Acute Febrile Muco-Cutaneous Lymph Node Syndrome in Young Children with Unique Digital Desquamation

(clinical observation of 50 cases observed at our institution)

Japan Kawasaki Disease Research Center

This booklet is a reprint of "指趾の特異的落屑を伴う小児の急性熱性皮膚粘膜淋巴腺症候群" (Acute Febrile Muco-Cutaneous Lymph Node Syndrome in Young Children with Unique Digital Desquamation), Arerugi (Jpn J Allergol) vol. 16, No. 3: pp178-222, 1967, and its English translation with an official allowance of the Japanese Society of Allergology.

Preface

Life sometimes takes strangest turns. From April 1948 through March 1949, I spent one year as an intern at the University Hospital of Chiba University Medical College. After rotating through various departments, I intended to specialize in pediatrics; After receiving the news of my passing the National Licensure examination, I applied and was admitted to the Department of Pediatrics of Chiba University Medical College. Because of the harsh living conditions after the end of the World War II, I emboldened myself to ask my professor to transfer me to a better position because it was financially difficult for me to remain a member of the medical staff at the university hospital. Fortunately, the professor referred me in December 1949 to the Department of Pediatrics, Japan Red Cross Central Hospital, which had no direct relationship with Chiba University. I took a position there starting in January 1950 and began receiving a salary, which was of small economic help to my family. Altogether, I remained a member of the university hospital staff for only 7 months. It is no exaggeration to state that my good fortune started from there.

On my first day at the Japan Red Cross Hospital, I was assigned to a child who had suffered from pertussis complicated by encephalopathy, a condition that was later found to be Pelger's familial anomaly of the leukocyte nucleus. Dr. Yutaka Kokubo, then the assistant chief of the department and my advisor, reported the case in the journal "Shonika Rinsho" (Japanese Journal of Pediatrics). I still remember the excitement I felt when I obtained the booklet with my name printed next to Dr. Kokubo's. Later, I encountered cases with diverse conditions and Dr. Jushichiro Naito, then the chief of the department, told me to introduce each case at the Tokyo Regional Academic Meeting of Pediatrics. We had more than 200 outpatients to attend to daily. In addition, 10 to 15 inpatients were assigned to each of us. Naturally, our daily schedule was quite full but we appreciated truly substantial clinical experiences. Thanks to superb guidance from Drs. Naito and Kokubo, I gained personal satisfaction working as a pediatrician.

In April 1956, Dr. Naito was transferred to head the Aiiku Hospital and Dr. Fumio Kosaki assumed the position of department head. From the beginning, Dr. Kosaki stated that the academism upheld at Tokyo University would be the basis of our training. Because Dr. Naito had placed a greater emphasis on clinical practice, we were somewhat perplexed at the start. However, under the influence of Dr. Kosaki, we learned to inject an academic element into our daily clinical practice. Under this condition, I began to hope for substantial work while working at the pediatric department of Japan Red Cross Hospital.

In January 1961 I was given a unique opportunity to observe a condition, which was later to be known as Kawasaki disease. Initially, I was unable to give a definitive diagnosis and had to discharge the patient with a diagnosis of unknown disease. One year later, in February 1962, while on night duty, I examined a patient who had been suspected to be suffering from septicemia. I immediately recalled the symptoms of the earlier patient. This time, the patient was admitted for further examination, which showed clinical symptoms that were identical to those of the first patient. I realized that there were at least two cases presenting unique clinical symptoms that have never been reported. Fortunately for me, patients with similar conditions were brought to us but occasional atypical cases confused me from time to time. After very careful studies over a period of 6 years, I compiled records on 50 cases. I was able to depict the unique nature of this new syndrome, which later earned international recognition as Kawasaki disease.

Burkitt, who reported the Burkitt's lymphoma, stated in his lecture to medical students: "You should not despair if you do not have access to sufficient research funds or research facilities: what is most important in conducting outstanding studies are steady observation and logical deduction." (Physicians whose names are remembered in acronyms, by Itakura, Naoe, and Hara, Medical Sense, April 2000). This statement indicates that anyone can be the second Burkitt or Cushing.

Be ambitious, young researchers!

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a specific non-profit organization

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指趾の特異的落屑を伴う小児の急性熱性皮膚粘膜淋巴腺症候群

（自験例50例の臨床的観察）

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（受付：1月19日，1967）

1. 緒　言

1876年 Fuchs[1] の発表した Herpes iris conjunctivae 以来，多数の学者によつて，眼，皮膚，粘膜を侵す一連の症候群に対して数多くの病名が与えられているが，1939～1940年 Franceschetti et Valerio[2]，1948年 Proppe[3] 等により眼皮膚粘膜症候群に統一され，多形滲出性紅斑の亜型と考えられるに至つた．我が国に於ても，1958年文部省綜合研究班[4][5]はこの症候群を整理して，

1） 多形滲出性紅斑症候群
2） Behcet 氏症候群
3） Reiter 氏病

の3群に大別されたことは衆知の通りであるが，私はこの範中に入り難い一症候群を経験した．即ち，昭和36年1月より昭和41年11月迄の約6年間に所謂眼皮膚粘膜症候群に似ているが，種々の相異点のある症候を示す50例を観察した．

その特異的症候を列記すれば，次の様である．

1） 種々なる抗生物質が使われているにも拘らず38度以上の発熱が6日以上持続する．
（大体1～2週間）……50例（100%）

2） 両側の眼球結膜の充血がある……49例（98%）

3） 皮膚の紅斑性発疹が，特に両手掌，両足蹠に特徴的にみられ，決して水疱形成をみることがない……43例（86%）

4） 口唇の発赤，乾燥糜爛，皺裂，時に出血，血痂，口腔粘膜の瀰蔓性充血及び苺舌が見られるが，水疱，潰瘍，偽膜或はアフタの形成が認められない……48例（96%）

5） 急性の頸部淋巴腺腫脹（拇指頭大以上）が認められるが，決して化膿しない……33例（66%）

6） 両手，両足が血管神経性浮腫状を呈する……22例（44%）

7） 指趾先の爪皮膚移行部よりの膜様落屑が主として第2病週中に始まる……49例（98%）

8） 過半数が2年以下である……27例（54%）

9） 再発がみられない．

10） 自然治癒し，後遺症をのこさいない．

11） 同胞感染がみられない．

私ははじめ，この特徴的な落屑に注目し，本症候群を猩紅熱に似て非なる落屑性疾患，即ち“非猩紅熱性落屑症候群について”と題して，昭和37年10月第61回千葉地方会に本症の7例について報告した[6]

その後症例を重ねるに従い，その眼症状，皮膚症状及び粘膜症状から，従来報告されてきた所謂眼皮膚粘膜症候群，特に Stevens-Johnson 氏病や Pluriorificielle Ectodermose よりは，種々の点で軽症ではあるが，一応この症候群に属するものではないかと考えて，昭和39年10月第15回東日本，第9回中部日本連合小児科学会（於松本）に於いて，“眼皮膚粘膜症候群の20症例”と題して，第2回目の報告を行つた[7]．

然し乍ら，その後所謂眼皮膚粘膜症候群（M.C.O.Sと略す）に関する従来の報告を仔細に検討した結果，我々の症候群が，今までに報告されて来た，M.C.O.S のどの Type にも一致しない，1つの Clinical Entity をなすものではなかろうかと考えられるに至つた．

故に，我々の経験した50例について，臨床的分析，検査所見を記すと共に，文献的考察を行い，ここに報告して諸賢の御批判を乞う次第である．

2. 症　例

ここに述べる症例はいずれも昭和36年1月より昭和41

Acute Febrile Muco-Cutaneous Lymph Node Syndrome in Young Children with Unique Digital Desquamation

(clinical observation of 50 cases observed at our institution)

Department of Pediatrics, Japan Red Cross Central Hospital (Chief: Dr. Fumio Kosaki)
Tomisaku Kawasaki

(Received on January 19, 1967)

1. Introduction

Since the 1876 report by Fuchs[1] on herpes iris conjunctivae, many names have been conferred on a series of syndromes affecting the eyes, skin, and mucous membrane. Franceschetti and Valerio[2] in 1939 to 1940 and Proppe[3] in 1948 placed them under the single nomenclature of oculo-muco-cutaneous syndrome, which was considered to be a subtype of polymorphic exudative erythema. It is well-known that in Japan, a Comprehensive Study Group organized by the Ministry of Education in 1958[4] classified this syndrome into the following 3 groups:

1) Polymorphic exudative erythema syndrome
2) Behçet's syndrome
3) Reiter's disease

However, the author encountered a syndrome that did not fit into any of these categories: specifically, during the 6 years between January 1961 and November 1966, 50 cases were observed that resembled the so-called oculo-muco-cutaneous syndrome but also exhibited several inconsistent features.

The unique symptoms of these cases are listed below:

1) In spite of the administration of several types of antibiotics, a fever exceeding 38 ℃ persists for more than 6 days.
(about 1 to 2 weeks)·····50 cases (100%)
2) The conjunctiva is congested in both eyes·····49 cases (98%)
3) Erythematous eruptions of the skin characteristically developing on both palms of the hands and soles of the feet but never forming bullae·····43 cases (86%)
4) The lips become red, dry, eroded, and cracked and they sometimes even bleed or form a bloody scab. The oral mucosa is characterized as diffusely hyperemic with the development of a strawberry tongue. No blisters, ulcer, false membrane, or aphthosis are recognized·····48 cases (96%)
5) Acute swelling of the cervical lymph nodes (exceeding the size of the tip of a thumb) develops but it never becomes abscessed·····33 cases (66%)
6) Both hands and feet develop an appearance like angioneurotic edema·····22 cases (44%)
7) Membranous desquamation affecting the onycho-cutaneous junction of the fingers and toes develops mainly in the 2nd week·····49 cases (98%)
8) More than half of the patients are under the age of 2 years·····27 cases (54%)
9) The condition does not recur.
10) The patients spontaneously recover without any sequelae.
11) There is no transmission among siblings.

Initially, I noted the unique desquamation characterizing this disease and named it "non-scarlet fever desquamative syndrome" (a desquamating condition that is similar but not identical to scarlet fever) and introduced 7 cases with the syndrome at the 61st meeting of the Chiba Regional Meeting in October 1962.[6]

With further observation of succeeding cases, however, the ocular, cutaneous, and mucous conditions of this syndrome began to resemble a mild form of the so-called oculo-muco-cutaneous syndromes, especially the Stevens-Johnson syndrome or pluriorificielle ectodermose. Thus I presented this condition for the second time in a report entitled "Twenty cases of oculo-muco-cutaneous syndrome" at the 15th Eastern Japan and 9th Central Japan Meetings on Pediatrics in October 1964.[7]

Upon examining past reports of the so-called oculo-muco-cutaneous syndrome (abbreviated to M.C.O.S.) further, I began to believe that the condition at hand constituted a new clinical entity that did not belong to any of the reported types of this syndrome.

Therefore, the results of the clinical examinations and the findings of diagnostic tests on the 50 cases we had encountered are presented together with a review of the literature. We would like to solicit any critiques that the readers may have.

2. Case studies

What follows are detailed descriptions of seven patients out of the 50 who were admitted to the Department of Pediatrics, Japan Red Cross Central Hospital from January 1961 through November 1966, for detailed clinical description. The patient numbers appearing in the temperature charts do not correspond to the case numbers that were given later (Table 1). Figures 1 to 4 are copies from the actual hospital records. It should be noted that the actual colors of the eyes, lips, and eruptions are in red.

Case Study [1] (patient No. 24), male, date of birth: September 15, 1956 (4 years 7 months of age)

年11月末迄に日本赤十字社中央病院小児科に入院した症例50例のうち，7例を選んで，精記した．体温表の症例番号は，後述の分類番号とは別に符した．図1—4はいずれも入院時に記されたもので，実際の眼，口唇及び発疹の色は赤である．

症例〔1〕　山○俊○（男）昭和31年9月15日生（4才3ヵ月）

入院　昭和36年1月5日（分類番号No. 24）

退院　昭和昭和36年2月9日

家族歴：父はアレルギー体質で生来湿疹が繰返し，薬物にもかぶれ易い．母は健康．

既往歴：出産正常．母乳栄養．乳児期の湿疹著明．発育は正常．感冒時はいつも喘鳴を併うという．

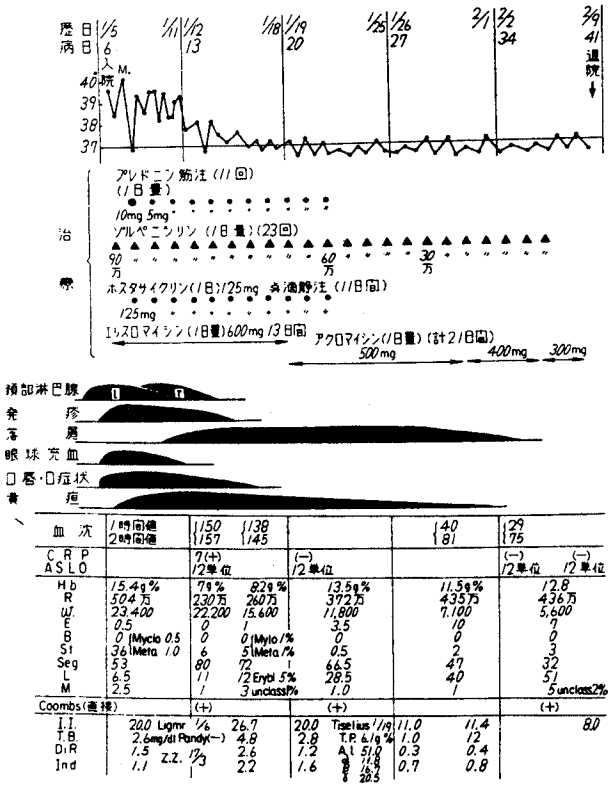
現病歴：昭和35年12月30日夜，頚部痛を訴え，左頚部の腫脹に気付いた．

12月31日　左頚部腫脹著明となり，触れると疼痛を訴えた．38.5℃

昭和36年1月1日　38.5～39.0℃，時々腹痛を訴えた．

1月2日　近医に受診し，アンギーナと診断された．薬を吐く．38.5℃～39.0℃

第1例　山添俊一（男）4才3ヵ月入院昭和36年1月5日退院昭和36年2月9日



血液	時間値 / 2時間値					
		1/5: 150 / 157	1/8: 138 / 145		1/26: 40 / 81	2/9: 29 / 175
CRP		7(+) / 12単位		(−) / 12単位		(−) / 12単位
ASLO						(−) / 12単位
Hb	15.4g%	79%	82g%	13.5g%	11.5g%	12.8
R	504万	230万	260万	372万	435万	436万
W.	23,400	22,200	15,600	11,800	7,100	5,600
E	0.5	0	1	3.5	10	7
B	0 Mycio 0.5	0	0 Mycio /%	0	0	0
St	36 Meta 1.0	6	5 Meta /%	0.5	2	3
Seg	53	80	72	66.5	47	32
L	6.5	11	12 Eryth 5%	28.5	40	51
M	2.5	1	3 unclass 7%	1.0	1	5 unclass 2%
Coombs(直接)		(+)		(+)		(+)
T.I.	20.0 Ligmx 1/6	26.7	20.0 Tisselius 1/19		11.0	11.4	8.0
T.B.	2.6mg/dl Pandy(−)	4.8	2.8 T.P. 6.1g%		1.0	12	
D.R	1.5 Z.Z. 1/3	2.6	1.2 Alb 51.0		0.3	0.4	
Ind	1.1	2.2	1.6 γ 16.9		0.7	0.8	
			β 28.5				

1月3日　嘔吐頻回．クロロマイセチン1日600mg投与された．38.5～39.0℃

1月4日　40℃となり，吐物がコーヒー残渣物様となる．

1月5日　入院す．

入院時所見：脱水状態で，顔貌やや重症感あり，呼吸促迫脈膊亢進す．意識明瞭．両側の眼球結膜が著明に充血し，口唇は鮮紅色，乾燥，摩爛皸裂がみられた．口腔粘膜は瀰蔓性に著しく発赤し，苺舌を呈していた．然し，偽膜，潰瘍或はアフタの形成は全く見られなかつた．左頚部淋巴腺は鶏卵大に瀰蔓性に腫れて，触ると著しく疼痛を訴えたが，局所の皮膚には発赤はみられず，恰も頚部腫瘍の感があつた．

両手掌，両足蹠は著しく発赤し，紅斑様を呈していた．他の部位の皮膚には特に発疹は見られなかつた．心肺には異常はなかつた．肝は辺縁を触知したが，脾はふれなかつた．

入院後の経過：体温表〔1〕参照．

1月5日　脱水がひどく，点滴輸液と共にホスタサイクリン（1日125mg）の投与を開始した．その他ペニシリンゾル1日90万単位筋注．

1月6日　皮膚に稍々黄疸が出現．髄液正常．プレドニン1日10mg筋注．

1月7日　黄疸と共に全身の皮膚に紅斑様発疹がみられた．高熱は依然として続いた．

1月9日　頚部淋巴腺は左が小さくなり，右が新たに腫脹して来た．

1月10日　両側の眼球結膜は依然として充血し，皮膚の紅斑及び軽い黄疸が全身に未だにみられた．然しやつと食物が経口的に摂取出来る様になつた．

1月12日　右の拇指先の爪皮膚移行部より膜様の落屑が始まつた．然し皮膚にはまだ紅斑がみられた．肝2横指．肝機能検査では，黄疸指数20，総ビリルビン値 2.6 mg/dl，直接「ビ」1.5mg，間接「ビ」1.1mg，CCF土，TAKATAーであつた．

1月13日　体温がやつと下降し始めた．全部の指先より落屑が始まつた．

1月14日　眼球結膜充血が殆んどみられず．黄疸のみ軽度にみられる．頚部淋巴腺も殆んどふれなくなつた．皮膚の紅斑も殆んど消失した．

1月16日　黄疸は依然として存在する．血液検査の結果，Hb 8.2gr，Rote 260万，Weiße，15,600，E 1，B 0，My. 1，Meta 1，St. 5，Seg. 72，L 12，M 3，

Admitted: January 5, 1961.

Discharged: February 9, 1961.

Family history: His father had an allergic tendency with life-long recurrences of eczema and drug reactions. His mother was in good health.

Past medical history: Being a product of a normal pregnancy and breast-fed, he suffered from severe eczema in infancy but achieved normal growth. Wheezes have been noted at times of upper respiratory infection.

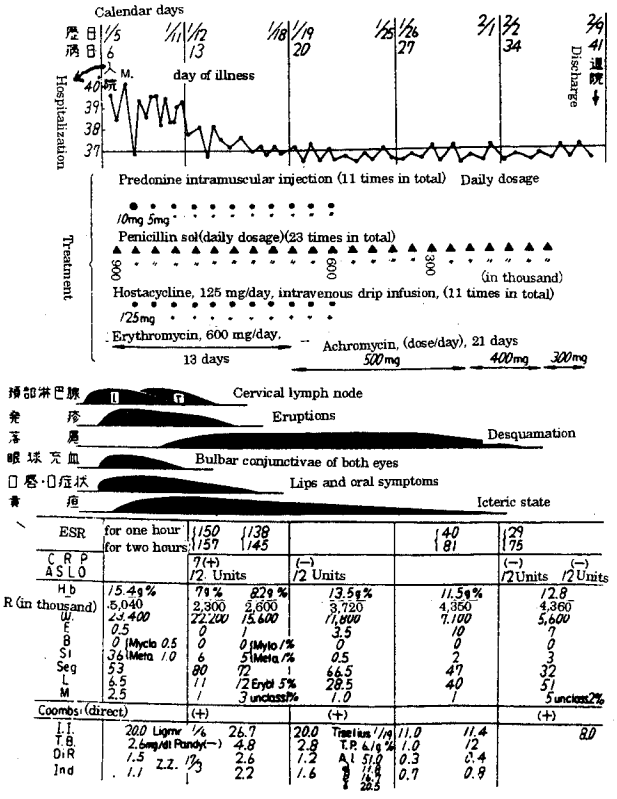
Present illness: In the evening of December 30, 1960, the patient complained of a neck pain and a swelling was found on the left side of his neck.

