%) and 19/55 (34.4%) of the infants at birth and 1 month, respectively. Further study will be continued at age of 6, 12 and 18 months of the children in order to verify HIV-1 vertical transmission rate.

INVESTIGATION ON THE BIOACTIVE THAI MEDICINAL PLANTS TO *YELLOW HEAD BACULOVIRUS* (YBV) IN BLACK TIGER PRAWNS *(PENAEUS MONODON)*

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The screening of selected Thai medicinal plants and weeds, which have antiviral activity has been carried out. Ethanol crude extract of thirteen species of plants were verified for their *in vivo* activities against *Yellow head baculovirus* (YBV) in black tiger prawns (*Penaeus monodon*). The scrutinized species are *Clinacanthus nutans, Cassia alata, Phyllanthus acidus, Phyllanthus amarus, Phyllanthus urinaria, Psitium guajava and Tinospora crispa*. The LD_{50} values and MIC were determined for their effects of the crude extracts. Water qualities effectuated by active extracts were also examined on BOD, COD, pH and alkalinity.

EVOLUTION AND TRANSLOCATION OF ACID PHOSPHATASE (PRESUMABLY PROTEIN TYROSINE PHOSPHATASE) IN *BURKHOLDERIA PSEUDOMALLEI* AND THEIR BIOLOGICAL SIGNIFICANCE

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JICA expert in Thai-NIH

Melioidosis is an endemic disease in South-east Asia and the largest number of cases has been reported from Thailand. The etiologic agent is *Burkholderia pseudomallei.* By screening assay with p-nitrophenyl phosphate as substrate, we found that most strains of *B. pseudomallei* have a high acid phosphatase activity. In an attempt to purify the enzyme from culture supernatant, cell-free extract, and the membrane fraction, we came to the suggestive observations that the acid phosphatase is glycoproteins evolved from premature enzyme proteins by glycosylation and translocated from the cytoplasm to the outermembrane and finally secreted into the environment. Tunicamycin inhibited the glycosilation without the effect on the cell viability, and modified the heat-sensitivity and pH-activity of the enzyme. Substrate-specificity assay revealed that tyrosine phosphate was a most effective one so far tested.

The affinity to the bacterial surface of the antienzyme sera was demonstrated by immunofluorescent microscopy. The cooperative study with other institutuion suggested the ligant-nature of the enzyme to asialo GM1 and GM2. These observations suggest that the enzyme is most probably protein tyrosine phosphatase which functions as a part of the signal transfer system to respond to the environmental stimuli. The abundant presence of the glycoproteins on the bacterial surface may constitute glycocalyx which give the cell the resistance to phagocytosis and chemotherapeutics. In this context, the enzyme will be stated to contribute to the pathogenicity of *B. pseudomallei.*

IMMUNODIAGNOSIS OF *PSEUDOMONAS PSEUDOMALLEI*

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An enzyme-linked immunosorbent assay (ELISA) with endotoxin preparation of *P.pseudomallei* as antigen was developed for detection of IgG antibodies from 47 melioidosis sera , 55 non-melioidosis sera and 50 blood donor sera. The sensitivity, specificity and accuracy of this ELISA were 95.7% , 94.2% and 94.7% , IHA were 81.0% , 91.4% and 88.1%, respectively. ELISA was judged to be more reliable than IHA. Detection of antigen in patientsû samples were used polyclonal antibodies compared with monoclonal antibodies to LPS or Protien fraction of *P. pseudomallei* by IFA. In 58 melioidosis samples and 43 non-melioidosis samples were tested. From 58 melioidosis samples gave positive in 54 samples (93.1%) with monoclonal antibodies, for anti-LPS and anti-protien fraction, polyclonal antibodies for guinea pig gave positive 81.0% and 84.5%, respectively. Anti-LPS as same as anti-protein fraction from rabbit gave positive 84.5%. Non-melioidosis samples gave positive 1 in 43 samples (2.3%). Monoclonal antibodies gave more specific than polyclonal antibodies and eliminated non-specific cross reactivity.

CHLAMYDIA TRACHOMATIS INFECTION IN THAILAND

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For detection chlamydial infection in Thailand, serological and bacteriological surveys have been performed. By micro-immunofluorescence test, chalmydial antibodies were found in all (12/12) of female prostitures , 25 (57%) of 44 unskillful male workers, 30 (60%) of 50 unskillful female workers, 11(38%) of 29 gynecological out-patients attending a hospital and 2(8%) of 25 blood donors. Although no *CHLAMYDIA* organisms were isolated from gynecological out-patients examined by cell culture. *Chlamydia trachomatis* is the leading pathogens of sexually transmitted diseases (STDs) in Thailand as well as in industrial countries.

HUMAN HERPESVIRUS 6 (HHV-6) AND 7 (HHV-7) INFECTIONS

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In 1986, a new herpesvirus which is now designated as human herpesvirus 6 (HHV-6) was isolated from patients with lymphoproliferative disorders and was recognized to be the causative agent of exanthem subitum (ES) in 1988. Recently HHV-6 is classified into two variants such as HHV-6A and HHV-6B. It is now beleived that HHV-6 persists in the host after primary infection and that can be reactivated later during immunosuppression invluding AIDS and organ transplantation. We recently found that HHV-6 can be reactivated during dengue virus infection in Thailand. Thirty patients with DHF were examined by virological and serological methods to determine the possible reactivation of HHV-6. While HHV-6 DNA was detected in 20 patients (67%) by polymerase chain reaction(PCR), HHV-6 was isolated in 12 of 30 DHF patients (40%) during the acute phase and also in 1 case during the convalescent phase. These data showed reactivation of HHV-6 in patients at a high frequency during acute DHF.

In 1990 a novel human herpesvirus, HHV-7, was isolated from $CD4^+$ lymphocytes of a healthy adult, but the clinical features of the primary infection to HHV-7 have not been established. We now describe the isolation of HHV-7 from patients having the typical clinical features of ES, and serologic studies from 15 other patients. HHV-7 was isolated from 2 infants with typical ES. The restriction enzyme-digested DNA patterns of the isolated viruses were very similar to that of the prototype HHV-7, but different from that of HHV-6. In addition, sera from another 15 children who had episodes of ES were serologically tested for antibodies to HHV-6 and HHV-7 by IFA test. Five of 7 patients had seroconversion to HHV-7 just after having typical signs and symptoms of ES. These results suggest that HHV-7 is also one of the causative agents of ES.

SPECIES SPECIFICITY AND INTERSPECIES RELATEDNESS IN HUMAN AND ANIMAL ROTAVIRUSES AS DETERMINED BY SEQUENCE ANALYSIS AND HYBRIDIZATION ASSAY

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Overall genomic relatedness and VP4 phylogenetic relationship among representative human and animal rotavirus strains were studied by VP4 sequence determination and RNA-RNA hybridization. It was found that there are multiple VP4 sequences in rotavirus strains from each animal species: three in horses, three in cows, two in pigs, two in cats, and one in dogs. In contrast, three examples of interspecies relatedness of VP4 sequences were observed : (i) between an equine strain (H1) and porcine strains (OSU and YM); ii) among canine (K9 and Cu-1) feline (Cat 97), and human strains (HCR3); and iii) between feline (Cat 2 and FRV-1) and human strains (K8 and AU-1). While overall genomic relatedness was high among rotaviruses from the same species, moderate or weak genomic relatedness was also detected between rotaviruses from different species. Thus, the present studies showed species specificity and interspecies relatedness of human and animal rotaviruses.