December 31: The left cervical swelling became more pronounced with complaint of pain when touched. The temperature was 38.5 ℃.

January 1, 1961: The temperature ranged 38.5 to 39.0 ℃. He complained of occasional abdominal pain.

January 2: Brought to a local physician who gave a diagnosis of *Angina* [translator: old term for sore throat]. He regurgitated the drug that had been given. The fever was in a range of 38.5 to 39.0 ℃.

Case 1 (No.24) a male, 4 years-and-3-months old, hospitalized on January 5 and discharged on February 9, 1961.



January 3: The vomiting became frequent. Chloramphenicol (600 mg/day) was administered. The temperature ranged from 38.5 to 39.0 ℃.

January 4: His temperature rose to 40 ℃ and the vomitus became coffee ground-like.

January 5: The patient was admitted to our hospital.

Findings at admission: The patient was dehydrated and moderately ill-appearing. Respiration was shallow and pulse was rapid. He was lucid. Both bulbar conjunctivae were markedly hyperemic and the lips were bright red, dry, eroded, and cracked. The oral mucosa was diffusely and markedly erythematous, accompanied by a strawberry tongue; however, it was totally free of pseudomembrane, ulcer, or aphtha. The left cervical lymph node was diffusely swollen to the size of a chicken egg and the patient complained bitterly of pain when touched. The overlying skin was not erythematous but had the appearance of a neck tumor.

Both palms and soles were markedly erythematous and macular. No skin eruptions were found on the rest of the body. His heart and lungs were normal. The liver edge was palpable but the spleen was not.

Hospital course: Refer to temperature chart [1]

January 5: Because of marked dehydration, intravenous fluid together with Hostacyclin (125 mg/day) was initiated. In addition, 900,000 units/day of penicillin was administered intramuscularly.

January 6: The skin became somewhat icteric. The cerebrospinal fluid findings were normal. Predonine (10 mg/day) was given intramuscularly.

January 7: In addition to jaundice, an macular erythematous eruption developed on his skin over the enire body. The high fever persisted.

January 9: The left cervical lymph node became reduced in size, while the right cervical node became enlarged.

January 10: Both bulbar conjunctivae were still hyperemic and macular rash and mild jaundice persisted throughout the body. However, the patient began taking foods by mouth.

January 12: Membranous desquamation began at the nail-skin junction of the right thumb but the skin was still erythematous. The liver edge was felt 2-finger-breadths below the costal margin. The liver function tests showed: icteric index 20; total bilirubin 2.6 mg/dL; direct bilirubin 1.5 mg/dL; indirect bilirubin 1.1 mg/dL; CCF ±, and TAKATA negative

January 13: His fever began to subside. Desquamation started from all fingertips.

January 14: Conjunctival injection was hardly noticeable. Only mild jaundice persisted. The cervical lymph nodes were barely palpable. Macular rash was almost completely gone.

January 16: Jaundice was still noticeable. The blood tests showed: Hemoglobin, 8.2 g/dL.; Rote 2,600,000; Weiße 15,600; Eosinophils 1%; Basophils 0; Myelocytes 1%; Metamyelocytess 1%; Stab cells 5%; Segmented cells 72%; Lymphocytes 12%; Monocytes 3%; Erythroblasts 5%; others 1%; Hematocrit 21%; icteric index26.7; total bilirubin 4.8 mg/dL; direct bilirubin, 2.6 mg; indirect bilirubin 2.2 mg; TTT, 4.0 (U; Gros (+); CCF (-); TAKATA (-). Accentuated anemia was noted.

January 18: Membranous desquamation started at

Ery. bl. 5，その他1，Ht. 21%，黄疸指数26.7，総ビリルビン値 4.8mg/dl，直接「ビ」2.6mg，間接「ビ」2.2mg，TTT 4.0μ. u. Gros (+)，CCF (−)，TAKATA (−)，で高度の貧血がみられた．

1月18日　趾先の爪皮膚移行部より膜様の落屑が始まつた．黄疸は稍々軽減した．

1月24日　はじめて笑つた．皮膚及び結膜の黄疸も殆んど消えた．肝も辺縁をふれるのみとなる．

2月1日　血清の黄疸指数11.4，総ビリルビン値 1.2mg/dl，直接「ビ」0.4mg，間接「ビ」0.8mgであつた．

2月9日　全治退院した．黄疸指数 8.0

治療：体温表に示す様に，プレドニン筋注を1月6日10mg（1日量），1月7日より5mg，10日間連用．ゾルペニシリン筋注は1月5日より1日90万単位ずつ11回，次で60万単位ずつ5回，30万単位ずつ7回計23回投与した．亦ホスタサイクリン1日 125mgを輸液やビタミン剤と共に，点滴静注にて11日間投与した．その他エリスロマイシン1日 600mg13日間，アクロマイシン1日 500mg，400mg及び 300mgを計21日間経口投与した．

検査所見：体温表に示す様に，この症例は一時高度の溶血性と思われる貧血の出現及び黄疸，自家血球凝集を思わせる高度の血沈速進（1時間値 150）があり，血沈棒を立てると，みるみるうちに血球が沈降して行つたので，Coombs test を行つたところ，直接クームスが陽性であつた．

この症例は我々の症例の第1号で，その頚部淋巴腺炎と両側眼球結膜充血，全身の皮膚特に両手掌，両足蹠の紅斑様発疹，口唇口腔粘膜の著明な充血，苺舌があり，然も外陰部肛門には異常なく，特に指趾先の爪皮膚移行部からの膜様落屑がはじまり，両手両足が恰も猩紅熱に於けるが如く，皮膚の膜様剝脱をみ，然も他の身体部位の落屑が全くなかつた点，等々，猩紅熱を疑つて猩紅熱に非ず，Stevens-Johnson 氏病或は Ectodermosis érosiva pluriorificialis を考慮して左に非ずで，結局本例の診断の結論は保留にした．

昭和36年度にはこの症例1例のみであつたが，翌年より毎年症例が集まり，本症候群の独自性に注目する様になつた．

症例〔2〕　高○浩○（男）1才8カ月

入院　昭和38年3月30日（分類番号No. 11）

退院　昭和38年4月13日

主訴：頚部淋巴腺腫脹，発熱

家族歴：父；健，母；患児を妊娠中，しばしば蕁麻疹が出現した．亦，ペニシリン疹ありと．

既往歴：初体重 3,100gr. 帝王切開にて出生：人工栄養．発育正常．乳児期；湿疹が軽度にあつた．感冒のとき喘鳴を伴う．

現病歴：

昭和38年3月23日　左頚部淋巴腺が小指頭大に腫れた．夜中に39℃となつた．

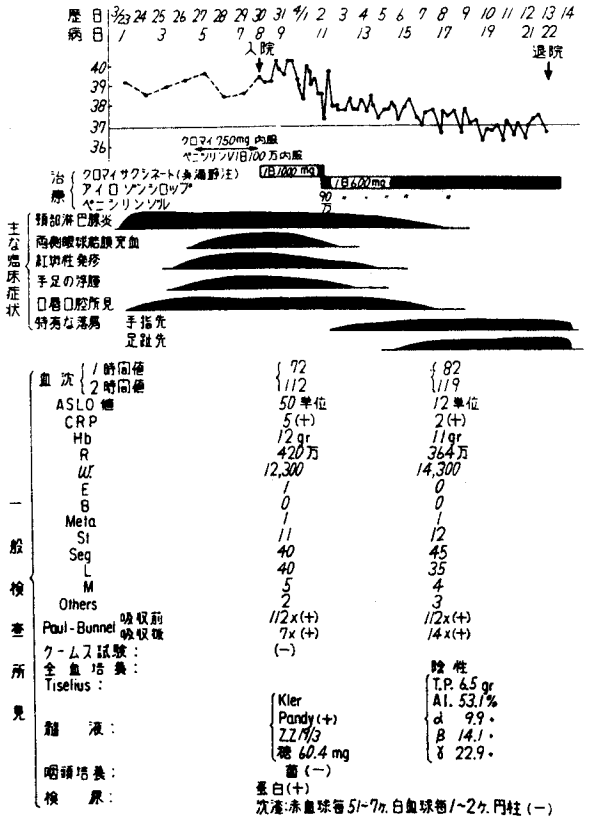
3月24日　朝左頚部淋巴腺が鶏卵大に腫れているのに気付いた．口唇が発赤，糜爛し，裂してきた．38.7℃でクロマイシロップを投与された．

3月25日　39℃で近医に頚部淋巴腺炎と診断された．白血球数17,600であつたと．

3月26日　39℃代で両手両足が腫れぼつたくなり，皮膚に紅斑が出現した．

3月27日　39.7℃で近医にて血沈検査をうけたところ，1時間値 106，2時間値 127で高度に速進していた．両側の眼球結膜充血及び両手掌，両足蹠が明かに紅斑状を呈し，両腕及び両脚の伸側にも紅斑が出現し，その医師からリウマチ熱を疑われた．この日よりクロマイ1日 750mgとペニシリン1日 100万単位の内服投与をう

第2例　高柳浩武（男）1才8カ月入院昭和38年3月30日退院昭和38年4月13日



the nail-skin junction of the toes. The jaundice improved slightly.

January 24: The patient smiled for the first time since the onset of the disease. The jaundice and conjunctival injection were no longer noticeable. Only the edge of the liver was palpable.

February 1: The serum jaundice index was 11.4; total bilirubin 1.2 mg/dL; direct bilirubin 0.4mg; and indirect bilirubin 0.8 mg.

February 9: The patient completely recovered and was discharged. The icteric index was 8.0.

Treatment: As was indicated on the temperature chart, intramuscular injection of Predonine was started at 10 mg/day on January 6, and was reduced to 5 mg/day on January 7 and continued for 10 consecutive days. Intramuscular injection of penicillin was started at a dose of 900,000 units /day on January 5 for 11 days, followed by 600,000 units/day for 5 days, and 300,000 units/day for 7 days, a total of 23 days. Hostacyclin at a dosage of 125 mg/day was infused together with an infusion fluid and vitamin preparations via an intravenous route for 11 days. Other medications included erythromycin (600 mg/day for 13 days) and oral Achromycin (at 500, 400, and 300 mg/day for a total of 21 days).

Test results: As shown in the temperature chart, this patient developed anemia and jaundice, suggestive of temporary intense hemolysis and marked elevation of erythrocyte sedimentation rate (150 in one hour), suggestive of auto-agglutination. When the sedimentation tube was placed vertically, the erythrocytes settled rapidly. Therefore, a direct Coombs' test was done, showing a positive result.

The case presented above was the first of a series of patients with similar conditions that we encountered. The major symptoms included: cervical lymphadenitis, bilateral hyperemia of the bulbar conjunctivae, macular erythema affecting the entire body, but especially remarkable in the palms of both hands and the soles of both feet, marked hyperemia of the lips and oral mucosa and a strawberry tongue. His external genitalia and anus were unaffected. Membranous desquamation started at the nail-skin junctions of the fingers and toes similar to scarlet fever, except that the rest of the body was unaffected by this desquamation. Stevens-Johnson syndrome and ectodermosis erosiva pluriorificialis were also considered but there were some contradictory features. Thus, the final diagnosis of this case remained inconclusive.

Only a single case with these features was detected in 1961. However, starting in 1962, an increasing number of patients with similar conditions came to our attention each year, which alerted us to a possible a unique syndrome.

Case Study [2] (patient No. 11), male, age 1 year 8 months

Admitted: March 30, 1963.

Discharged: April 13, 1963.

Chief complaints: Swelling of the cervical lymph nodes and fever.

Family history: Father was in good health.Mother, while she was pregnant with the patient, experienced repeated bouts of urticaria. She also experienced penicillin rash.

Past medical history: The patient was delivered by Cesarean section. His birth weight was 3,100 g. He was bottle-fed and showed a normal growth pattern. During infancy, he often developed mild eczema. Wheezing occurred when he caught colds.

Present illness:

March 23, 1963: The left lymph node was swollen to the size of the end of a little finger. During the night, his temperature rose to 39 ℃.

March 24: In the morning, the left cervical lymph node was found to be swollen to the size of a chicken egg. The lips were erythematous, erosive, and cracked. Because his temperature had risen to 38.7 ℃, Chloramphenicol syrup was administered.

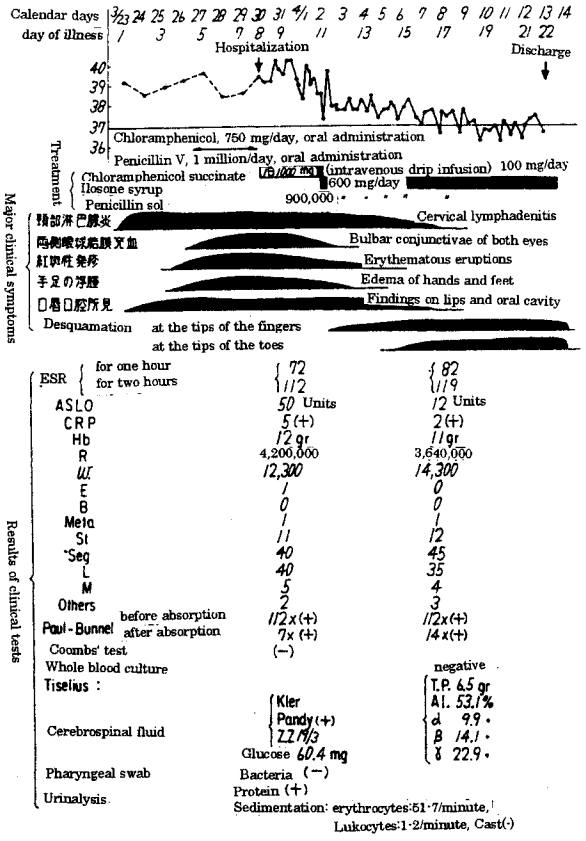
March 25: His temperature rose to 39 ℃. A diagnosis of cervical lymphadenitis was made by a local physician. The leukocyte count was 17,600.

March 26: The temperature remained in the 39s ℃ and both hands and feet appeared to be swollen. Macular erythema appeared on the skin.

March 27: His temperature registered 39.7 ℃ and an erythrocyte sedimentation rate obtained by a local physician was 106 at one hour and 127 at 2 hours. Both bulbar conjunctiva were hyperemic. The palms of both hands and the soles of both feet were evidently erythematous. Erythema was also noted at the extensor surfaces of both arms and legs. His physician suspected rheumatoid fever and prescribed 750 mg/day of Chloramphenicol and 1,000,000 units/day of penicillin to be administered orally.

March 28: Temperature 38.5 ℃. The ocular and dermal symptoms became more pronounced.

Case 2 (No.11) a male, one-year-and-8-months old, hospitalized on March 30 and discharged on April 13, 1963



けた.

3月28日　38.5℃で眼症状，皮膚症状が更に著明となつた.

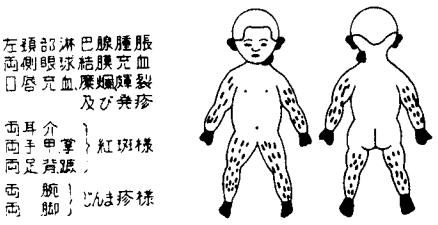
3月29日　その医師から敗血症の疑いをうけ紹介されて，翌3月30日当小児科に入院した.

入院時所見：

両側の眼球結膜が著明に充血し，口唇は乾燥，発赤，糜爛，皸裂がみられ，口腔粘膜全体が著しく充血していたが，アフタ形成，潰瘍或は偽膜等はなかつた．左頚部淋巴腺が鶏卵大以上に腫脹し（写真17)，硬く弾力性で，触つたり，動かしたりすると，ひどく疼痛を訴えた．然し局所の皮膚には殆んど発赤はみられなかつた.

発疹は図1の如く主として両上肢，両下肢に紅斑様，蕁麻疹様のものがみられたが，躯幹には発疹はなかつた．両手，両足が著明に血管神経性浮腫状を呈して，所謂“パンパン”に腫れていた．外陰部，肛門には異常はみられなかつた.

図1　高柳例（1才8月）



入院後の経過：体温表〔2〕参照

3月30日　頚部淋巴腺を穿刺したが，針先に僅少の血液がついて来ただけであつた．之を培養したが，菌は証明されなかつた.

4月1日　発疹がややうすくなつてきた.

4月2日　両側の眼球結膜充血が殆んどみられなくなつた.

4月3日　発疹が殆んど消えて，うすく色素沈着がみられた．右拇指先の爪皮膚移行部より膜様の落屑がはじまつた.

4月4日　両手足の浮腫が全くみられなくなつた.

4月6日　右第1趾先の爪皮膚移行部より膜様落屑がはじまつた.

4月8日　頚部の淋巴腺が全くふれなくなつた．亦，口唇の糜爛，皸裂もとれた.

4月13日　両手両足の膜様落屑のみを残して，全治退院した.

検査所見：体温表（2）参照

4月2日血沈1時間値72，2時間値 112でCRP5（十)，ASLO50単位，白血球数12,300で後骨髄球迄の左方核移動がみられた．Paul-Bunnel 陰性，クームス試験陰性，血液培養陰性，Tiselius では γ-Gl が22.9%であつた．髄液もほぼ正常で咽頭培養で菌が陰性．検尿では蛋白陽性，沈渣には赤血球が少数認められた．然し腎炎所見はなかつた.

治療：紹介医師によると，4月24日からクロマイパルミテート液を，4月27日より29日迄はペニシリンで1日100万単位及びクロマイ1日 750mgが内服投与された.

入院後は表の如く，3日間はクロマイサクシネート1日1gを輸液と共に点滴静注し，以降アイロゾンシロップ1日 600mgの内服，及び4月2日よりペニシリンゾル1日90万単位6回筋注が行われた.

副腎皮質ホルモンは全く投与しなかつた

症例〔3〕　目○善○（男）8カ月

入院　昭和40年8月30日（分類番号No. 4）

退院　昭和40年9月11日

主訴：発熱，発疹

家族歴：父は健，母は生来蕁麻疹が出来易いという．且絆創膏等にもかぶれ易い.

既往歴：生下時体重 2,400gr．人工栄養，発育正常．湿疹軽度に存す．首据り3カ月．お坐り6カ月.

現病歴：昭和40年8月23日朝，38.4℃で近医に受診しアンギーナと診断された．夜40℃.

8月24日　朝38.8℃で夜は40℃．クロマイの筋注をうけた由.

8月25日　朝39℃で夜40℃．右頚部淋巴腺が鶏卵大に腫れているのに気付いた．硬く，触れると，痛がつた．両手掌，両足蹠が赤くなつているのに気付いた.

8月26日　両手足が真赤になり，浮腫気味となつた．口唇の乾燥，発赤，糜爛，皸裂を認めた．体温は39℃～40℃であつた.

8月27日　両側の眼球結膜充血に気付いた．紅斑様発疹が両手足特に両手掌，両足蹠に限局し，且浮腫気味であつた．体温は39℃～40℃で，ピレチアの注射をうけた.

8月28日　発疹は四肢以外に腹部，胸部，背部の皮膚に風疹様，蕁麻疹様に出現した．頚部淋巴腺は稍々小さくなつて来た．体温は39℃～40℃であつた.

8月29日　右頚部淋巴腺は拇指頭大に小さくなり，さわっても痛がなくなった．発疹は全身に紅斑様となった．体温は39.3℃，38℃及び39℃であった.

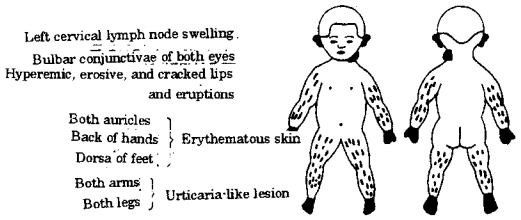
8月30日　高熱が続き，紹介されて，当小児科に入院

March 29: His attending physician suspected septicemia and referred the patient to our department. He was admitted to our pediatric ward on March 30.

Findings at admission: The bulbar conjunctivae of both eyes were markedly hyperemic. The lips were dry, erythematous, erosive, and cracked. The entire mucosal surface of the mouth was markedly hyperemic but there was no aphtha, ulcer, or pseudomembrane formation. The lymph node on the left side of the neck was swollen to the size greater than a chicken egg (Photo 17) and felt firm but elastic. The patient complained of severe pain when the lesion was touched or moved. However, the overlying skin was hardly erythematous.

As indicated in Fig. 1, macular and urticaria-like skin rash occurred in all extremities sparing the truncal region. Both hands and feet were markedly edematous, similar to angioneurotic edema making the overlying skin tense as a drum. The external genitalia and anus appeared normal.

Figure 1 No.11 (20-month-old)



Hospital course: Refer to temperature chart [2].

March 30: The cervical lymph node was lanced, yielding only a small amount of blood at the needle tip. This blood sample was cultured but no bacteria grew.

April 1: The rash appeared to have decreased.

April 2: The conjunctival injection was now barely recognizable.

April 3: Skin eruptions were almost entirely gone, leaving minimal pigmentation. Membranous desquamation started at the nail-skin junction of the right thumb.

April 4: Edema of hands and feet had totally disappeared.

April 6: Membranous desquamation started at the nail-skin junction of the right first toe.

April 8: The cervical lymph node was no longer palpable. The lips were free of erosion or cracking.

April 13: The patient recovered completely with the exception of membranous desquamation of hands and feet and was discharged.

Laboratory findings: Refer to temperature chart (2).

April 2: Erythrocyte sedimentation rate 72 at 1 hour, 112 at 2 hours; CRP5 (+). ASLO 50 units; leukocyte count 12,300 with leftward shift as far as metamyelocytes; Paul-Bunnellnegative; Coombs' test negative; bacterial culture of the blood negative; and Tiselius γ-G1 22.9%. The cerebrospinal fluid was generally normal. Pharyngeal culture yielded no organisms. Urinalysis indicated protein (+) and a few erythrocytes in the sediment. However, there was no sign of nephritis.

Treatment: The personal physician had prescribed Chloramphenicol palmitate solution starting on April 24. Between April 27 and 29, oral penicillin (1,000,000 units/day) and Chloramphenicol (750 mg/day) were given.

Following hospital admission, Chloramphenicol succinate (1 g/day) was infused via an intravenous route, together with an infusion fluid for 3 days, followed by oral administration of 600 mg/day of Ilosone syrup. Starting on April 2, 900,000 units/day of penicillin was injected intramuscularly 6 times. Throughout the clinical course, no adrenal cortical hormone was given.

Case Study [3] (patient No. 4), male, age 8 months.

Admitted: August 30, 1965.

Discharged: September 11, 1965.

Chief complaint: Fever and skin eruption.

Family history: Father in good health. Mother prone to urticaria (she was hypersensitive even to adhesive bandages).

Past medical history: Birth weight 2,400 g. He was bottle-fed and had shown normal growth. He suffered from mild eczema. His neck became steady in 3 months and he was able to sit up in 6 months.

Present illness: In the morning of August 23, 1965, he was found to have developed a temperature of 38.4 ℃. A local physician examined him and gave a diagnosis of *Angina* [old term for sore throat]. The temperature further rose to 40 ℃.

August 24: His temperature was 38.8 ℃ in the morning and 40 ℃ in the evening. It was reported that he received an intramuscular injection of Chloramphenicol.

August 25: The temperature was 39 ℃ in the morning and 40 ℃ in the evening. It was noted that his right cervical lymph node had swollen to the size of a chicken egg and was hard. The patient complained of pain when the lesion was touched. It was also noted that both hands and feet were erythematous.

August 26: Both hands and feet became deeply red and edematous. The lips were dry, erythematous, erosive, and cracked. The temperature ranged from 39 to 40 ℃.

August 27: Both bulbar conjunctivae had become injected. Erythematous eruptions were limited to both hands and feet, especially the palms and soles,which were somewhat edematous. The temperature ranged from 39 to 40 ℃. He received a Pyrethia injection.

August 28: In addition to the rash already affecting the extremities, rubella- or urticaria-like skin eruptions appeared on the skin of the abdomen, thorax, and the back. The cervical lymph node became somewhat smaller. The temperature ranged from 39 to 40 ℃.

August 29: The right cervical lymph node was now the size of the end of a thumb and the patient no longer cried when the lesion was touched. The skin eruptions became erythematous over the entire body. The temperature fluctuated: 39.3, 38, and 39 ℃.

August 30: With persistent fever, the patient was referred to us and admitted to the department of pediatrics at our hospital. (He had been treated with intramuscular administrations of Chloramphenicol, oral medication with Ilosone syrup, together with administration of sulpyrine, VB2, and Pyrethia.)

した（入院迄にクロマイ筋注，アイロゾンシロップ内服，その他スルピリン，VB_2 剤，ピレチア等が使用された由）．

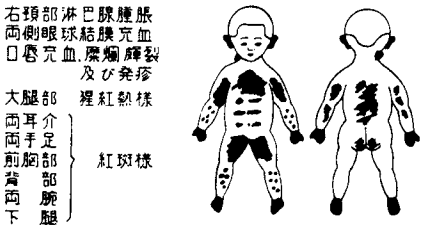
入院時所見：

両側の眼球結膜が充血し，口唇の乾燥，充血，糜爛，皺裂がみられた．口腔粘膜は瀰蔓性に充血し，苺舌を呈していたが，アフタや潰瘍や偽膜の形成はなかつた．右頸部淋巴腺が拇指頭大にやや硬くふれた．全身の皮膚に一部紅斑様，一部猩紅熱様の発疹がみられたが，特に両手掌，両足蹠の紅斑が特徴的であつた（図2）．

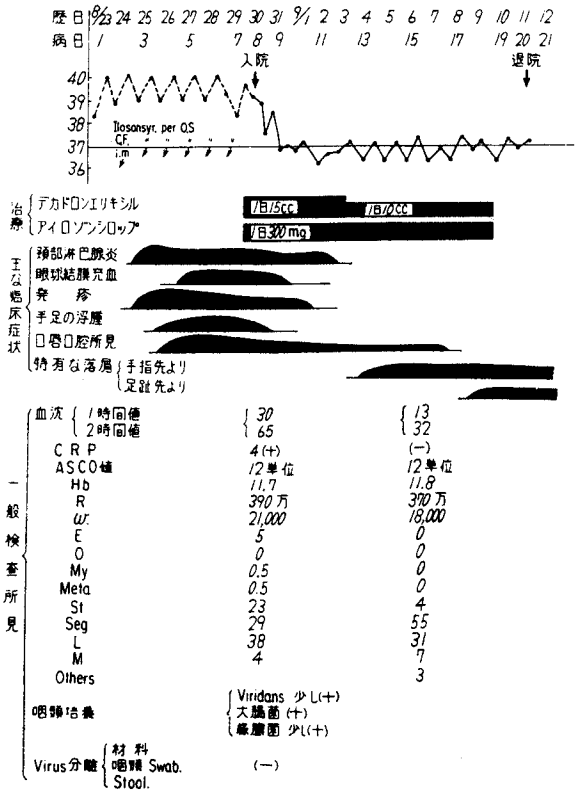
入院後の経過：体温表（3）参照

8月31日　両側の眼球結膜充血は殆んどみられなくなつた．

図2　目黒例（8カ月）



第3例　目黒義幸（男）8カ月入院昭和40年8月30日退院昭和40年9月11日



9月1日　背部に猩紅熱様，紅斑様の発疹がみられるのみで，他の部位の発疹は消えた．

9月3日　発疹は全く消えて，頸部の淋巴腺もふれなくなつた．

9月4日　両側の拇指先及び左人差指先の爪皮膚移行部より膜様の落屑がはじまつた．

9月6日　口唇及び口腔の変化も殆んどなくなつた．

9月9日　両側の第1趾先の爪皮膚移行部より膜様の落屑がはじまつた．

9月11日　両手両足の膜様落屑のみを残して全治退院した．

検査所見：表に示す様に，入院当初，血沈は1時間値30，2時間値65で，CRP 4（十），ASLO12単位，白血球数21,000，血像では骨髄球を含む左方核移動がみられたが，9月6日にはほぼ正常となつた．入院当初の咽頭ヌグイ液及び便よりウイルス分離を依頼したが，いずれも成功しなかつた（予研芦原博士）．

治療：表の如く，入院後直ちにデカドロンエリキシル1日15cc（1.5mg）及びアイロゾンシロップ1日300mgの内服投与を行つたところ，翌日午後より下熱した．

症例〔4〕　加○修（男）5才1カ月

入院　昭和41年4月5日（分類番号No. 26）

退院　昭和41年4月24日

主訴：発熱，右頸部淋巴腺腫脹

家族歴：父は時々蕁麻疹が出来る．父方の祖母に喘息がある．父の弟が喘息と蕁麻疹がある．その子（即ち甥児のいとこ）もひどい喘息であると．母は健康．同胞2人，姉は健．

既往歴：初体重 3,600gr 人工栄養，発育正常．乳児期にも，それ以後にも喘息或は湿疹は認められなかつた．

現病歴：

昭和41年3月30日午前0時頃，右頸部痛を訴えた．発熱には気付いたが測らなかつた．

3月31日　近医に受診し，右頸部淋巴腺炎と診断された．1日中首を痛がり，触らせなかつた．アイロゾン600mg，ベトネラン 1.5mgの投与をうけた．朝38.2℃，昼37.8℃，夜37.9℃であつた．

4月1日　食欲全くなく，終始首を痛がつた．朝37.8℃，昼38.0℃，夜39.0℃であつた．

4月2日　朝37.7℃，昼39.0℃で解熱剤を与え，夜37℃となつた．依然右頸部痛を訴えた．

4月3日　朝両側の眼球結膜充血に気付いた．赤口唇

Findings at admission:

Both bulbar conjunctivae were congested. The lips were dry, hyperemic, erosive, and cracked. The oral mucosa was diffusely hyperemic, and there was a strawberry tongue; However, no aphtha, ulcer, or pseudomembrane had formed. The right cervical lymph node felt somewhat hard and was swollen to the size of the end of a thumb. The skin of the body was characterized by eruptions that were macular in some parts and scarlatiniform in others. Erythema of the palms of the hands and soles of the feet was particularly notable (Fig. 2).

Clinical course after admission: Refer to temperature chart (3).

August 31: The hyperemic condition of the bulbar conjunctivae was barely noticeable.

September 1: Scarlatiniform rash was now confined to the back. The skin on the remainder of the body had become normal.

September 3: Eruptions were completely gone, and the cervical lymph node was no longer palpable.

September 4: Membranous desquamation started at the nail-skin junction of both thumbs and left index finger.

September 6: The lips and oral mucosa had become almost normal.

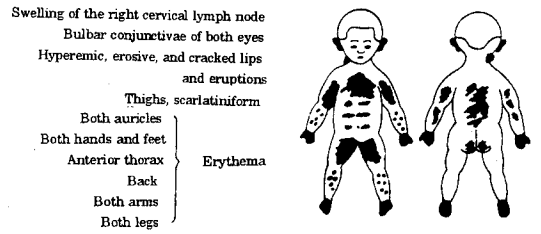
September 9: Membranous desquamation started at the nail-skin junction of the first toes of both feet.

September 11: The condition cleared up completely except the membranous desquamation of both hands and feet. The patient was discharged.

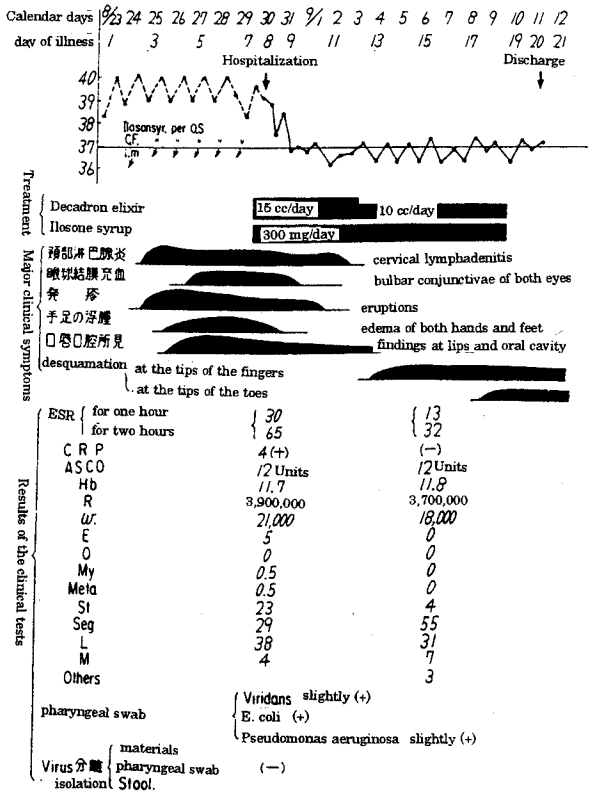
Test results: As indicated in the table, the results of the tests conducted at admission were: erythrocyte sedimentation rate 30 at one hour, and 65 at 2 hours; CRP4 (+); ASLO 12 units; leukocyte count 21,000; and the leftward nuclear shift of the blood cells including myelocytes. By September 6, these results were almost normal. At the time of hospital admission, viral culture was requested from the pharyngeal swab and the fecal specimen. The test was unsuccessful(report by Dr. Ashihara of the National Institute of Infectious Diseases).

Treatment: As indicated in the table, the patient was treated with 15 cc (1.5 mg)/day of Decadron elixir and 300 mg/day of Ilosone syrup immediately after hospitalization. The fever broke in the afternoon of the next day.

Figure 2 No. 4 (8-months-old)



Case 3 (No.4) a male, 8-months-old
hospitalized on August 30 and discharged on Sept. 11, 1965.



Case Study [4] (patient No. 26), male, age 5 years 1 month.

Admitted: April 5, 1966.

Discharged: April 24, 1966.

Chief complaints: Fever and swelling of the right cervical lymph node.

Family history: His father suffers from occasional urticaria. The paternal grandmother has asthma. A paternal uncle suffers from asthma and urticaria. His son (the patient's cousin) also suffers from severe asthma. His mother was well. He had an older sister and she was healthy.

Past medical history: He weighed 3,600 g at birth and was bottle-fed. His growth was normal and he never experienced asthma or eczema during infancy or childhood.

Present illness:

At midnight on March 30, 1966, the patient complained of pain in the right side of the neck. He was found to have fever but the temperature was not recorded.

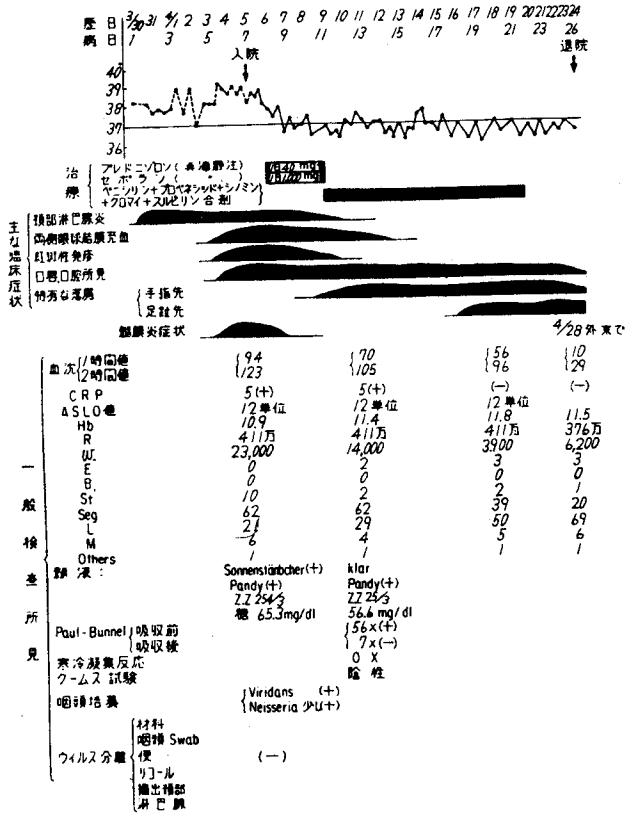
March 31: A local physician examined him and made a diagnosis of right cervical lymphadenitis. . The neck pain persisted throughout the day, and the patient would not let others touch it. Ilosone (600 mg) and Betnelan (1.5 mg) were administered. Temperature was 38.2, 37.8, and 37.9 ℃ in the morning, noon, and evening, respectively.

April 1: The patient had no appetite and complained of the pain in his neck. His temperature was recorded to be 37.8, 38.0 and 39.0 ℃ in the morning, noon, and at night, respectively.

April 2: His temperature was 37.7 ℃ in the morning and 39.0 ℃ at noon. Treatment with an antipyretic reduced it to 37 ℃ in the evening; however, the patient still complained of the pain at the right side of his neck.

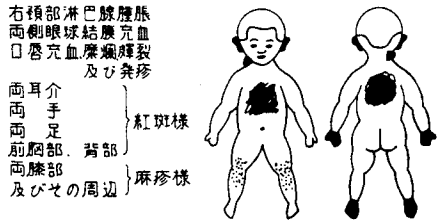
April 3: In the morning, congestion of both bulbar conjunctivae was noted. His lips were dry, erythematous, erosive, and cracked. His forehead and both earlobes were also red. Around noon, the palms of both hands and the soles of both feet were also

第4例　加藤修（男）5才1カ月入院昭和41年4月5日退院昭和41年4月24日



の乾燥，発赤，糜爛，皺裂を認めた．前額部と両耳介が紅斑様に発赤していた．昼頃より両側の手掌，足蹠の紅斑に気付いた．亦前頭部に激しい頭痛を訴え，水分も嘔吐する様になつた．朝38.2℃，昼38.2℃，夜38.6℃であつた．

図3　加藤例



4月4日　右の頸部淋巴腺の腫脹はやや小さくなつた．が依然として激しい頭痛と嘔吐が続いた．朝39℃，昼38.7℃，夜39℃であつた．

4月5日　朝39.5℃で前胸部と背部に新たな紅斑が出現した．頭痛が激しく，紹介されて，日赤中央病院小児科に入院した．

入院時所見：顔貌やや苦悶状で，両側眼球結膜が著明に充血していた．右頸部淋巴腺がウズラの卵大に硬くふれ，圧痛があつた．口唇は乾燥，発赤，糜爛，皺裂し，口腔粘膜は瀰蔓性に充血し，苺舌を認めた．皮膚は図3の如く，両耳介，両手掌，足蹠が著明に紅斑様を呈し，手甲及び足背は紅斑と健康な皮膚とに鮮明な境界を示していた．亦前胸部，背部には紅斑が，両下肢の伸側には麻疹様の発疹が散在した．両側の膝蓋腱反射は亢進し，項部強直を認めた．ブルジンスキー陽性．然し，バビンスキーその他の病的反射は陰性であつた．

入院後の経過：体温表（4）参照

4月5日　入院後直ちに髄液を検べたところ，Pandy（＋），細胞数254/3，糖65.3mg/dlで漿液性髄膜炎が合併していることが判つた．

4月6日　口唇の皺裂部より出血し，血痂がみられた．外科に依頼し，頸部淋巴腺の摘出を行つたが（太中外科梶谷Dr.），腫脹した淋巴腺は胸鎖乳様筋の下，深く存在していたので，皮下組織中の米粒大の淋巴腺2コをとつて，組織学的及びウイルス学的検査を行つた．同時に皮膚の紅斑部の生検も行つた．

4月7日　発疹は殆んど消え，僅かに全指の小関節部に一致して，発赤し，両手掌に軽度の紅斑が残るのみとなつた．

4月9日　発疹は消え，全指先の爪皮膚移行部より膜様の落屑がはじまつた．

4月10日　薬物誘発試験として，ペニシリンG散40万＋プロベネシッド0.5g＋シノミン0.3gr＋クロロマイセチン400mg＋スルピリン0.6gr＋スルフィソミジン1.0grの合剤を1日量として投与を開始した．

4月12日　両側の眼球結膜充血は殆んど認められなくなつた．

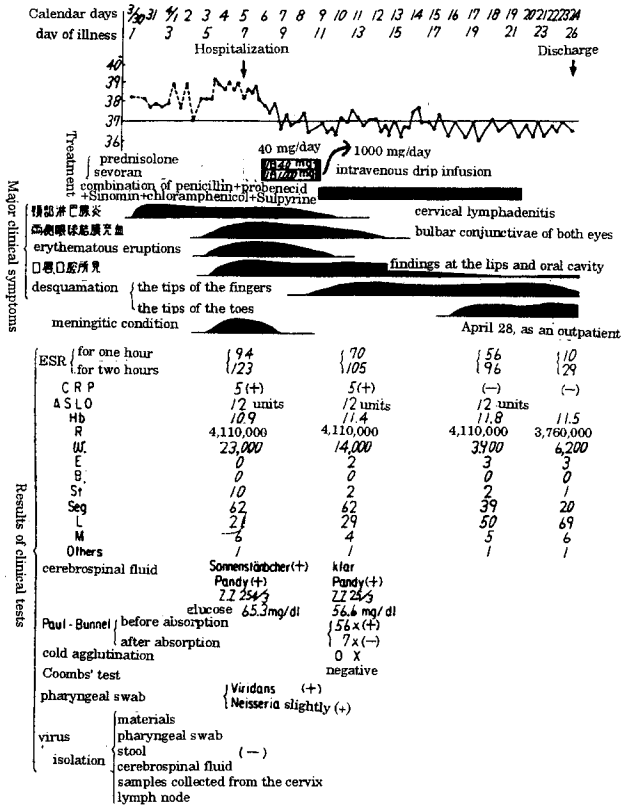
4月16日　左第1趾先の爪皮膚移行部より膜様の落屑がはじまつた．薬物誘発試験では何の反応も示さなかつた．

4月24日　口唇口腔所見もほぼとれて，両手足の膜様落屑のみを残し，全治退院した．

検査所見：入院時血沈1時間値94，2時間値123，CRP5（＋），ASLO12単位，白血球数23,000，血像では桿核10%で軽度の左方核移動があつた．髄液は塵埃様混濁（＋）で，Pandy（＋），細胞数は254/3（殆んど単核細胞），糖65.3mgであつた．この髄液所見は急速に改善し，4月11日には細胞数が25/3となつた．その他Paul-Buunel陰性，寒冷凝集反応陰性，クームス試験陰性であつた．E.K.G.にも異常はなかつた．

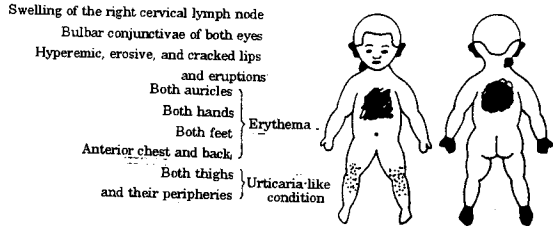
治療：入院翌日の4月6日よりプレドニン1日40mg及

Case 4 (No.26) a male, 5 years-and-one-month-old hospitalized on April 5 and discharged on April 24, 1966



erythematous. The patient complained of a severe frontal headache and vomited everything he ate including liquid. His temperature was recorded to be 38.2, 38.2, and 38.6 ℃ in the morning, noon, and night, respectively.