LABORATORY SUPPORTING ON POLIO ERADICATION PROGRAM

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In 1988, the World Health Organization committed itself to the aradication of poliomyelitis from the world by the year 2000. From this policy, Ministry of Public Health has prepared a National Plan of Action for poliomyelitis eradication which has included in 7th National Health Development Plan. The polio diagnosis laboratory at Virus Research Institute (VRI), Thailand was nominated as the regional Reference Laboratory for supporting polio eradication program in Southeast Asia Region in June 1992. For laboratory supporting on this program in Thailand, The results of laboratory confirmed in 1992 showed that 119 cases of AFP were isolated and 13 were indentified as polio type 1, 8 were indigenous cases and 5 were imported cases. In 1993, 18 out of 156 AFP cases were isolated as polio, 9 were indigenous cases and 4 were imported cases, while in 1994 from January to March, 1 out of 41 AFP cases were found as polio type 1 and indigenous case. All of imported cases were found in children under 6 years while most of indigenous cases were found over 6 years of age. All of polio isolated strains in Thailand during this period were further analysed for intratypic differentiation using ELISA and probe hybridization test. Forty-five percents of this isolates were still being wild strain. The results of laboratory diagnosis of 73 stool specimens which sent from other countries revealed that 24 were polio type 1, 4 were type 2 and 5 were type 3. To achieve the target of polio eradication program in Thailand, monitoring of poliovirus isolated from specimens which collected from environment is mainly concerned and will be performed in the near future.

A NATIONAL COLLABORATIVE OF RESISTANCE TO ANTIMICROBIAL AGENT IN *STREPTOCOCCUS PNEUMONIAE* AND *HAEMOPHILUS INFLUENZAE*

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Pneumonia is the first cause of death in children in Thailand. The most common bacterial agents of community-acquired pneumonia in children are *Streptococcus pneumoniae* and *Haemophilus influenzae.* In order to reduce severity of and mortality from pneumonia, the national collaborative drug susc eptibility surveillance system for these two bacteria was established under the sponsorship of WHO. With the collaboration of Division of Tuberculosis as an co-ordinating center; 6 hospitals from Bangkok, Chonburi, Pitsanulok, Khonkaen, Nakornratchasima, Songkhla as the collection team ; 5 Regional Medical Sciences Centers as the clinical laboratory team and the Division of Clinical Pathology as the central supply and the reference laboratory. In the period of February 1993 to February 1994, nasopharyngeal swabs were collected from one thousand eight hundred of children at the age of less than 5 year old with acute respiratory tract infection seen at the outpatient unit of 6 hospitals. The occurence, sensitivity pattern using disk diffusion method and minimum inhibition concentration value of *S. pneumoniae* and *H. influenzae* were determined. The prevalence of ampicillin resistance *H. influenzae,* penicillin resistance *S. pneumoniae*, chloramphenicol and co-trimoxazole resistance *S. pneumoniae* and *H. influenzae* will be presented in the seminar. The correlation of resistance to the existence of antimicrobial in urine will be revealed.

LABORATORY DIAGNOSIS OF *CLOSTRIDIUM DIFFICILE* ASSOCIATED DIARRHOEA

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C. difficile was isolated from 4.8% of overall age group of diarrhoeal patients and from 2.6% of controls. Faecal cytotoxin of*C. difficile* was detected in 52.5% of 203 diarrhoeal patients and in 17 (22.4%) of 76 controls. Whereas enteric pathogens other than *C. difficile* were detected in 0.7-7.4 % of the patients studied. These data suggest that *C. difficile* associated disease may be frequently encountered in such a developing region studied.

The reactivity of a commercial latex test (C.D. D-1 latex test, Mitsubishi Chemical Industries, Tokyo) with thirty-three species of bacteria was tested. Toxigenic and nontoxigenic strains of *C. difficile* gave a positive result in the C.D. D-1 latex test. Cross-reactions were also given by *C. putrificum, C. sporogenes* and proteolytic *C. botulinum.*

Culture filtrates from standard toxigenic strains of *C. difficile* A 4897, *C. sporogenes* and *C. putrificum* ATCC 25784 were used for protein purification. Four major peaks (A1, A2, A3 and A4) were obtained from *C. difficile* A4897. Positive hemagglutinating fractions (A1 and A2) and cytotoxic active fractions (A3 and A4) obtained from *C. difficile* indicated that they are enterotoxin and cytotoxin, respectively. *C. sporogenes* gave two major (B1, B2) and two minor (B3, B4) peaks. Whereas only one peak (C1) has been separated from *C. putrificum* ATCC 25784. Interestingly, the *C. difficile* latex agglutinating antigen was detected in fractions B1 and B3 from *C. sporogenes*; and fraction C1 from *C. putrificum. C. sporogenes* contained at least two latex agglutinating antigens with molecular weight approximately 70,000 and 50,000 as determined from SDS-PAGE.