Figure 3 No.26



April 4: The swelling at the right side of the neck appeared to have been reduced slightly but the severe headache and vomiting persisted. The temperature was 39, 38.7, and 39 ℃ in the morning, noon and at night, respectively.

April 5: The temperature rose to 39.5 ℃ in the morning and erythematous lesions spread to the anterior chest and back. The severe headache persisted. The patient was referred and was admitted to the pediatric ward of the Japan Red Cross Hospital.

Findings at admission: The discomfort was evident in the patient's facies. The bulbar conjunctivae of both eyes were markedly injected. The lymph node at the right side of the neck was enlarged to the size of a quail's egg, hard and painful to touch. The lips were dry, erythematous, eroded, and cracked. The oral mucosa was diffusely hyperemic, with a recognizable strawberry tongue. As shown in Fig. 3, the skin was markedly erythematous at both earlobes, palms, and soles, while clear demarkations with normal skin were noted at the dorsa of the hands and feet. Occasional red macular spots were found at the anterior thorax and back and morbilliform lesions were scattered on the extensor surfaces of both legs. The patellar tendon reflex was exaggerated in both legs. Nuchal rigidity was noted. Brudzinski's sign was positive but the Babinski and other pathological reflexes were negative.

Clinical course following admission: Refer to temperature chart (4).

April 5: An examination of the cerebrospinal fluid conducted immediately after admission revealed the following: Pandy (+); cell count 254/3; and glucose 65.3 mg/dL. These indicated that the condition was complicated with serous meningitis.

April 6: The cracks on the lips bled, forming bloody crusts. A request was made to the Department of Surgery to excise the cervical lymph node (the procedure was conducted by Dr. Kajiya of Professor Futonaka's Department of Surgery). Because the swollen lymph node was situated deeply under the sternocleidomastoid muscle, two subcutaneous lymph nodes the size of of rice grain were collected for histological and viral examinations. At the same time, a biopsy was obtained of the erythematous lesions of the skin.

April 7: The skin eruptions were almost completely gone except for the erythematous lesions at the small joints of all fingers and mild erythema of both palms.

April 9: Skin eruptions dissipated and membranous desquamation started at the nail-skin junctions of all fingers.

April 10: For a drug provocation test, the administration of daily doses of the combination of the following drugs was started: 400,000 units of penicillin G powder + 0.5 g of probenecid + 0.3 g of Sinomin + 400 mg of Chloramphenicol + 0.6 g of sulpyrine + 1.0 g of sulfisomidine.

April 12: The hyperemic condition of the bulbar conjunctivae of both eyes was hardly recognizable.

April 16: Membranous desquamation started at the nail-skin junction of the left first toe. No reaction was found to the drug provocation test.

April 24: The lips and oral cavity were almost normal and the skin lesions had cleared except for the membranous desquamation. The patient was discharged.

Test results: At admission, erythrocyte sedimentation rate was 94 at one hour and 123 at 2 hours; CRP 5 (+); ASLO, 12 units; leukocyte count 23,000; differential count, stab cells 10%, indicating slight shift to the left; and cerebrospinal fluid, turbid with flocculation (+), Pandy (+), cell count 254/3 (almost all monocytes)and glucose 65.3 mg. These cerebrospinal fluid findings on improved rapidly. The cell count declined to 25/3 by April 11. A Paul-Bunnell test, cold agglutination reaction, and Coombs' test were all negative. The electrocardiography was within normal limits.

Treatment: On April 6 (the day after admission), we began intravenous infusion of Predonine 40 mg/day and sevoran 1 g , together with other agents. These medications were discontinued after 3 days when the systemic and local symptoms improved markedly. The clinical course remained satisfactory

びセポラン1gr を他の薬剤と共に点滴静注した．3日間で全身症状及びその他の諸症状も大部分とれたので中止した．その後も比較的順調に経験し，薬物誘発試験も陰性であつた．

例症〔5〕　浅○山○夫（男）1才2ヵ月

入院　昭和37年5月18日（分類番号No. 42）

退院　昭和37年6月7日

主訴　発熱

家族歴：父は蕁麻疹が出来易い．父方祖父に喘息があつた．母は健康．

既往歴：出産正常，発育順調，人工栄養．乳児期に湿疹はなかつた．

現病歴：昭和37年5月14日朝37.9℃に発熱し，耳鼻科にて中耳炎と診断された．右頸部に僅かに発疹がみられた．夜39　代となつた．

5月15日　38℃から39.2℃で，四肢の先端に紅斑様発疹が明かとなつた．

5月16日　口唇及び口腔内があれて来た．発熱は38.2℃～39.2℃であつた．

5月17日　両側の眼球結膜充血が認められた．39℃～39.5℃であつた．

5月18日　高熱を主訴として入院した．

入院時所見：図4の如く，両手両足の紅斑様発疹が著明で，浮腫状を呈していた．頸部及び外陰部，肛門周囲にも紅斑がみられた．両側の眼球結膜充血があり，口唇の乾燥，発赤，糜爛，皺裂及び口腔粘膜全体の著明な瀰蔓性充血があつた．苺舌も認めた．然し，頸部淋巴腺及びその他の部位の淋巴腺の腫脹は全く認めなかつた．アンギーナもなかつた．

入院後の経過：（体温表（5）参照）

5月18日より3日間エリスロマイシンとゾルベニシリンを使用したが発熱は続いた．

5月21日よりプレドニン1日10mgの内服投与を行つた．

5月22日より37.6℃～38℃代となり，臨床的な諸症状がほぼ見られなかつた．

5月23日より右拇指先の爪皮膚移行部より膜様落屑がはじまつた（第11病日）．

6月2日より趾先の落屑がはじまつた．

6月7日両手足の落屑のみを残して，全治退院した．

検査所見：入院時血沈1時間値78，2時間値99，血色素量12gr 赤血球数 435万，白血球数30,600，血像ではE 0，Meta 1，St 20，Seg 63，L13，M 3，その他1で，CRP 2（十），ASLO12単位，全血培養陰性，クームス試験陰性，咽頭培養ではナイセリヤ菌（卄），β溶連菌少し（十）であつた．

この症例は頸部淋巴腺腫脹の伴わない症例であつた．

症例〔6〕　竹○砂○子（女）1才7ヵ月

入院　昭和39年11月4日〔分類番号No. 10〕

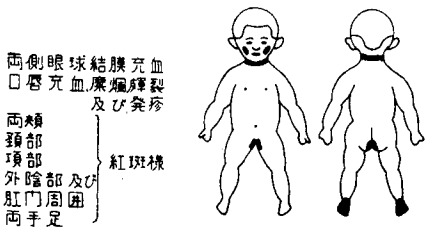
退院　昭和39年11月16日

主訴：発熱と食欲不振

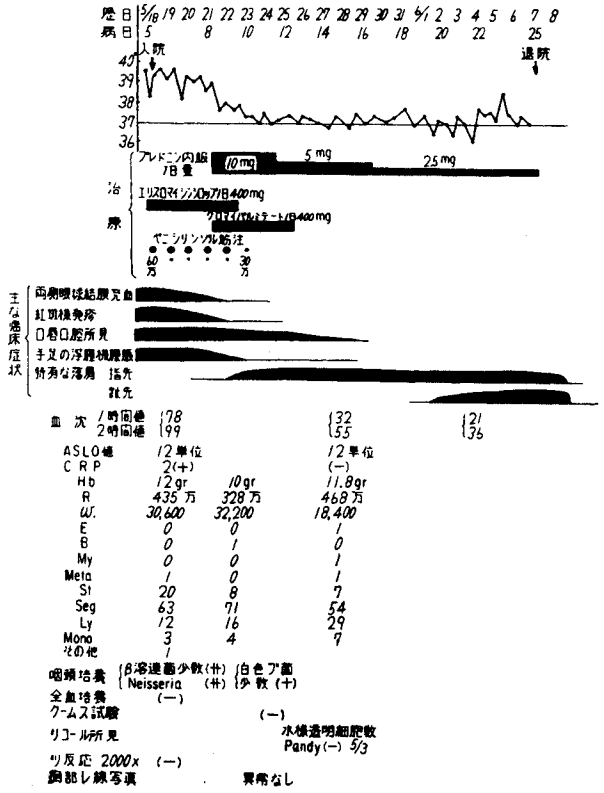
家族歴：父母共健康でアレルギーの家族歴は全くない．本人も乳児期に湿疹はなかつた．

現病歴：昭和39年10月27日朝から不機嫌で昼急にひきつけた．この際体温は40℃であつた．咳（—），くしやみ（—），鼻汁（—）．

図4　浅生山例（1才2月）



第5例　浅生山秀夫（男）1才2ヵ月入院
昭和37年5月18日　退院昭和37年6月7日



therafter. The result of the drug provocation test was negative.

Case Study [5] (patient No. 42),male, age 14 months.

Admitted: May 18, 1962.

Discharged: June 7, 1962.

Chief complaint: Fever.

Family history: Father is prone to urticaria. Paternal grandfather suffered from asthma. His mother was normal.

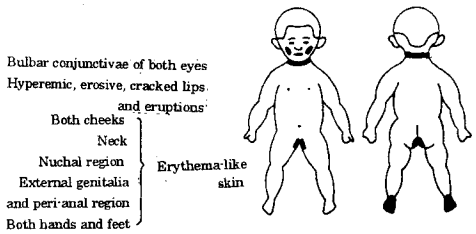
Past medical history: The patient was delivered normally and has achieved normal growth on bottle-feeding. He experienced no eczema during infancy.

Present illness: On May 14, 1962, the patient developed a fever of 37.9 ℃. Diagnosis of otitis media was made by an otorhinologist. A mild eruption was noted on the right side of his neck. His temperature rose to 39 ℃ in the evening.

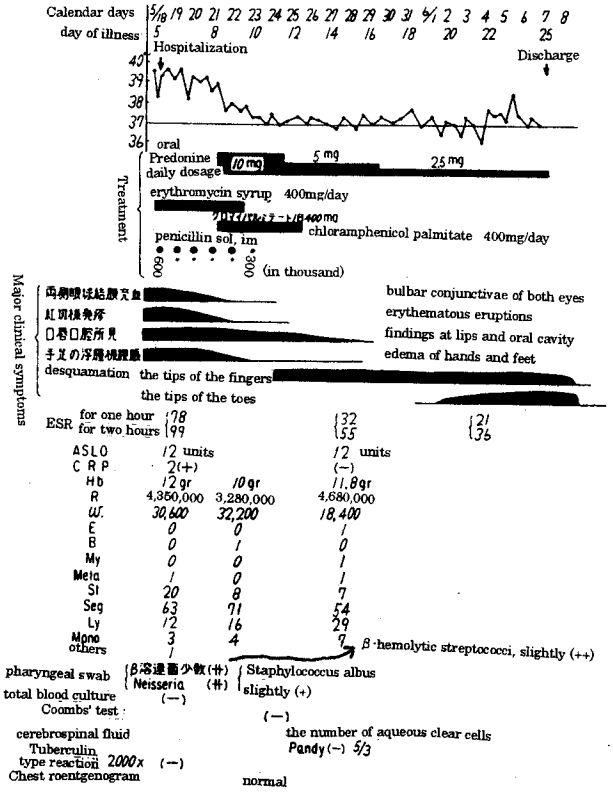
May 15: The temperature ranged from 38 ℃ to 39.2 ℃. Erythema became evident at the distal ends of his extremities.

May 16: The lips and oral mucosa became inflamed. The fever ranged from 38.2 ℃ to 39.2 ℃.

Figure 4 No.42 (14-month-old)



Case 5 (No.42) a male, 14-month-old
Hospitalized on May 18 and discharged on June 7, 1962.



May 17: Congestion of the bulbar conjunctivae of both eyes was noted. Temperature ranged from 39 ℃ to 39.5 ℃.

May 18: The patient was admitted to our hospital with a chief complaint of high fever.

Findings at admission: As shown in Fig. 4, erythematous eruptions were evident at both hands and feet, which were also edematous. Erythema was also noted in the neck, external genitalia, and peri-anal region. The bulbar conjunctivae of both eyes were injected. The lips were dry, erythematous, eroded, and cracked. The oral mucosa was markedly hyperemic throughout with the development of a strawberry tongue. The lymph nodes of the neck and other regions were totally free of swelling. There was no *Angina* [old term for sore throat].

Hospital course: Refer to temperature chart (5). The patient was treated with erythromycin and penicillin for 3 days starting on May 18, but the fever persisted.

Starting on May 21, he was treated with 10 mg/day of oral Predonine.

The fever was reduced to a level of 37.6 to 38 ℃ and most of the clinical symptoms were eliminated.

On May 23, membranous desquamation began at the nail-skin junction of the right thumb (day 11 since onset).

Desquamation started at the toes on June 2.

On June 7, the symptoms have entirely disappeared (except desquamation of both hands and feet) and the patient was discharged.

Test results: At admission, the erythrocyte sedimentation rate was 78 at one hour and 99 at 2 hours; hemoglobin 12 g; erythrocyte count 4,350,000; and leukocyte count 30,600. Differential counts were: Eosinophils 0%; Metamyelocytes 1%; Stab cells 20%; Segmented neutrophils 63%; Lymphocytes 13%; Monocytes 3%; others 1%. Other test results included: CRP 2(+); ASLO 12 units; all blood cultures negative; Coombs' test negative; pharyngeal swab *Neisseria* (++); and (hemolytic streptococci slightly (+).

This case represents a clinical subtype without swelling cervical lymphadenitis.

Case Study [6] (patient No. 10), female, age 1 year 7 months

Admitted: November 4, 1964.

Discharged: November 16, 1964.

Chief complaints: Fever and anorexia.

Family history: Both parents are healthy with no family history of allergic diseases. The patient did not suffer from eczema during infancy.

Present illness: On the morning of October 27, 1964, the patient was in an bad mood and suddenly developed convulsions at noon. Her temperature was 40oC then. Coughs (-), sneezing (-), and nasal discharge (-).

November 1: The lips appeared eroded.
November 2: The bulbar conjunctivae of both eyes were found to be hyperemic. Her temperature was 39.3 ℃, and the attending physician noted swelling of the left cervical lymph node.

November 3: Her temperature remained around 39 ℃. It was noted that both hands and feet were edematous but no skin eruptions were seen then.
November 4: The patient was admitted to the pediatric ward in our hospital.

11月1日　口唇が糜爛して来た.

11月2日　39.3℃で両側の眼球結膜充血に気付いた. 亦左の頸部淋巴腺腫脹を近医に指摘された.

11月3日　39℃代で両手両足が浮腫状となつているのに気付いた. 発疹には気付かなかつた.

11月4日　当小児科に入院した.

入院時所見：皮膚には発疹がみられない. 両側の眼球結膜は著明に充血している. 口唇の発赤, 糜爛及び皺裂がみられ, 乾燥している　舌はやや平滑で光沢を帯び, 苺舌ではなかつた.

口腔粘膜全体が瀰蔓性に充血していたが, アフタや偽膜の形成はなかつた. 左頸部で下顎角直下に淋巴腺が拇指頭大に腫脹し, やや硬く, 触ると疼痛を訴えた. 局所皮膚の発赤はみられなかつた. 両手甲, 手掌が著明に浮腫状であつた.

入院後の経過：(体温表(6)参照)

11月5日　両側の眼球結膜充血及び両手の浮腫がとれて下熱した.

11月10日　右拇指先の爪皮膚移行部より膜様落屑がはじまつた.

11月11日　口唇の糜爛, 皺裂はまだみられた.

11月16日　指の落屑を少し残してほぼ全治退院した.

検査所見：11月5日血沈1時間値34, 2時間値73, 咽頭培養では緑連菌(+). 血液検査では血色素量11gr%, 赤血球数 375万, 白血球数12,500, 血像ではE 1.5, My 0.5, Meta 0.5, St 10, Seg 56, Ly 27, M 4, その他5で, CRP 2(+), ASLO12単位, 寒冷凝集反応16倍, クームス試験陰性, Paul-Bunnel 陰性であつた. この症例は発疹は認められなかつたが, 指先の爪皮膚移行部からの膜様落屑がみられた女児例で, 比較的軽い症例であつたので, 入院後全く薬剤を使用せずに観察することが出来た.

症例〔7〕　市木好美(女) 2才4ヵ月

入院　昭和41年8月25日(分類番号No. 15)

退院　昭和41年9月6日

主訴　発熱と発疹

家族歴：父はトクホンにかぶれ易い. 母は健康. 患児は一卵性双生児で, もう1人は健康である. 他に5才の姉がいるが健康.

既往歴：生下時体重 1,600gr. 人工栄養, 乳児期に湿疹なし. 首据り4ヵ月, 歩行1年6ヵ月, 風邪は引き易いが, 喘鳴を伴うことはない.

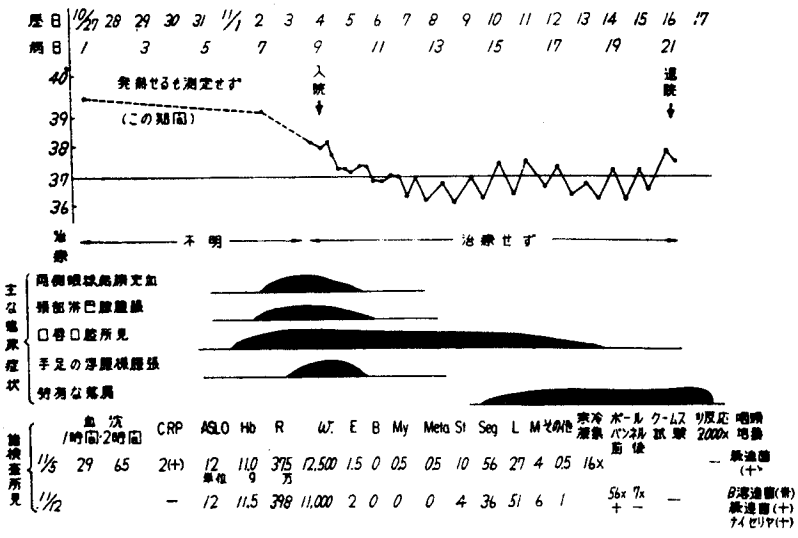
現病歴：昭和41年8月21日　夕方急に元気がなくなり, ぐつたりしていた. 発熱に気付いたが測らなかつた. 右側の首を痛がり, 母親は右側の頸部淋巴腺腫脹に気付いた(午後7時頃).

8月22日　朝38.2℃で外科に受診し, 頸部淋巴腺炎と診断された. 夜39.4℃となる.

8月23日　朝38.2℃で耳鼻科に受診したところ, 中耳炎ではなくて, 頸部淋巴腺炎であるといわれた. 昼37.6℃. 夜8時頃39.9℃となり, 近くの小児科に受診した.

8月24日　朝37.2℃. 戸外で遊んだ. 夜38.4℃で, 午後10時頃両手足が紅斑様なのに気付いた. 同時に目を開けた際, 両側の眼球結膜の充血にも気付いた.

第6例　竹内砂代子(女) 1才7ヵ月
入院昭和39年11月4日　退院昭和39年11月16日



Findings at admission: The skin had no eruptions. The bulbar conjunctivae of both eyes were markedly hyperemic. The lips were red, eroded, cracked, and dry. The tongue was somewhat smooth and lustrous, but did not have the appearance of a strawberry tongue.

The oral mucosa was diffusely hyperemic without the formation of aphtha or a pseudomembrane. On the left side of the neck immediately below the maxillary angle, a lymph node was swollen to a size that approximated the end of a thumb. It felt hard and produced pain when palpated. No erythema was found on the overlying skin. The dorsa of both hands and feet were markedly edematous.

Hospital course: Refer to temperature chart (6).

November 5: Hyperemia of the bulbar conjunctivae of both eyes and edema of both hands have dissipated and the patient's temperature has returned to normal.

November 10: Membranous desquamation started at the nail-skin junction of the right thumb.

November 11: The lips were still eroded and cracked.

November 16: Except for residual desquamation of the fingers, the patient was free of symptoms and was discharged.

Test results: On November 5, erythrocyte sedimentation rate was 34 at one hour and 73 at 2 hours. A pharyngeal culture yielded *Pseudomonas aeruginosa* (+). The results of hematological examinations were: hemoglobin11 g/dL; erythrocyte count 3,750,000; leukocyte count 12,500; differential count Eosinophils 1.5%, Myelocytes, 0.5%, Metamyelocytes 0.5%, Stab cells 10%, Segmented cells 56%,Lymphocytes 27%, Monocytes 4%, and others 5%. CRP was 2 (+); ASLO, 12 units; cold agglutination reaction 16 x; Coombs' test negative; and Paul-Bunnell test negative. This patient exemplifies a clinical course in which membranous desquamation occurred at the nail-skin junction of her fingers without the development of skin eruptions. It was a relatively mild course and the patient was observed without administration of any medications.

Case Study [7]: (patient No. 15, female, age 2 years 4 months.

Admitted: August 25, 1966.

Discharged: September 6, 1966.

Chief complaints: Fever and skin eruptions.

Family history: Her father developed hypersensitivity reactions to medicated plasters. Her mother was healthy. The patient is one of monozygotic twins and her twin sister is normal. Another 5-year-old sister is also in good health.

Past medical history: At birth, she weighed 1,600g and was bottle-fed since then. She suffered no eczema during early infancy. Her head became steady at 4 months and she learned to walk at 18 months. She often caught a cold but did not develop wheezing.

Present illness: In the evening of August 21, 1966, she suddenly became lethargic. She appeared febrile but no temperature was recorded. She complained of pain on the right side of her neck. Her mother noted that a swollen lymph node at that site (around 7 o'clock in the evening).

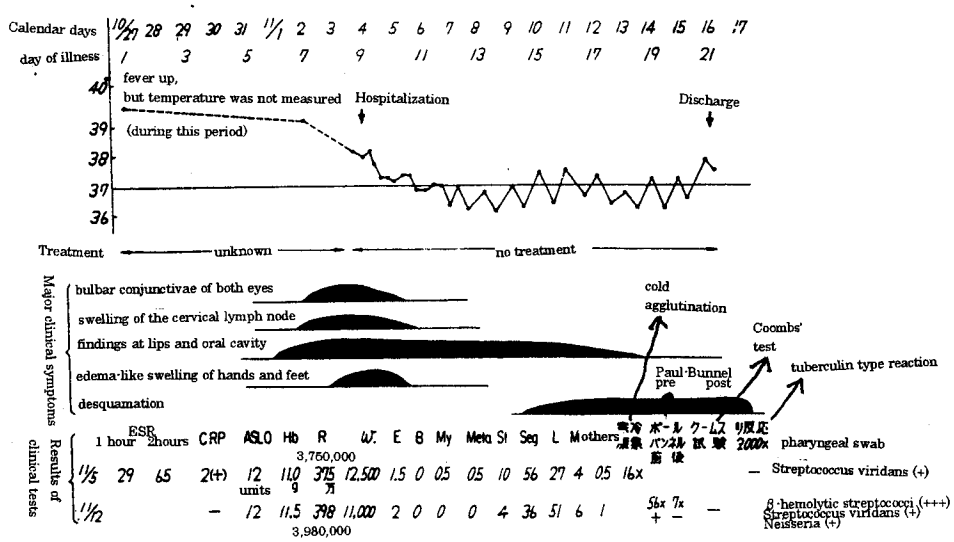
August 22: The patient developed a fever of 38.2 ℃ in the morning and was brought to the department of surgery, where a diagnosis of cervical lymphadenitis was given. Her temperature rose to 39.4 ℃.

August 23: The fever registered 38.2 ℃ .After the patient was examined by an otorhinologist for suspicion of otitis media, the diagnosis was changed to cervical lymphadenitis. The temperature was 37.6 ℃ at noon and 39.9 ℃ around 8 in the evening. She was brought to a neighborhood pediatric clinic.

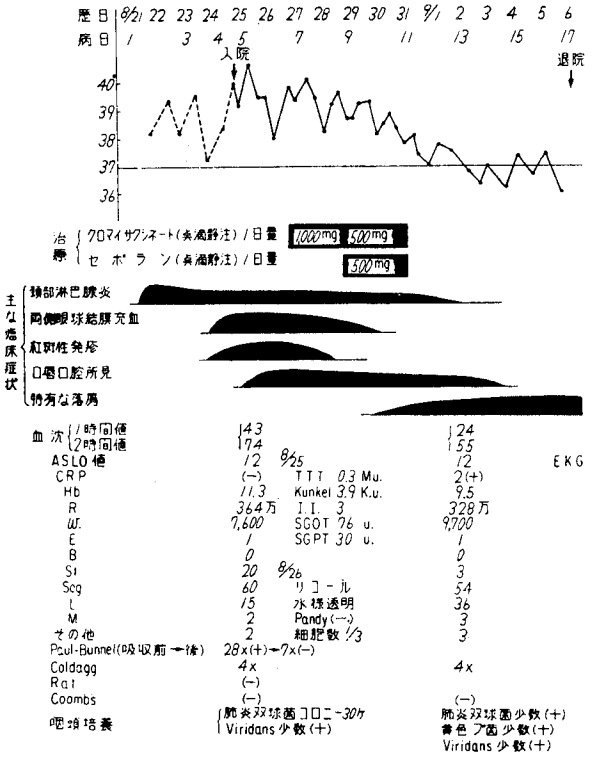
August 24: Her temperature was 37.2 ℃ in the morning and she felt well enough to play outside. In the evening, the temperature rose to 38.4 ℃. Around 10 o'clock in the evening, it was noted that her hands and feet were erythematous. It was also noted when she opened her eyes that the bulbar conjunctivae of both eyes were hyperemic.

August 25: Her temperature was 40 ℃ in the morning. The patient was in an ill mood, crying occasionally, dozing off from time to time, and

Case 6 (No.10) a 19-month-old female
Hospitalized on Nov. 4 and discharged on Nov. 16, 1964.



第7例　市○好○（女）2才4ヵ月
入院昭和41年8月25日　退院昭和41年9月6日



8月25日　朝40℃．不機嫌で泣いたり，うとうとしたり亦口を痛がつたりした．手足のみならず躯幹にも紅斑が現われたので，当小児科に紹介されて入院した．

入院時所見：栄養は中等度．両側の眼球結膜が著明に充血し，口唇の乾燥，発赤，糜爛，皺裂をみる．口腔粘膜は瀰蔓性に充血し，咽頭発赤も著しいが，偽膜や潰瘍やアフタの形成はない．舌苔を被るも，一部露出し，乳頭が著明に腫脹して，所謂苺舌を呈していた．右頚部淋巴腺がウズラの卵大に腫脹し，稍々硬く，弾性があり，触れると疼痛を訴えた．局所の皮膚の発赤はない．皮膚は紅斑様発疹が全身特に両手掌，両足蹠に著明であるが，どこにも水疱はみられない．胸部理学的所見では，肺に異常なく，心音も純で，腹部では肝脾をふれない．外陰部，肛門には全く異常を認めない．

入院後の経過：体温表（7）参照

8月25日　諸検査を行う．血沈1時間値43，2時間値74，CRP（−），ASLO12単位，RA Test（−），寒冷凝集反応4倍，Paul-Bunnel 陰性，肝機能検査では黄疸指数3，SGOT76，SGPT30，TTT 0.3μ.u. Kunkel 3.9k.u. で血液検査では血色素数11.3gr. 赤血球数364万，白血球数 7,600でE1，B0，ST20，Seg. 60，Ly 15，M2，その他2の血像であつた．咽頭培養では肺炎双球菌がコロニー30コ，Viridans が少数（+）．検尿はほぼ正常であつた．

8月26日　皮膚の組織学的検査を右第3趾先と臀部の共に紅斑部位に於て施行した．髄液は外観水様透明，Pandy（−），細胞数1/3で正常であつた．両側の眼球結膜充血及び皮膚の紅斑様発疹がやや消褪しはじめた．

8月27日　8月25，26，27日の3日間に亘つて採取した咽頭ヌダイ液及び糞便及び髄液合計8検体を予研芦原博士にウイルス分離を依頼した．

8月28日　発疹殆んど消えた．が発熱は依然として続いている．

8月29日　両側の眼球結膜充血がとれた．

8月30日　口唇の乾燥発赤，糜爛，皺裂は依然として著明である．右頚部淋巴腺はやや小さくなり，拇指頭大で硬い．発疹は全くない．右拇指先の爪皮膚移行部から膜様落屑が始まる．

8月31日　右側のほぼ全指先の特異的な膜様落屑がみられた．

9月1日　下熱し，37℃代となる．

9月2日　口唇所見も大分とれて来た．右頚部淋巴腺も殆んどふれなくなつた．

9月3日　右第1趾先の爪皮膚移行部より，膜様落屑が始まつた．

9月6日　両手両足の指趾に限局した膜様落屑のみを残して，ほぼ全治退院した．

検査所見：8月25日の検査所見は上記したが9月2日（第13病日）に血沈1時間値24，2時間値55，CRP2（+），ASLO12単位，寒冷凝集反応4倍，クームス試験陰性，血液検査では血色素量 9.5gr. 赤血球数 328万，白血球数 9,700，血像はE1，B0，St. 3，Seg. 54，Ly 36，M3，その他3で，咽頭培養は黄色ブ菌少数（+），肺炎双球菌少数（+），Viridans 少数（+）であつた．

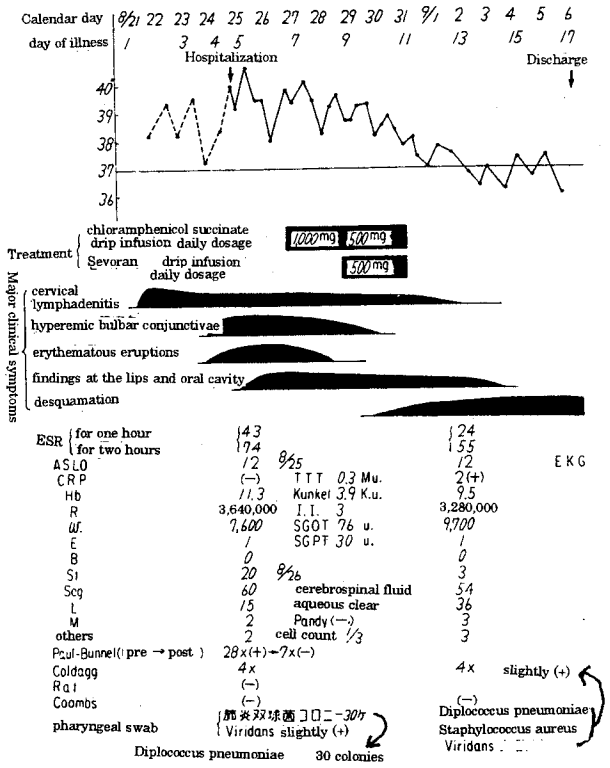
9月6日　心電図でPQの延長を認めた．そこで退院後も全く治療を行わずに観察し，3ヵ月後の12月8日に再び心電図をとつて検べたところ，今回は全く正常所見であつた．勿論臨床的にも全く異常なく，健康に生活していた．

予研にお願いしたウイルス分離の結果はまだ結論を得られなかつた．

治療：

8月25日と26日は全く治療せずに観察した．

Case 7 (No.15) a 28-month-old female
Hospitalized on August 25 and discharged on Sept. 6, 1966.



complained of pain in her mouth. Erythema affected not only the hands and feet but also the torso. She was referred to our pediatric department and was admitted.

Findings at admission: The child's nutritional status was fair. Both bulbar conjunctivae were markedly hyperemic. The lips were dry, erythematous, eroded, and cracked. The oral mucosa was diffusely hyperemic. The pharynx was also markedly erythematous without the formation of pseudomembrane, ulcer, or aphtha. The tongue was coated but the papillae were partly exposed and markedly swollen, presenting the features of a so-called strawberry tongue. The lymph node at the right side of the neck was swollen to the size of a quail's egg, somewhat hard and resilient. The patient complained of pain when the lesion was touched. The skin over the lesion was not erythematous. The erythematous eruptions covered her entire body, especially on both palms and the soles. These lesions were not accompanied by blisters. A physical examination found the lungs to be normal. The heart sounds were clear. The liver and spleen were not felt when the abdominal region was examined. The external genitalia and anus were completely normal.

Hospital course: Refer to temperature chart (7).

The following tests were conducted on Aug. 25: Erythrocyte sedimentation rate 43 at one hour and 74 at 2 hours; CRP (-); ASLO 12 units; RA test (-); cold agglutination reaction 4 x; Paul-Bunnell negative. The results of the liver function tests were: icteric index3; SGOT 76; SGPT 30; TTT 0.3 μ u; Kunkel 3.9 k.u. Hematological examinations produced the following results: hemoglobin 11.3 g; erythrocyte count 3,640,000; leukocyte count 7,600; differential count:Eosinophils 1%; Basophils 0; Stab cells 20%; Segmented cells 60%; Lymphocytes 15%; Monocytes 2%; and others 2%. A pharyngeal culture yielded 30 colonies of Diplococcus pneumoniae and a few *Streptococcus viridans* (+). The results of urinalysis were generally normal.

August 26: A histological examination was conducted on the erythematous skin collected from the third toe of the right foot and the buttocks. The results of cerebrospinal fluid examination were normal: clear in appearance, Pandy (-), and cell count 1/3. Hyperemia of both bulbar conjunctivae and erythematous eruptions of the skin began to disappear.

August 27: Pharyngeal swabs collected over a 3-day period (between August 25 to 27), fecal specimens, and cerebrospinal fluid samples (total, 8 specimens) were sent to Dr. Ashihara of the National Institute of Infectious Diseases for virus isolation.

August 28: Skin eruptions have almost entirely disappeared but her fever persisted.

August 29: The bulbar conjunctivae were no longer congested.

August 30: The lips were still dry, red, eroded, and cracked. The lymph node at the right side of the neck was somewhat reduced in size (to the size of the tip of a thumb) and felt hard. The skin was completely devoid of eruptions. Membranous desquamation started at the nail-skin junction of the right thumb.

August 31: Membranous desquamation of a unique pattern was seen on each finger of the right hand.

September 1: The fever broke and the temperature remained around 37 ℃.

September 2: The oral mucosa returned almost to normal. The right cervical lymph node was now hardly palpable.

September 3: Membranous desquamation started at the nail-skin junction of the first toe of the right foot.

September 6: Except for membranous desquamation localized at the toes and fingers, all symptoms had disappeared and the patient was discharged.

Test results: the findings of the tests conducted on August 25 were shown above. Those from tests conducted on September 2 (day 13 following onset) are given below: erythrocyte sedimentation rate 24 after at hour and 55 after 2 hours; CRP 2 (+); ASLO 12 units; cold agglutination reaction 4 x; Coombs' test negative. The results of hematological tests were: hemoglobin 9.5g; erythrocyte count3,280,000; leukocyte count 9,700; differential count: Eosinophils 1%; Basophils 0; Stab cells 3%; Segmented neurtrophils 54%; Lymphocytes 36%; Monocytes 3%; and others 3%. Pharyngeal culture yielded a few *Staphylococcus aureus* (+), *Diplococcus pneumoniae* (+), and *Streptococcus viridans* (+).

September 6: ECG exhibited prolongation of the PQ interval. Therefore, the patient was observed after discharge without any active treatment. A second ECG, conducted 3 months later (on December 8) found her to be perfectly normal. She was also clinically normal and is currently enjoying normal activities.

The results of viral isolation have not come in yet.

Treatment:

The patient was observed without any treatment

8月27日よりクロマイサクシネート1日1gを輸液と共に点滴静注を行つた.

8月29日よりクロマイサクシネートを1回 0.5gr とし，セボラン1日 0.5gr との併用とした.

8月31日　すべての治療を中止した.

全経過中皮質ホルモンは使わなかつた.

3. 自験50例の症候学

我々の症例は主症状の1つである頚部淋巴腺腫脹の有無によつて，2つの大きなグループに分けることが出来る．即ち，

第1のグループは頚部淋巴腺が拇指頭大から鶏卵大或はそれ以上に腫脹する群で，之を一応CLA（十）群（Cervical Lymphadenitis の略）とした.

第2のグループは頚部淋巴腺腫脹のないグループで，之をCLA（一）群とした.

第1表は以上の2大別に従い，各々年令順に各症例を整理分類したものである（表1）.

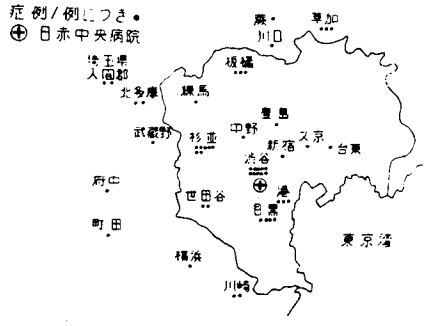
症例番号（又は分類番号）No. 1からNo. 33迄の33例がCLA（十）群に属し，症例番号No. 34からNo. 50迄の17例が，CLA（一）群に属している.

これから述べようとする，本症候群の症状分析は一応CLA（十）群とCLA（一）群とを合せた全例50例について行つたものであるが，必要に応じて，この両者間の相異点にふれるつもりである.

1） 地理的分布（地理的分布図及び表）

図及び表に示す様に各症例間に相互関係や流行等は全く見られなかつた.