The usefulness of detecting leucine arylamidase activity of *C. difficile* was evaluated for rapid identification of suspected *C. difficile* colonies. All toxigenic and nontoxigenic strains of *C. difficile* tested showed positive leucine arylamidase activity within 4 hour while none of other species of clostridia except *C. bifermentans* gave a positive reaction. However, the colonies of *C. bifermentans* and *C. difficile* could be easily differentiated on the basis of their morphology. Therefore, leucine arylamidase activity testing appears to be very useful for the rapid identification of *C. difficile* isolated.

MOLECULAR EPIDEMIOLOGY OF *SALMONELLA ENTERITIDIS* BY PULSED-FIELD GEL ELECTROPHORESIS AND RIBOTYPING

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Salmonella enteritidis isolates of three different phage types obtained from patients and food suspecting the causes of outbreaks of food-poisoning in Japan were characterized for epidemiological studies by pulsed-field gel electrophoresis (PFGE) and ribotyping. The results of PFGE of BlnI digested genomic DNAs showed that among isolates of the same phage type the isolates obtained from the same outbreaks revealed the identical PFGE patterns or minor different (1 or 2 bands different) patterns; whereas, the isolates from different outbreaks displayed distinct PFGE patterns. No identical PFGE patterns were observed among isolates of different phage types. Digestion of all *S. enteritidis* isolates genomic DNAs with EcoRI followed by hybridization with 23S 16S rRNAs of *E. coli* revealed one ribopattern. The results from this study suggested that PFGE of BlnI digested genomic DNA is useful to discriminate *S. enteritidis* isolates, the frequent causative agent of egg-related food-poisoning.

ENVIRONMENTAL IMPACT ASSESSMENT OF PESTICIDE HEALTH EFFECTS TO AGRICULTURISTS IN THE UPPER NORTHEASTERN AREAS

Vichai Prasartthong, Pratoomwan Kittiapibool, Darawas Viengyos and Supaporn Veateewootachrn
Regional Medical Sciences Center: Khon Kaen

The economic growth has been growing in the upper northeastern areas of Thailand. It has created environmental impacts due to unsustainable pesticide use to increase the agricultural productivity. Environmental impact on pesticide health effects to agriculturists were therefore studied and the strategic management for their safety were implemented. Cholinesterase activity were determined in 634 blood samples from agriculturists in four provinces of the northeastern areas. Eight cases or 1.3 persent of the agriculturists had the toxic levels. The information from the public were assessed by oral interview and questionaires. Among the agriculturists, 420 persons or 66.2 percents used organophosphate pesticides. The 255 agriculturists or 40.2 percents showed visible signs of illness. They were the persons who donot protect themselves of the ones who though care themselves while working with pesticides but handling unproperly. These findings showed a significant data of toxic exposure to the pesticides. Information and eduction of the public were assessed by oral advice and displayed exhibition for the public at their farming community sites in order to guide proper handling, storing and applying the pesticides. The pesticide masks were also given to approximate 290 households for proper protection. Environmental impact assessment on auditing, laboratory mornitoring and public education were forcused for effective management to solve local health problems for farmers in the upper northeastern areas.

A PILOT PROGRAME FOR NEONATAL SCREENING IN THAILAND

Charoensiriwatana W., Janejai N., Tankananond W., Arpornsuwan T.,
Krasao P., Suttipiromkul K. and Bhumisawasdi J.,
Health Science Research Institute, Nonthaburi, Thailand.