地理的分布図



年度別地理的分布表　　日赤中央病院：渋谷区

年度	渋谷	杉並	目黒	港	板橋	草加	世田谷	川崎	北多摩	入間	中野	台東	練馬	新宿	文京	豊島	川口	武蔵野	府中	町田	横浜	計
1961			1																			1
1962	3	1	1	1			1		1			1										9
1963	1	1	1	1	1				1				1									7
1964	1	1					1	1						1	1		1					7
1965	3	2			2				1	1							1					10
1966	2	2	2		2	1		1		1			1			1		1	1	1	1	16
計	10	7	4	3	3	3	2	2	2	2	1	1	1	1	1	1	1	1	1	1	1	50

2） アレルギーの家族歴（表2）

父母に蕁麻疹に罹り易い傾向がみられた.

3） 年度別及び季節別頻度（表3）

表の如く昭和37年度より症例数が急に増加しているが，症例が増したためか，発見率が高くなつたためかは明かでない．季節別にみると10，11，12及び2月が他に比して頻度が低く，全体の傾向としては，春から夏にかけてやや多く，秋から冬にかけてやや少い様にみえる.

4） 年令別（表4）

表に示す様に，2才以下の乳幼児が27例（54%）で過半数を占めている点が特徴的である.

年令の分布は生後2カ月の乳児から9才1カ月の学童に迄及んでいるが（表1参照），6才以上は僅かに5例で（10%），本症候群が主として乳幼児の疾患であることがわかる.

5） 性別（表5）

男32例，女18例で，約5：3の比で男児に多い.

6） 初発症状，主訴の分析その他（表6）

ここに述べる症状分析は入院中のものは，入院病歴に基いたものであるから，比較的正確といえるが，入院迄の症状や所見は，一部の症例を除いて（医師の経過報告書持参の症例）大部分が家族，特に母親の言によるので，その正確さは期待し難い．或る母親は入院前の熱型を非常によく記載してあるが，他の母親は単に記憶のみで答えるという具合で，色々であつた.

後述の治療の項に於ける各症例毎の体温表も，入院迄の部分は以上の様な各件での資料に基ずくこと並に入院後の体温測定は2才以下は主に肛門検温によることを参考とされ度い.

初発症状（表6の1）

発熱ではじまる例が圧倒的に多く，前駆症状としては，“首の痛み”を4例，“咳嗽”を2例，“頚部淋巴腺腫脹”，“不機嫌でぐずる”及び“腹痛”をそれぞれ1例ずつ認めたにすぎない（表中（　）内数字）.

即ち，一般的な所謂風邪症状等の前駆症状は大部分の症例に欠けていた.

主訴の分析（表6の2）

入院時又は来院時の主訴は，圧倒的に，“発熱”であつた（48例，96%）.即ち近医の治療をうけているにも拘らず，高熱が続くので，大多数の例は，その医師の紹介により来院したケースである．次で“発疹”，“頚部淋巴腺腫脹”，“目が赤い”の順となつている.

on August 25 and 26.

Starting on August 27, 1 g/day of Chloramphenicol succinate was given by intravenous infusion together with the maintenance fluid.

Starting on August 29, the dosage of Chloramphenicol succinate was reduced to 0.5 g/day and administered in combination with 0.5 g/day of sevoran.

On August 31, all medications were stopped.

Throughout the course, no adrenal cortical hormone was administered.

3. Symptomatology of the 50 patients

The patients were divided into two main groups: those in whom the cervical lymph node was swollen (one of the major symptoms); and those in whom there was no lymph node swelling.

In the first group, tentatively called CLA (abbreviation for cervical lymphadenitis) (+), the cervical lymph node was swollen approximating the size of the end of a thumb to a chicken egg.

The second group, composed of those with no swelling of the cervical lymph nodes, was assigned the nomenclature of CLA (-).

In Table 1, each patient has been assigned to one of these two groups and listed in ascending order of age.

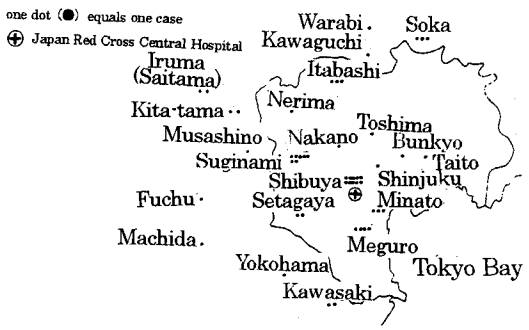
Patient (or classification) Nos. 1 through 33 represent 33 patients who belong to the CLA (+) group, while Nos. 34 through 50 are 17 in the CLA (-) group.

The analysis of symptoms of this syndrome, which will be introduced below, will involve all 50 patients. Differences between the two groups will also be discussed whenever it is deemed necessary.

1) Geographic distribution (a figure and table showing the geographic distribution)

As indicated in the figure or table, there was no correlations between cases or area-specific epidemics.

Geographical Distribution of Patients



Geographical Distribution of Patients by Year Japan Red Cross Central Hospital:Shibuya

year	Shibuya	Suginami	Meguro	Minato	Itabashi	Soka	Setagaya	Kawasaki	Kita-tama	Iruma	Nakano	Taito	Nerima	Shinjuku	Bunkyo	Toshima	Kawaguchi	Musashino	Warabi	Machida	Fuchu	Yokohama	Total
1961				1																			1
1962	3	1	1	1			1		1			1											9
1963	1	1	1	1	1				1					1									7
1964	1	1					1	1							1	1			1				7
1965	3	2				2				1	1							1					10
1966	2	2	2		2	1		1		1			1				1			1	1	1	16
total	10	7	4	3	3	3	2	2	2	2	1	1	1	1	1	1	1	1	1	1	1	1	50

2) Allergic tendencies seen in family histories (Table 2)

Tendencies for urticaria were noted in mothers or fathers.

3) Annual and seasonal incidences (Table 3)

As shown in the table, the number of cases listed increased suddenly since 1962. It is not certain whether this is so because the number of cases increased or more cases were uncovered. When the incidence is examined by season, it is slightly lower in October, November, December, and February. There is an overall trend toward a slight increase in spring and summer and a drop in fall and winter.

4) Age factor (Table 4)

As shown in this table, it is noteworthy that more than half of the patients (54%) are infants and children below the age of 2 years.

The age of patients ranges from 2 months to 9 years and one month (Table 1) but only 5 (10%) are over the age of 6 years. It is evident that this syndrome mainly affects infants and very young children.

5) Sex factor (Table 5)

Males number 32 and females, 18 or a sex ratio of roughly 5:3.

6) Initial symptoms, analysis of chief complains, and others (Table 6)

The symptoms of those who had been hospitalized were analyzed, based on the records kept at the hospital. The data are considered to be reasonably accurate. With the exception of a few (those reports submitted by attending physicians), the symptoms and findings prior to hospital admission were obtained from family members (especially the mothers) and the accuracy of these data cannot be relied upon. Some mothers documented the fluctuating fever patterns in detail prior to hospitalization, while others gave vague descriptions from memory.

The pre-hospitalization portion of the temperature charts for individual patients, which will be discussed in the section entitled "Treatment", was also prepared from the sources described above. Following hospitalization, the rectal temperature was used mainly for children under 2 years of age.

Initial symptoms (Table 6-1)

For an overwhelming number, fever was the initial symptom. Prodromal symptoms included "pain in the neck" (4 cases) and "coughing" (2 cases). "Lymph node swelling", "bad mood and fussiness", and "abdominal pain" were recorded for only one case each (figures in parenthesis in the table).

It was concluded that common prodromal conditions, such as the so-called "cold-like symptoms" were lacking in most of the cases.

Analysis of the chief complaints (Table 6-2)

An overwhelming number (48 cases, 96%) reported "fever" as the major complaint when admitted to the hospital or examined at the clinic. Most of them were first treated by a local physician but because of a persistent high fever, they were referred to our hospital. Other major complaints included "skin eruptions", "swelling of the cervical lymph nodes", and "redness of the eyes".

Diagnosis given by other physicians (Table 6-3)

The diagnosis given by physicians who attended the patients prior to visiting our hospital varied

表1　自験50例の年令順，主症状別，整理分類表　No. 1—33CLA（＋）群，No. 34—50CLA（－）群 *

症例番号	氏名	年令	性別	発熱	頸部淋巴腺炎	皮膚 発疹	皮膚 落屑	眼球結膜充血	口腔所見口唇	手足の腫状腫脹浮	症例番号	氏名	年令	性別	発熱	頸部淋巴腺炎	皮膚 発疹	皮膚 落屑	眼球結膜充血	口腔所見口唇	手足の腫状腫脹浮
1	原	4　月	男	＋	＋	＋	＋	＋	＋	－	26	加藤	5才 1月	男	＋	＋	＋	＋	＋	＋	－
2	村田	6　月	男	＋	＋	＋	＋	＋	＋	－	27	桑原	5才 8月	女	＋	＋	＋	＋	＋	＋	－
3	岡田	8　月	男	＋	＋	＋	＋	＋	＋	＋	28	飯島	5才10月	男	＋	＋	＋	＋	＋	＋	－
4	目黒	8　月	男	＋	＋	＋	＋	＋	＋	＋	29	梅本	6才 4月	女	＋	＋	－	＋	＋	＋	－
5	松田	8　月	男	＋	＋	－	＋	＋	＋	－	30	矢島	6才 9月	男	＋	＋	＋	＋	＋	＋	－
6	山本	11　月	男	＋	＋	＋	＋	＋	＋	＋	31	桜井	7才 1月	女	＋	＋	＋	＋	＋	＋	－
7	小川	1　才	女	＋	＋	＋	＋	＋	＋	＋	32	東川	8才 7月	男	＋	＋	＋	＋	＋	＋	－
8	男沢	1才 2月	男	＋	＋	＋	＋	＋	＋	＋	33	中坪	9才 1月	男	＋	＋	＋	＋	＋	＋	－
9	三上	1才 2月	女	＋	＋	＋	＋	＋	＋	＋	34	大沢	2　月	男	＋	－	＋	＋	＋	＋	－
10	竹内	1才 7月	女	＋	＋	－	＋	＋	＋	＋	35	森下	3　月	女	＋	－	－	＋	＋	＋	－
11	高柳	1才 8月	男	＋	＋	＋	＋	＋	＋	＋	36	内山	6　月	男	＋	－	＋	＋	＋	＋	＋
12	石田	1才 9月	女	＋	＋	＋	＋	＋	＋	＋	37	呉	7　月	男	＋	－	＋	＋	－	＋	＋
13	今田	1才10月	男	＋	＋	＋	－	＋	＋	＋	38	加山	8　月	男	＋	－	＋	＋	＋	＋	－
14	奥山	1才11月	男	＋	＋	＋	＋	＋	＋	＋	39	海老沢	9　月	男	＋	－	＋	＋	＋	＋	－
15	市木	2才 3月	女	＋	＋	＋	＋	＋	＋	－	40	佐藤	11　月	男	＋	－	＋	＋	＋	－	－
16	高井	2才10月	男	＋	＋	＋	＋	＋	＋	＋	41	永沼	11　月	男	＋	－	＋	＋	＋	＋	－
17	中村	3才 3月	女	＋	＋	＋	＋	＋	＋	＋	42	浅生山	1才 3月	男	＋	－	＋	＋	＋	＋	＋
18	川田	3才 4月	女	＋	＋	＋	＋	＋	＋	－	43	金井	1才 5月	男	＋	－	＋	＋	＋	＋	＋
19	田部井	3才 6月	女	＋	＋	＋	＋	＋	＋	－	44	立川	1才 7月	男	＋	－	＋	＋	＋	＋	＋
20	高山	3才 7月	男	＋	＋	＋	＋	＋	＋	－	45	錦谷	1才10月	男	＋	－	＋	＋	＋	＋	－
21	高橋	3才 9月	女	＋	＋	＋	＋	＋	＋	＋	46	柳沢	1才11月	男	＋	－	＋	＋	＋	＋	＋
22	竹浪	4才 1月	女	＋	＋	＋	＋	＋	＋	＋	47	河村	2才 2月	男	＋	－	＋	＋	＋	－	－
23	岩淵	4才 2月	女	＋	＋	＋	＋	＋	＋	－	48	伊藤	2才 3月	女	＋	－	－	＋	＋	＋	－
24	山添	4才 3月	男	＋	＋	＋	＋	＋	＋	－	49	入之内	2才 7月	男	＋	－	－	＋	＋	＋	＋
25	松本	4才 7月	男	＋	＋	－	＋	＋	＋	－	50	上野	3才 4月	女	＋	－	＋	＋	＋	＋	－

*CLA＝Cervical Lymphadenitis の略

表2　アレルギーの家族歴（50例中46例）

	喘息	蕁麻疹	薬疹	湿疹及びアトピー性皮膚炎	ストロフルス
父方 祖父		1	1		
父方 祖母	2	1			
母方 祖父					
母方 祖母					
父	1	12	3	3	
母		10	3	1	
父の兄妹	1	2			
母の兄妹	1		1		
本人の同胞			1	3	
本人					
乳児期			1	13	
その後					2

表3　年度別及び季節別頻度

	1月	2月	3月	4月	5月	6月	7月	8月	9月	10月	11月	12月	計
昭和36年	1												1
37				1	3	1	2		1		1		9
38	1	2	2	1								1	7
39			1	1		1	1	1	1		1		7
40			1		2	2	1	3	1				10
41	2		2	1		1	4	2	2	2			16
合計	4	2	6	4	5	5	8	6	5	2	2	1	50例

他医の診断（表6の3）

来院前に診察をうけた医師による診断は，その時期によつて，まちまちであるが，病初期では，感冒，頸部淋

Table 1. All 50 cases observed at our institution arranged in ascending order of age with a listing of major symptoms, Nos.1 – 33, CLA (+) group; Nos.34 – 50, CLA (+) group*

patient No.	name	age	sex	fever up	cervical lymphadenitis	skin		conjunctivae hyperemia of bulbar	findings of the lips and oral cavity	edematous tumidity of the hands and feet
						eruption	desquamation			
1		4m	M	+	+	+	+	+	+	-
2		6m	M	+	+	+	+	+	+	-
3		8m	M	+	+	+	+	+	+	+
4		8m	M	+	+	+	+	+	+	+
5		8m	M	+	+	-	+	+	+	-
6		11m	M	+	+	+	+	+	+	+
7		1y	F	+	+	+	+	+	+	+
8		1y2m	M	+	+	+	+	+	+	+
9		1y2m	F	+	+	+	+	+	+	+
10		1y7m	F	+	+	-	+	+	+	+
11		1y8m	M	+	+	+	+	+	+	+
12		1y9m	F	+	+	+	+	+	+	+
13		1y10m	M	+	+	+	-	+	+	+
14		1y11m	M	+	+	+	+	+	+	+
15		2y3m	F	+	+	+	+	+	+	-
16		2y10m	M	+	+	+	+	+	+	+
17		3y3m	F	+	+	+	+	+	+	+
18		3y4m	F	+	+	+	+	+	+	-
19		3y6m	F	+	+	+	+	+	+	-
20		3y7m	M	+	+	+	+	+	+	-
21		3y9m	F	+	+	+	+	+	+	+
22		4y1m	F	+	+	+	+	+	+	+
23		4y2m	F	+	+	+	+	+	+	-
24		4y3m	M	+	+	+	+	+	+	-
25		4y7m	M	+	+	-	+	+	+	-

patient No.	name	age	sex	fever up	cervical lymphadenitis	skin		conjunctivae hyperemia of bulbar	findings of the lips and oral cavity	edematous tumidity of the hands and feet
						eruption	desquamation			
26		5y1m	M	+	+	+	+	+	+	-
27		5y8m	F	+	+	+	+	+	+	-
28		5y10m	M	+	+	+	+	+	+	-
29		6y4m	F	+	+	-	+	+	+	-
30		6y9m	M	+	+	+	+	+	+	-
31		7y1m	F	+	+	+	+	+	+	-
32		8y7m	M	+	+	+	+	+	+	-
33		9y1m	M	+	+	+	+	+	+	-
34		2m	M	+	-	+	+	+	+	-
35		3m	F	+	-	-	+	+	+	-
36		6m	M	+	-	+	+	+	+	+
37		7m	M	+	-	+	+	-	+	+
38		8m	M	+	-	+	+	+	+	-
39		9m	M	+	-	+	+	+	+	-
40		11m	M	+	-	+	+	+	-	-
41		11m	M	+	-	+	+	+	+	-
42		1y3m	M	+	-	+	+	+	+	+
43		1y5m	M	+	-	+	+	+	+	+
44		1y7m	M	+	-	+	+	+	+	+
45		1y10m	M	+	-	+	+	+	+	-
46		1y11m	M	+	-	+	+	+	+	+
47		2y2m	M	+	-	+	+	+	-	-
48		2y3m	F	+	-	-	+	+	+	-
49		2y7m	M	+	-	-	+	+	+	+
50		3y4m	F	+	-	+	+	+	+	-

*CLA=Cervical Lymphadenitis

Table 2. Family history of allergy (46 of 50 cases)

		asthma	urticaria	drug eruption	eczema & atopic dermatitis	strophulus
Paternal	Grandfather		1	1		
	Grandmother	2	1			
Maternal	Grandfather					
	Grandmother					
Father		1	12	3	3	
Mother			10	3	1	
Father's siblings		1	2			
Mother's siblings		1		1		
Patient's siblings				1	3	
Patient						
Infancy				1	13	
Post-infancy						2

Table 3. Occurrence by year and season

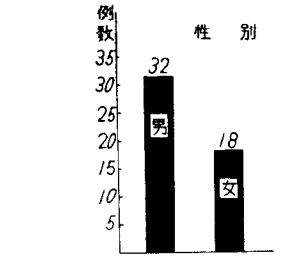
	January	February	March	April	May	June	July	August	September	October	November	December	total
1961	1												1
1962				1	3	1	2		1		1		9
1963	1	2	2	1								1	7
1964			1	1		1	1	1	1		1		7
1965			1		2	2	1	3	1				10
1966	2		2	1		1	4	2	2	2			16
total	4	2	6	4	5	5	8	6	5	2	2	1	50 cases

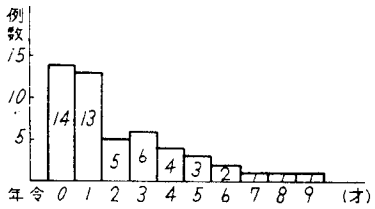
widely. In the early stage, common diagnoses were cold, lymphadenitis, or *Angina* [old term for sore throat]. Later, many were diagnosed as having

表4　年令分布

年令	0才	1	2	3	4	5	6	7	8	9	10	計
CLA(+)群	6	8	2	5	4	3	2	1	1	1	0	33例
CLA(−)群	8	5	3	1	0	0	0	0	0	0	0	17
合　計	14	13	5	6	4	3	2	1	1	1	0	50

表5　性別：男32例　女18例





巴腺炎，アンギーナ等と診断された例が多く，後には，ムンプス，麻疹，猩紅熱，敗血症等と診断された例が多い．

表にかかげた診断名の多様性は，そのまま，本症候群の症状の複雑性を如実に物語つていて興味深い．

入院病日（表6の4）

殆んど第3病日から第9病日の間に入院している．特に第4，5，6病日に集中しているのは，発疹や眼球結膜充血等の主症状が出そろつてくるからであろう．恐らく治療にあたられていた医師が，普通の疾患とは違うと判断されて，我々のもとに紹介下さつたものと思う．

7)　主な臨床症状（表7）

本症候群の主な臨床症状をまとめると表7に示す如くである．以下各症状について詳述する．

イ）発熱（表8～12）

本症候群の最も重要な症状の1つは発熱である．全例に38℃以上41℃に至る高熱が少くとも6日間以上みられた．最高体温は46例（92%）が39℃以上で，38℃代に終始した例は僅か4例にすぎなかつた（表8）.38℃以上の発熱持続期間は殆んど6日から20日迄で大多数は15日以内であつた（表9）.後に治療の項で，各症例毎の熱型を示すが，38℃以下となつても，37℃代の微熱が比較的長く続く例が時々みられた．

入院期間や退院病日は，発熱及びその他の検査所見と密接な関係をもつものであるが，表10の如く，入院期間は大体9日から30日迄であり，退院病日は第16病日から第35病日迄で，それ以上は例外的であつた（表11）.発熱

表6　初発症状，主訴の分析，医師（来院前の）の診断及び入院病日

1)　初発症状

発熱	不機嫌ぐずる	首の痛み	頚部淋巴腺腫脹	咳嗽	咽頭痛	食欲不振	鼻汁鼻閉	吐気嘔吐	腹痛
43例	7（1）	6（4）	4（1）	3（2）	2	2	1	1	1（1）

（　）内は発熱以前に訴えた症状又は認められた症状と症例数（9例）

2)　主訴の分析

発熱	発疹	頚部淋巴腺腫脹	眼が赤い	食欲不振	元気がない歩けない	鼻閉	下痢	嗜眠状
48例	19	11（1）	6	3	1（1）	1	1	1

（　）内は主訴に発熱が含まれなかつた症例（2例）

3)　他医の診断（来院前に診察をうけた医師による）

頚部淋巴腺炎	アンギーナ	麻疹	感冒	猩紅熱	ムンプス	敗血症	風疹	ストロフルス	ピリン疹
12例	6	5	9	3	3	2	2	1	1

薬疹	リウマチ熱	咽頭結膜炎	中耳炎	自家中症毒	腺熱	髄膜炎	アレルギー性疾患	ウイルス性疾患
1	1	1	1	1	1	1	1	1

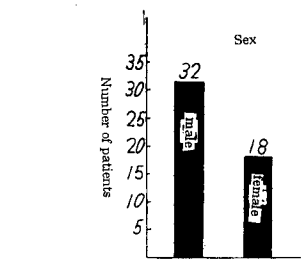
4)　入院病日

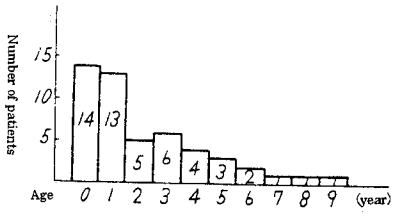
病日	1日	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	計
症例数	0	0	3	11	11	11	4	5	2	0	1	0	0	0	0	2	0	0	50例

Table 4. Age distribution

age	0 y.o.	1	2	3	4	5	6	7	8	9	10	total
CLA(+)	6	8	2	5	4	3	2	1	1	1	0	33 cases
CLA(-)	8	5	3	1	0	0	0	0	0	0	0	17
total	14	13	5	6	1	3	2	1	1	1	0	50

Table 5 Sex: 32 males and 18 females





mumps, measles, scarlet fever, or septicemia.

Variability of diagnoses (as shown in the table) attests to the symptomatic complexity of this syndrome.

First visiting day to the hospital (Table 6-4)

Almost all were admitted to the hospital between days 3 and 9 after the onset. There is a cluster of cases admitted on days 4, 5, and 6, which can probably be explained by the fact that major symptoms, such as skin eruptions and congestion of the bulbar conjunctivae, develop around this time. Perhaps the attending physicians recognized the extraordinary nature of this syndrome then and decided to refer their patients to our department.

7) Major clinical symptoms (Table 7)

The major clinical symptoms of this syndrome, which are described below, are compiled in Table 7.

a) Fever (Tables 8 through 12)

Fever is one of the primary symptoms. All suffered from a high fever that exceeded 38 ℃ (and rose as high as 41 ℃ in some) and persisted for 6 days or longer. For 46 cases (92%), the maximum temperature exceeded 39 ℃: only 4 cases had a maximum temperature that remained in the 38s ℃ (Table 8). The duration of this febrile state with a temperature exceeding 38 ℃ ranged from 6 to 20 days; but for most, it was 15 days or less (Table 9). The fever pattern for individuals is described in the section entitled "Treatment." Occasionally there were patients whose temperatures declined below 38 ℃ but thereafter suffered from a lingering low-grade fever around 37 ℃ for a relatively long period.

The length of stay at the hospital and timing of discharge are closely related to the fever and results of various laboratory tests. As shown in Table 10, the length of stay generally ranges from 9 to 30 days, and timing of discharge, from days 16 to 35 after the onset with a few exceptional cases of longer hospital stays. (Table 11). It was suspected that the duration of fever might be largely affected by the therapy given, especially administration of adrenal cortical hormones. To resolve this, comparison was made between those who had and had not been treated with these hormones (22 and 28 cases, respectively). There was no major difference in fever duration between these two goups (Table 9). However,

Table 6. Symptoms at onset, analysis of major complaints, diagnosis by local physicians, and the days of illness at hospitalization

1) Symptoms at onset

fever	irritable mood	neck pain	swollen cervical lymph node	cough	sore throat	anorexia	rhinorrhea/ nasal obstruction	nausea vomiting	stomach ache
43 cases	7(1)	6(4)	4(1)	3(2)	2	2	1	1	1(1)

Numbers in parentheses are numbers of symptoms reported or noticed before the fever.

2) Analyses of main complaints

fever	eruption	swollen cervical lymph node	bloodshot eyes	anorexia	lethargy/ inability to walk	nasal obstruction	diarrhea	drowsiness
48 cases	19	11(1)	6	3	1(1)	1	1	1

Numbers in parentheses are numbers of cases without fever.

3) Diagnosis by local physicians (given prior to hospitalization)

cervical lymphadenilis	angina	measles	common cold	scarlet fever	mumps	septicemia	rubella	strophulus	eruption caused by aspirin
12 cases	6	5	9	3	3	2	2	1	1

drug eruption	rheumatic fever	pharyngo-conjunctival fever	otitis media	auto intoxication	glandular fever	meningitis	allergic disease	viral disease
1	1	1	1	1	1	1	1	1

4) The days of illness at hospitalization

day of illness	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	total
No. of cases	0	0	3	11	11	11	4	5	2	0	1	0	0	0	0	2	0	0	50 cases

表7　主な臨床症状

1)	発熱(38℃以上)が6日間以上持続	50例（100%）
2)	頸部淋巴腺腫脹（拇指頭大以上）	33例（66%）
3)	両側眼球結膜充血	49例（98%）
4)	皮膚の紅斑様発疹	43例（86%）
5)	両手，足の血管神経性浮腫様腫脹	22例（44%）
6)	口唇糜爛，皸裂，口腔粘膜瀰蔓性充血，時に苺舌	48例（96%）
7)	指，趾の爪皮膚移行部よりの膜様落屑	49例（98%）

表8　最高体温と例数

体温	40℃以上	39℃以上	38℃以上	計
例数	22	24	4	50例

但し，2才以下は肛門検温（入院中）

期間は治療，特に副腎皮質ホルモンの使用如何に影響されることが，大きいのではないかと考えて皮質ホルモン使用例（22例）と，不使用例（28例）とを比較したところ，両者間に大差はなかつた（表9）.然し乍ら，皮質ホ

表9　発熱持続期間（38℃以上）及び皮質ホルモン使用例と不使用例との比較

有熱期間	6日	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	31	計
皮質ホルモン使用例	3	1	5	5	1	2	1	0	1	0	0	1	1	0	0	0	1	22例
皮質ホルモン不使用例	2	5	4	7	3	2	2	1	0	1	0	0	0	0	1	0	0	28例
合計	5	6	9	12	4	4	3	1	1	1	0	1	1	0	1	0	1	50例

表10　入院期間（日数）と症例数

入院期間	6日	9	11	12	13	14	15	16	17	18	19	20	21	24	25	26	27	28	29	36	38	81	計
症例数	1	2	2	1	4	2	3	3	4	3	2	3	8	2	2	1	1	1	1	2	1	1	50例
合計	12例						26例							7例					5例				50例

表11　退院病日と症例数

退院病日	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	32	33	34	40	41	53	88	計
症例数	2	2	1	6	5	2	6	2	5	2	3	2	0	2	2	2	1	1	1	1	1	1	50例
合計	18例						20例							12例									50例

表12　二相性発熱例（8例）

No.	症例	年令	第一次下熱	第二次発熱（病日）	第三次発熱（病日）	退院病日	備考
1	松○	10月	第12病日	18, 19病日（39代）	23, 27病日（38代）	40病日	肛門検温，ステロイド使用
2	石○	1才6月	9	11, 12, 13, 14（38～39代）		18	腋窩検温，「ス」使用
3	森○	3月	11	23より32病日迄（37.5～38.2℃）		32	肛門検温，「ス」使用
4	田○井	3才6月	7	12, 13, 14, 15, 16, 17（38～39℃）		32	腋窩検温，「ス」使用
5	佐○	11月	8	13, 14, 15, 16, 17（38～37℃）	22, 23, 24, 25（37.8～37.9℃）	26	肛門検温，「ス」使用
6	錦○	1才10月	6	14, 15, 16（38代）	20, 21, 22, 23（39代）*	25	肛門検温，「ス」不使用 * 中耳炎
7	柳○	1才11月	11	23, 24, 25（38代）		30	肛門検温，「ス」不使用
8	伊○	2才3月	9	12, 13, 14, 15, 16（38～39代）		21	腋窩検温，「ス」不使用

Table 7. Main clinical symptoms

1) Fever: high fever (over 38.0℃) lasting over 6 days	50 cases (100%)
2) Swollen cervical lymph node (thumb-tip sized)	33 cases (66%)
3) Hyperemia of bulbar conjunctivæ of both eyes	49 cases (98%)
4) Erythematous eruption of the skin	43 cases (86%)
5) Angioneurotic edema-like condition of the hands and feet	22 cases (44%)
6) Erosive cracked lips and diffuse hyperemia of the oral mucosa with occasional strawberry tongue	48 cases (96%)
7) Membranous desquamation of the nail-skin junctions of the fingers and toes	49 cases (98%)

Table 8. Maximum body temperature and the number of cases

Body temperature	40℃+	39℃+	38℃+	total
No. of cases	22	24	4	50 cases

Anal temperature was recorded for those under 2 years of age (during hospitalization)

occasionally adrenal cortex hormones has been observed to produce dramatic improvements in fever and other clinical symptoms. Thus,one cannot judge the efficacy of these hormones on this syndrome

Table 9. Duration of fever (over 38°C) and a comparison of cases treated or not treated with adrenal cortical hormones

duration of fever	6 days	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	31	totla
with adrenal cortical hormone	3	1	5	5	1	2	1	0	1	0	0	1	1	0	0	0	1	22 cases
without adrenal cortical hormone	2	5	4	7	3	2	2	1	0	1	0	0	0	0	1	0	0	28 cases
total	5	6	9	12	4	4	3	1	1	1	0	1	1	0	1	0	1	50 cases

Table 10. Duration (days) of hospital stay and the number of patients

duration of hospitalization	6 days	9	11	12	13	14	15	16	17	18	19	20	21	24	25	26	27	28	29	36	38	81	total
No. of cases	1	2	2	1	4	2	3	3	4	3	2	3	8	2	2	1	1	1	1	2	1	1	50 cases
total	12 cases						26 cases							7 cases					5 cases				50 cases

Table 11. Day of illness at discharge and the number of patients

day of illness at discharge	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	32	33	34	40	41	53	88	total
No. of patients	2	2	1	6	5	2	6	2	5	2	3	2	0	2	2	2	1	1	1	1	1	1	50 cases
total	18 cases						20 cases							12 case									50 cases

Table 12. Cases with bi-phasic fever (8 cases)

No.	tient N	age	primary decline of fever	secondary onset of fever (days of illness)	tertiary onset of fever (days of illness)	days of illness at discharge	remarks
1	5	10m	12 days of illness	18,19 (39s℃)	23,27 (38s℃)	40 days of illness	anal temperature steroid used
2	12	1y6m	9	11,12,13,14 (38s-39s℃)		18	axillary temperature steroid used
3	35	3m	11	23-32 (37.5-38.2℃)		32	anal temperature steroid used
4	19	3y6m	7	12,13,14,15,16,17 (38s-39s℃)		32	axillary temperature steroid used
5	40	11m	8	13,14,15,16,17 (38s-37s℃)	22,23,24.25 (37.8-37.9℃)	26	anal temperature steroid used
6	45	1y10m	6	14,15,16 (38s℃)	20,21,22,23 (39s℃)*	25	anal temperature steroid not used *otitis media
7	46	1y11m	11	23,24,25 (38s℃)		30	anal temperature steroid not used
8	48	2y3m	9	12,13,14,15,16 (38s-39s℃)		21	axillary temperature steroid not used

ルモンが，発熱及び臨床症状の改善に劇的な効果を示した例を時々経験したので，有熱期間の比較だけで，本症候群に対する皮質ホルモンの效果の良し悪しを論ずることは出来ない．一方この表9は本症候群が，皮質ホルモンの使用なしでも，よく治癒しうることを示している．二次性発熱を伴つた8例をみると（表12),皮質ホルモン使用例がやや多く，亦，二次性発熱時には，発疹とか両側眼球結膜充血等の他の症状を伴うことがなく，単に発熱のみであつた．

熱型の詳細は治療の項の各症例別体温表をみて戴き度い．

ロ）頸部淋巴腺腫脹（表13～18，写真1，4，17）

本症候群に於ける特徴の1つで，深部の頸部淋巴腺が犯され（最も多いのは下顎角の部位で胸鎖乳様筋の下の淋巴腺である),大きさは拇指頭大から鶏卵大又はそれ以上に達し，外部から触知すると硬い腫瘤としてふれ，局所の発赤や熱感が全くないか，あつても僅かで一般に疼痛は強い（表13).亦，しばしば疼痛のために斜頸を認めた．多くは片側であるが，左右差はない（表14).出現病日（表15）は，発病第1，2病日に圧倒的に多く，本症候群と頸部淋巴腺炎との病因的関係を示唆している．消失病日及び持続日数は比較的記載の明らかな例のみについて表にしてみた（表16，17).扨てはじめに本症候群をCLA（＋）群とCLA（－）群とに分けて分類してみたが，その年令分布をみると明らかに両群の間に相異がみられる（表18).即ち，CLA（＋）群33例中2才以下は14例（42.4%）であるのに，CLA（－）群17例中2才以下は13例（76.5%）でCLA（＋）群は年長児に多く，CLA（－）群は比較的年少児に多い傾向がみられた．CLA（－）群でも，小豆大，米粒大，大豆大或は小指頭大以下の淋巴腺を頸部或は他の部位（腋窩，ソケイ部，後頭部等）にふれた例が8例あつたが，CLA（＋）群の如く明瞭ではなかったので，CLA（－）群に一括した．5例に頸部淋巴腺穿刺を行つたが，いずれも内容物を吸引出来ず，針先についた僅かな血液等を培養したが，菌は全く証明出来なかつた．本症候群に於ける頸部淋巴腺炎の特徴は決して化膿しないことである．33例中化膿した例は1例もなかつた．組織学的検査を症例番号No. 1原例，No. 6山本例，No. 26加藤例の3例に実施した．組織学的所見の精細は別項で後述する．この材料の一部を予研芦原博士に依頼し，ウイルス分離を試みて戴いたが，現在迄のところ，如何なるウイルスも分離されていない．この頸部淋巴腺の病理組織学的検査及び病因学的検索（細菌やウイルス分離，蛍光抗体法等）は，重要なので今後共追求して行く予定である．

表13　頸部淋巴腺腫脹の大きさ（入院時）

大きさ	鶏卵大又はそれ以上	チャボ卵大	ウズラ卵大	拇指頭大	計
例数	14例	3	5	11	33例

表14　頸部淋巴腺腫脹の部位

部位	右側	左側	両側	計
例数	13例	13	7	33例

表15　頸部淋巴腺腫脹の出現病日と例数

病日	1日	2	3	4	5	6	7	8	9	10	計
例数	11	10	4	2	4	0	1	1	0	0	33例

表16　頸部淋巴腺腫脹消失時期
（比較時記載の明かなもの）26例

病日	7	8	9	10	11	12	13	14	15	16	17	18	19	20	計
例数	1	1	3	1	1	3	5	5	4	1	1	0	0	0	26例

表17　頸部淋巴腺腫脹持続期間
（比較的明かなもののみ）22例

日数	5	6	7	8	9	10	11	12	13	14	15	16	17	18	計
例数	2	1	0	2	2	4	2	2	3	2	1	1	0	0	22例

表18　頸部淋巴腺腫脹の有無と年令（症例数）

頸部淋巴腺＼年令	0才	1	2	3	4	5	6	7	8	9	10	計
CLA（＋）群	6	8	2	5	4	3	2	1	1	1	0	33例
CLA（－）群	8	5	3	1	0	0	0	0	0	0	0	17例

ハ）両側の眼球結膜充血（表19，写真16，19）

正確には眼球結膜毛細血管拡張と称すべきであろう．写真に示す様に，毛細血管の一本一本が明らかに拡張して相互に区別することが出来る．毛様充血はみられない．眼脂は全くないか，あつても余りひどくはない．眼科的には，“単なる結膜炎とも云えるが，恐らく発疹その他の症状と同じく全身性の血管反応の一部分現象であろう”．との意見であつた（眼科梶部長）．

本症状出現時期は記載の明らかな43例について検べて

simply on the basis of fever duration. From Table 9, it can be seen that this syndrome can be controlled satisfactorily without the aid of these hormones. Among the 8 patients who developed a secondary fever (Table 12), those treated with adrenal cortex hormones slightly outnumbered the others. It should also be noted that the secondary fever was a simple febrile condition not accompanied by other symptoms, such as skin eruptions and bilateral conjunctival injection.

Refer to the temperature chart for each patient in the section entitled "Treatment" for the details in fever types.

b) Swelling of the cervical lymph nodes (Tables 13 through 18, Photos 1, 4, and 17)

One of the symptomatic features of this syndrome is the involvement of the deep-seated cervical lymph nodes (most frequently involved was the one located at the mandibular angle below the sternocleidomastoid muscle). The swelling ranged from the size of the tip of a thumb to a chicken egg or larger and it had the texture of a hard nodule when palpated from outside. It was totally devoid of or minimally accompanied by local redness or heat but was generally associated with exquisite tenderness (Table 13). It was often associated with torticollis due to this tenderness. Many were unilateral but there was no preference for sidedness (Table 14). This swelling occurred on day 1 or 2 in most of the patients (Table 15), suggesting a cause-effect

Table 13. Size of swollen cervical lymph node (at hospital admission)

size	Equal to or larger than hen's egg	Smaller than hen's egg	quail egg size	size of the end of the thumb	Total	total
No. of cases	14 cases	3	5	11		33 cases

Table 14. Site of the swollen cervical lymph node

site	right	left	bilateral	total
No. of patients	13 case	13	7	33 cases

Table 15. Appearance time of cervical lymph node swelling and the number of cases

days of illness	1 day	2	3	4	5	6	7	8	9	10	total
No. of cases	11	10	4	2	4	0	1	1	0	0	33 cases

Table 16. Disappearance time of cervical lymph node swelling

26 cases clearly recorded

dasy of illnsee	7	8	9	10	11	12	13	14	15	16	17	18	19	20	total
No. of cases	1	1	3	1	1	3	5	5	4	1	1	0	0	0	26 cases

Table 17. Duration of cervical lymph node swelling (Only 22 obvious cases)

days	5	6	7	8	9	10	11	12	13	14	15	16	17	18	total
No. of cases	2	1	0	2	2	4	2	2	3	2	1	1	0	0	22 cases

Table 18. Swollen cervical lymph node and age (number of cases)

cervical lymph node	age (year) 0	1	2	3	4	5	6	7	8	9	10	total
CAL(+)	6	8	2	5	4	3	2	1	1	1	0	33 cases
CAL(-)	8	5	3	1	0	0	0	0	0	0	0	17 cases

relationship between this syndrome and cervical lymphadenitis. The day when the swelling disappeared and the duration of the symptom are listed in Tables 16 and 17, based on only the case histories that appeared reliable. The patients were first assigned to either of two groups for analysis: CLA (+) and CLA (-). An obvious difference was noted in the age distributions, i.e., 14 of 33 children (42.4%) in CLA (+) were under 2 years, while 13 of the 17 children (76.5%) in CLA (-) were under 2 years of age (Table 18). Evidently more of those children belonging to the former were older; and the latter group was mostly composed of younger children. Even in the CLA (-) group, however, 8 patients with lymph nodes that were the sizes of red bean, rice grain, soy bean, or even as large as the tip of a little finger. Such small lymph nodes were found not only in the cervical region but also in other areas (e.g., the axilla, inguinal region, and occipital region), and were not as obvious as those found in the CLA (+) group. It was decided, therefore, that these 8 patients belonged to the CLA (-) group. Some cervical lymph nodes had been lanced but attempts to draw the contents of the swelling were unsuccessful. A small amount of blood or other fluid attached to the needle tip was used as a sample to isolate the microorganisms. No bacteria were identified. The characteristic of the cervical lymphadenitis of this syndrome is that it never becomes suppurative. None of the 33 patients developed a purulent condition. Histological examinations were conducted on 3 patients (patient No. 1, patient No. 6, and patient No. 26), the details of which will be introduced in another section. Part of the material used for this study was also used for viral isolation by Dr. Ashihara of the National Institute of Infectious Diseases but no virus has been isolated. The results from the histological study and etiological investigation of the cervical lymph nodes (e.g., viral and bacterial isolation and fluorescent antibody technique) are considered important. We plan to continue this avenue of investigation in the future.

c) Congestion of bilateral bulbar conjunctivae (Table 19 and Photos 16 and 19)

To be precise, the condition should be called capillary dilatation of the bulbar conjunctiva. As shown in the photographs, each capillary is clearly dilated and can be outlined individually. There is no sign of ciliary congestion. The eyes are free of or show very little discharge. And ophthalmologically, "it may be classified as simple conjunctivitis; but like skin eruptions and other symptoms, it is most likely an ocular expression of a phenomenon caused by a systemic vascular reaction." (a comment by Dr. Kaji, Chief of the Department of Ophthalmology).