A pilot screening programme has been strarted since 1991 by collecting hell-prick blood spots from neonates aged 48 hours upward. The specimens were collected from 13 provinces in North, north-eastern and southern part of the country and posted to a governmental central laboratory, Department of Medical Sciences for assay of Thyroid Stimulating Hormones (TSH) and Phenylalanine using home-made IRMA TSH Blood Spot kit and Guthrieûs test, respectively. The cut off level for sample recall were 25 mU/L for TSH and 4 mg/dl for Phenylalanine. 20,442 specimens were assayed and results showed the incident of Congenital Hypothyroid (CHT) 1:2,920 and Phenylketonuria (PKU) 1:10,221 in spite of the fact that only 35% of cases could be recalled for CHT and 15% for PKU. The treatment was taken immediately after identification and no retardation was observed in all cases. In addition, a model for detection of CHT and PKU neonates by utilization of rural area laboratories has also been worked out be means of modification of locally available technology so that the National Screening Programme can be set up effectively using local resources in the near future.

④　プロジェクト終了式におけるスピーチ

プロジェクト終了式におけるスピーチ

(1) パンヤ保健省医科学局長
(2) 在タイ日本大使館熊本一等書記官
(3) JICAタイ事務所浅野次長
(4) ソンポップＮＩＨ所長
(5) 金井プロジェクト・リーダー
(6) 山崎最終評価専門家チーム団長

Closing Ceremony of the Research Promotion Project
in National Institute of Health, Thailand
On Friday, June 24, 1994 At 2.00 P.M.
At National Institute of Health, Nonthaburi, Thailand

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1. Ceremony : at NIH, room A-204

1.1 Addressing :
By Director-General of DMSc
By First Secretary of Embassy of Japan in Thailand
By Resident Representative of JICA Thailand Office

1.2 Presenting the review of the Project :
By Director of NIH, DMSc
By Leader of Japanese Evaluation Team
By Project Team Leader of the Research Promotion Project in NIH

1.3 Presenting the future plan :
Future communication between NIH Thailand and NIH Tokyo
By Director-General of DMSc

1.4 Tree Planting :
By Dr. Ryosuke Murata,
Chairman of Japanese Advisory Committee of the Project
By Dr. Nadhirat Sangkawibha, Honorable Consultant, DMSc

2. Tea Party : at NIH, room A-203

Speech by Dr. Panya, Director General,
Department of Medical Sciences, Ministry of Public Health

Distinguished guests, ladies and gentlemen,

It is indeed a great privilege to me to participate in this closing ceremony, today.

So, after a years of close technical cooperation between Japan and Thailand, the Research Promotion Project will come to end this July. I would not talk about the good result or impact that were produced by the project, as it will be presented later in the following session. What I would like to express here is what we thank and what we feel about the project.

It is really very difficult for me to express in words our thought and feeling towards the project. There is an old teaching, saying that, if somebody is hungry and you love him, give him cooked fish to relieve his hunger. But if you love him more, don't give the cooked fish but the raw one and teach him how to cook to help him not only to relieve his hunger, but also to satisfy his taste and appetite. But if you love him most, don't give him the fish, give him the fishing hook or net and train him how to catch fish and also how to cook.

And now, we know how to catch and how to cook the fish although not to the best level of expertise, but at least to the extent that we can feed ourselves and we can cook forward to cooperating with others to train those in need of the technics.

Nine years is not a short period of time. Not only a large amount of money that has been put into the project for establishing the infrastructure and learning, but also the tremendous amount of energy and patience on the part of the experts. This, naturally, induce deep feeling of respect and gratitude among those students counterpart towards their teacher's experts. You can witness such kind of feeling from what they did during the seminar and during the coming weekend.

Finally, on behalf of the Department of Medical Sciences, I would like to join all of you here to congatulate the organising,as well as the advisory committee for the admired success of the project. And also, we would like to express again, our sincere respect and gratitude to everyone involved in this Project and we are certain as always the buddhists that the good merits from what you have done in the past 9 years will bring all of you good fortune and prosperity in your life and your work.

Thank you

Speech by Mr. Kumamoto, First Secretary,
Embassy of Japan

Dr. Panya Sonkom, Director-General,
Department of Medical Sciences,
Ministry of Public Health;
Dr. Nadhirat Sangkawibha;
Dr. Sompop Ahandrik, Director of NIH;
Dr. Ryosuke Murata, Chairman of the
Advisory Committee in Japan;
Dr. Komi Kanai, Team Leader;
Dr. Shudo Yamazaki, Leader of the Japanese
Evaluation Team;
Distinguished Guests;
Ladies and Gentlemen;

I feel very honoured and pleased to be given this opportunity to say a few words, on behalf of the Government of Japan, on this auspicious occasion of the Closing Ceremony of the NIH Project, the result of which to date say a lot for the quality of work being done.

Thailand and Japan have a long history of cooperation in various fields of medical science. All of them are regarded as success stories of international cooperation between the both countries. In particular, it is not too much to say that this nine-year period project is considered to be one of the most successful cases. The NIH

staff with its energy and enthusiasm indicate this. I am, therefore, very happy and proud that the Government of Japan made a modest contribution.

Needless to say, as health is indispensable to everyone, so health laboratory services and health research activities are essential to every country for its efficient medical care and effective disease control measures. Now that the NIH has modern equipment, laboratory technologies and above all an army of willing staff with improved morale, I am confident the NIH activities will enjoy further growth and diversification and are also sure to play a pivotal role in tackling various kinds of health and medical issues. It is my hope that we can continue to work together. In this context, I do view this closing ceremony today as the start of what shall turn out to be a long mutually rewarding relationship. I think emphasis on other types of technical cooperation would open new opportunities to continue the growth of our relationship.

In addition, I believe that the

importance of this project lies not only in the dissemination of new knowledge and techniques, but also in the provision of an opportunity for the concerned doctors and officers to get together, share the experiences of both countries and develop regional and international cooperative relationship. I sincerely hope that you all will maintain the channels created during this project.

Finally, I would like to express my sincere appreciation to all the outstanding doctors and officials concerned with this program. Without their competence and devotion, this project would not have been possible. In this regard, our special thanks should go to Dr. Ryosuke Murata and Dr. Komi Kanai, whose untiring efforts have been a key to the success of this project since its inception.

Thank you.

SPEECH

Delivered by Mr.Toshio ASANO
Assistant Resident Representative, JICA Thailand office
at the Closing Ceremony of the Research Promotion Project
in the National Institute of Health
on Friday, June 24, 1994
at NIH Nonthaburi

Dr.Nadhirat Sangkawibha, Honarable Consultant,department of Medical Sciences.
Dr.Panya Sornkom, Director General, Department of Medical Sciences.
Dr.Sompop Ahandrik, Director, National Institute of Health
Dr.Ryousuke Murata, Chairman, Advisory Committee of JICA
Dr.Komi Kanai, NIH Project Leader
Dr.Shudou Yamazaki, Director General, National Institute of Health
Distinguished Guests,
Ladies and Gentlemen.

It is my great honor to extend congratulation, on behalf of Japan International Cooperation Agency, on the occasion of the Closing Ceremony of the Research Promotion Project in the National Institute of Health.

During nine years' life of the Project, The Project of National Institute of Health established brilliant achievements and reputation thanks for continuous efforts and sincere collaboration of Japan and Thai personnel concerned. As JICA, we would like to express our deep sense of gratitude for all members who did and are doing the smooth implementation of this Project. Particularly we would like to appreciate efforts of first period of the project. Dr. Nadhirat and Dr.Murata are pioneers of the cooperation and their attendance to this ceremony really shows their ever-lasting dedication to this project.

JICA was established on August 1, 1974 under the Japan InternationalCooperation Law and it is going to cerebrate its 20th anniversary on August 1 this year. After JICA has extended its assistance since 1950 in Thailand JICA and DMS are keeping a close relationship through ~~technical~~ grant aid and technical cooperation in the medical and sanitary fields. Especially, it is widely said that this NIH Project is one of the most proud and successful projects in the world, which JICA has been conducting during its history of 20 years.

As you have known already, at present the NIH activities has been acknowledged not only in Thailand but also at the international level. This is one objective we have been seeking, so making efficient use of accumulated results, we do hope that NIH should take key role and play an important part as a leading research center among neighboring countries. For attaining this purpose, JICA is willing to cooperate with NIH and the Ministry of Public Health in the coming future.

Finally, I would like to take this opportunity to repeat my appreciation for the cooperation and assistances of Japanese and Thai authorities concerned.

Thank you.