When 43 cases with fairly accurate clinical descriptions were investigated, this ocular symptom develops around days 3, 4, or 5 after onset in most and disappears toward the end of the 2nd week

表19　両側眼球結膜充血の出現—，消失—，持続日数（明かな例のみ）

出現病日	1日	2	3	4	5	6	7							計
例数	3	6	8	14	9	2	1							43例
消失病日	6日	7	8	9	10	11	12	13	14	15	16	23		計
例数	4	2	7	4	5	5	4	4	5	1	1	1		43例
持続日数	2日	3	4	5	6	7	8	9	10	11	12	22		計
例数	1	5	6	6	4	3	4	3	4	1	1	1		39例

みると，第3，4，5病日に多く，大体第2病週の終り迄に消失する（表19）．その持続日数はまちまちであるが，大多数は10日間以内であつた．この眼症状は本症の診断には欠くことの出来ない重要な所見で50例中49例（98%）にみられた．又偽膜の形成や癒着或は角膜潰瘍等の合併症や後遺症は1例もなかつた．

ニ）発疹（表20～23，写真5，6，7，8，9，10，11，12，18，20，21）

本症候群の発疹は紅斑が主体で，時に麻疹様，風疹様，猩紅熱様，蕁麻疹様，稀に汗疹様を併うことであり，その頻度は表20の如くである．発疹のみられた43例中3例は麻疹様のみ，3例は麻疹様と猩紅熱様のみで，いずれも紅斑様の発疹が伴われていない点は注意を要する．亦表にはないが，両足外側から足背にかけて針先大の小紫斑が散在した乳児2例を経験した．然し所謂紫斑病に見られる様な紫斑を伴つた例は1例もなかつた．亦全く発疹に気付かれなかつた7例はいずれも後述する特異的な指先からの落屑がみられたので，指先の紅斑性病変が存在したことは確実である．発疹の出現病日（表21）は第3～第5病日に多く，第2病週に入つてから，発疹がみられることは，極く例外的と考えてよい．発疹の持続日数（表22）は大部分は1週間以内であるが，僅か1日か，2日で消える例もあるから注意を要する．発疹発現順序は（表23）四肢特に手掌，足蹠の紅斑から始まる場合が，顔首或は胸腹背部より始まる場合より，かなり多く，且手掌，足蹠及び指趾の末端に限られる場合が，しばしばあるから注意して観察する必要がある．時に指の各関節に一致して紅斑がみられることもある．頭髪内に発疹のみられた例も時に認められた．

表20　発疹の性状，頻度及び組合せ

1. E	12例	7. E＋M＋U	3例
2. E＋M	13〃	8. E＋U	2〃
3. E＋M＋S	4〃	9. E＋S＋U＋汗	1〃
4. M	3〃	10. E＋汗	1〃
5. S＋M	3〃	11. NONE	7〃
6. E＋S	1〃		

E：紅斑様
M：麻疹様風疹様
S：猩紅熱様
U：蕁麻疹様
汗：汗疹様

表21　発疹出現病日（記載の明かな例）

病日	1	2	3	4	5	6	7	8	9	10	11	12	13	14	計
例数	4	3	10	10	6	4	2	0	0	0	1	0	0	0	40例

表22　発疹持続日数

日数	1	2	3	4	5	6	7	8	9	10	11	12	13	14	計
例数	4	2	3	2	6	9	6	1	4	1	1	0	1	0	40例

表23　発疹の出現順序

1）四肢特に手掌，足蹠より出現	29例（58%）
2）胸腹背部又は顔，首より出現	14例（28%）
3）無疹例（気付かれなかつた例）	7例（14%）

ホ）両手，両足の血管神経性浮腫様腫脹（写真22～25）

写真にみられる様に，両手，足，特に全指，全趾，両手甲，両手掌，両足背，両足蹠が，所謂“パンパン”に腫れて，しばしば皮膚に光沢がみられ，指圧で圧痕が出来ない点が特徴である．

この所見は全症例50例中22例（44%）にみられた．この22例中，2才以下が17例（77.3%）で圧倒的に年少児に多く，この症状は主として2才以下の乳幼児の症状と云えよう．この所見は手足の紅斑とは必ずしも一致しないので，一応独立した症状として記載したが，その発生病理は或は同じかも知れない．

ヘ）口唇及び口腔粘膜症状（写真1，2，3，17）

写真の様に口唇の乾燥，発赤，糜爛，皺裂，時に出血，血痂がみられ，口腔粘膜は全体に瀰蔓性の著明な充血がみられる．然し乍ら，口唇や口腔粘膜には水疱，偽膜，潰瘍或はアフタ等の形成が殆んどみられない点が特徴と言えよう．亦舌は厚い舌苔を被る時もあるが，その下から苺舌となるか，はじめから乳頭が隆起して苺舌を

Table 19. Onset, disappearance, and duration of bilateral bulbar conjunctivae (Evident cases only)

day of illness at onset	1 day	2	3	4	5	6	7						total
No. of cases	3	6	8	14	9	2	1						43 cases
day of illness at disappearance	6 day	7	8	9	10	11	12	13	14	15	16	23	total
No. of cases	4	2	7	4	5	5	4	4	5	1	1	1	43 cases
duration in days	2 days	3	4	5	6	7	8	9	10	11	12	22	total
No. of cases	1	5	6	6	4	3	4	3	4	1	1	1	39 cases

(Table 19). The duration of the symptom varies but for most, it was 10 days or less. The recognition of this ocular symptom was an absolutely essential part of the diagnosis of this syndrome and was observed in 49 of 50 patients (98%). None of them suffered from sequelae or complications, such as pseudomembrane formation, adhesion, or corneal ulceration.

d) Skin eruptions (Tables 20 to 23, Photos 5 through 12, 18, 20, and 21)

Skin eruptions associated with this syndrome are mostly macular erythema, which is occasionally accomapnied by rashes resembling measles, rubella, scarlet fever, urticaria, and rarely miliaria. The incidence of these skin eruptions is listed in Table 20. Among the 43 patients with skin eruptions,there were 3 patients who developed only morbilliform rash and 3 others with morbilliform and scarlatiniform rashes and not accompanied by erythematous macules. Although not listed in the table, two infants had punctate purple lesions the size of a needle head that were scattered from the lateral side to the back of both legs. However, none exhibited typical purplish

Table 20. Characteristics, frequency and combination of skin eruptions

1 E	12 cases	7 E+M+U	3 cases	E:eryhtematous
2 E+M	13	8 E+U	2	M:Morbilliform
3 E+M+S	4	9 E+S+U	1	S:scarlet-fever-like
4 M	3	+Mil		U:urticaria-like
5 S+M	3	10 E+Mil	1	Mil:miliaria-like
6 E+S	1	11 NONE	7	

Table 21. Date of development of skin eruptions (only cases clearly recorded)

days of illness	1	2	3	4	5	6	7	8	9	10	11	12	13	14	total
No. of cases	4	3	10	10	6	4	2	0	0	0	1	0	0	0	40 cases

Table 22. Duration of skin eruptions (in days)

days	1	2	3	4	5	6	7	8	9	10	11	12	13	14	total
No. of cases	4	2	3	2	6	9	6	1	4	1	1	0	1	0	40 cases

Table 23. Sequence of development of skin eruptions

1) Starting at the extremities, especially palms and soles of feet	29 cases (58%)
2) Starting at the chest, abdomen, and back or face and neck	14 cases (28%)
3) No eruptions (eruption not noticed)	7 cases (14%)

blotches associated with purpura diseases. All of the 7 children who did not exhibit obvious signs of eruptions later developed the specific pattern of desquamation at their fingertips (described later). Therefore it is certain that erythematous lesions existed at the fingertips of these patients. The skin eruptions developed between days 3 and 5 after onset (Table 21): only in exceptional cases did skin conditions develop in the second week. The duration of skin eruptions was one week or less in most (Table 22) but it should be noted with caution that in a few exceptional cases these eruptions come and go in one or two days. The erythematous eruptions started at the extremities, especially the palms and soles, more often than at the neck, face, thorax, abdomen, or back. The conditions may be limited to the palms, soles, or ends of the fingers and toes. Close observation is necessary to find these skin lesions. Erythema may be even limited to the finger joints. The rashes may be rarely limited to the scalp, which are obscured by hair.

As described above, skin eruptions in this syndrome, represented by erythema affecting the hands and feet, are symmetrical on right and left (more specifically, the palms and soles). Because they never form blisters or ulcers, they may be "polymorphic" but not "exudative."

e) Angioneurotic edema-like swelling of both hands and feet (Photos 22 to 25)

As shown in the photos, both hands and feet, especially all ten fingers and toes, the dorsal sides of the hands and feet, palms, and soles, become conspicuously swollen and tense like a drum. Characteristically, the overlying skin becomes lustrous. However, a digital pressure by the examiner on the skin does not leave any indentation.

This symptom was found in 22 of the 50 patients (44%), the majority of whom were infants under two years (17 or 77.3%). It may be concluded that this is a symptom that affects mainly infants under two. The condition does not necessarily coincide with the erythema that also affects the hands and feet, and so this indurative edema was treated as a separate symptom. However, both symptoms may originate from a single pathological process.

f) Symptoms affecting the lips and oral mucosa (Photos 1, 2, 3, and 17)

As indicated in the photos, the lips become dry, erythematous, eroded, and cracked: they may even bleed or become encrusted with dried blood. The entire oral mucosa is affected by diffuse and marked hyperemia. Characteristically, blisters, pseudomembranes, ulcers, or aphtha rarely forms on these lips or oral mucosa. A heavy coating may cover the tongue, under which a strawberry tongue may develop. The papillae become raised from the beginning, assuming the appearance of a strawberry tongue. *Angina* [old term for sore throat] was very rare at admission. (As was previously mentioned, some patients had manifested angina at the outset, according to the attending physicians).

These symptoms affecting the lips and oral mucosa were very frequent [in 48 of 50 patients (96%)]. There is a strong possibility that in addition to an inflammatory process, dehydration may play a role in the development of these symptoms. Other frequent symptoms of the mucosa included nasal

呈する事が多い．腺窩性アンギーナの所見を呈した例は入院時には殆んどみられなかつた（アナムネーゼには病初にアンギーナがあつたとの医師の診断をうけた例数は上述した）．

この口唇，口腔所見は50例中48例（96%）にみられて，頻度の高い所見である．この変化は炎症性の他に，脱水がかなり関与している可能性がある．他の粘膜症状として，鼻カタルを併発していた例がかなり見られたが，正確な症例数は明かでない．肛門や外陰部の皮膚粘膜移行部の変化は，軽いカタル性変化が1～2例に認められた以外，殆んど異常がなかつた．

ト）指趾先の爪皮膚移行部からの膜様落屑（表24，25，写真13，14，15，26，27，28）

表24　指趾の爪皮膚移行部よりの膜様落屑開始病日と症例数

病日		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	計
例数	指先							3	2	4	8	5	6	6	4	3	
	趾先										1	2	1	2	3	4	

病日		16	17	18	19	20	21	22	23	24	25	26	27	28	29	31	計
例数	指先	2			1		1									1	46例
	趾先	2	1	5	5	2			1	1	1						31例

写真にみられる様に非常に特徴的で，指先特に拇指先の爪皮膚移行部にはじめ皺裂が生じ，間もなく膜様に僅かな皮膚の剝離がはじまる．落屑開始の時期は一般に第2病週即ち第7乃至14病日である（表24）．落屑の範囲は次の3通りがみられた．即ち，

1）膜様落屑が指先の末節関節より先端に限られる．

2）指の基部即ち基関節と手掌との境界周辺迄膜様の落屑をみる．

3）手甲，手掌を含む腕関節周辺迄膜様落屑がみられる．

趾及び足の落屑方式は指及び手と大体同じであるが，指先のみで足には落屑のなかつた例もあつた．趾先の落屑開始は指先より一般に遅れる（表25）．手足以外の皮膚

表25　指先と趾先との膜様落屑開始時期の日数差（明かな例のみ）

日数差	同時	1日	2	3	4	5	6	7	8	9	10	11	12	13	14	計
例数	2	1	2	3	5	6	5	3	2			1	1		1	32例

表26　症例毎の主症状出現順序（その1）
症例No. 1—17

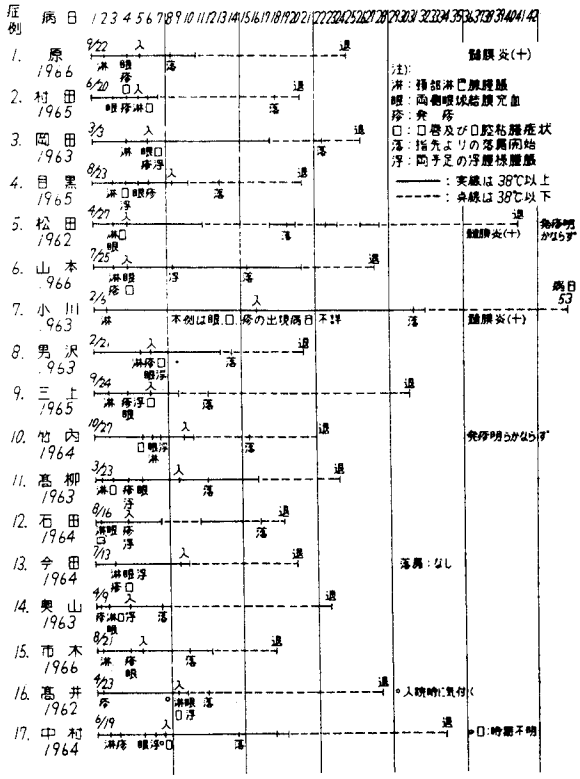
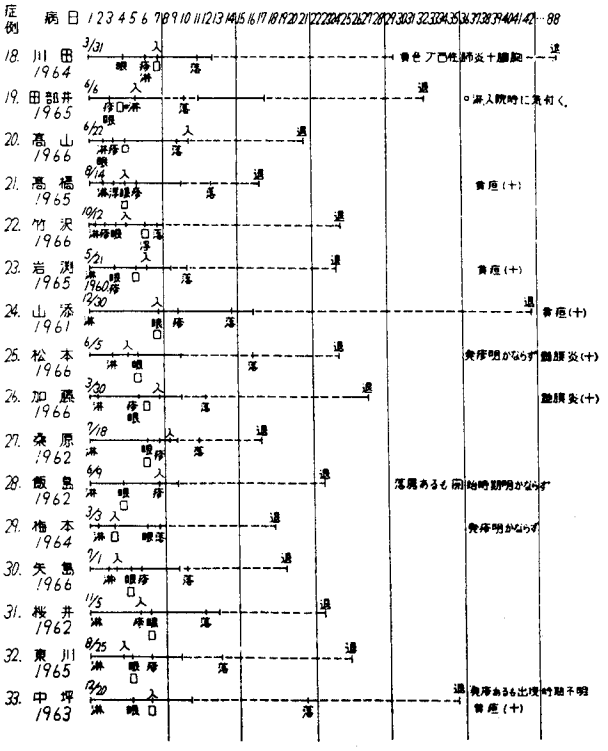


表27　症例毎の主症状出現順序（その2）
症例No. 18—33



catarrh but no accurate measure of their incidence is available. The skin-mucosal junction of the anus or external genitalia almost never showed any changes, except for mild catarrh in one or two cases.

g) Membranous desquamation of the nail-skin junction of the fingers and toes (Tables 24 and 25, Photos 13-15 and 26-28)

As evident in the photographs, the symptom shows a pattern that is unique to this syndrome. Initially, cracks develop at the fingertips, especially at the nail-skin junction of the thumb, shortly followed by gradual membranous dehiscence of a small amount of skin. This desquamation process commonly occurs during the second week (i.e., between days 7 and 14, Table 24). The process progresses in one of the following 3 ways:

Table 24. Date when desquamation started at the nail-skin junctions of the fingers and the number of cases

days of illness		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	total
No. of cases	finger tips							3	2	4	8	5	6	6	4	3	
	toe tips										1	2	1	2	3	4	

days of illness		16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	
No. of cases	finger tips	2			1		1										1	46 cases
	toe tips	2	1	5	5	2			1	1	1							31 cases

1) It is limited to the end of the fingers beyond the distal interphalangeal joint,

2) It extends to the base of the fingers, i.e., the border between the proximal interphalangeal joint and the palm, or

3) It extends to the area around the wrist joint (including the dorsum and palm of the hand).

The manner by which desquamation affects the soles and entire feet corresponds to that for the hands and fingers. There were some cases in which the process only affected the fingertips but not the feet. Desquamation involving the soles usually followed that of the fingertips (Table 25). In addition to the skin of the hands and feet, slight furfuraceous [bran-like] desquamation was noted on the buttocks and other regions. We have not seen a single case of membranous desquamation involving other areas besides hands and feet. It is the unique feature of this symdrome that membranous desquamation is limited to the fingers, ankles, hands, and feet and does not extend beyond the wrist joint. When the desquamation process is limited to the fingertips, in particular, it may be overlooked. It is necessary to examine the patient carefully even after the patient's temperature returns to normal. If one encounters an

Table 25. Duration (days) between the start of hand and foot desquamation (Evident cases only)

duration (days)	same day	1 day	2	3	4	5	6	7	8	9	10	11	12	13	14	total
No. cases	2	1	2	3	5	6	5	3	2			1	1		1	32 cases

Table 26. Sequence of development of major symptoms for each patient (No. 1 of 3) Patient Nos. 1 - 17

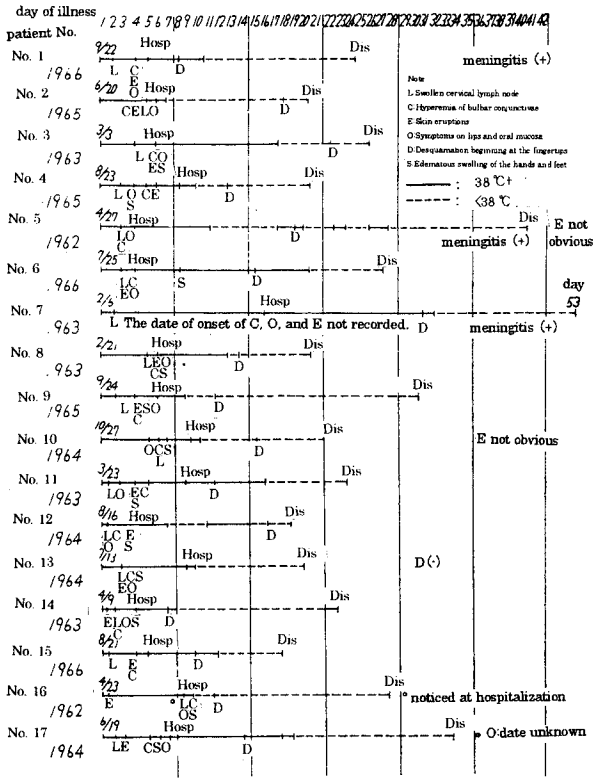
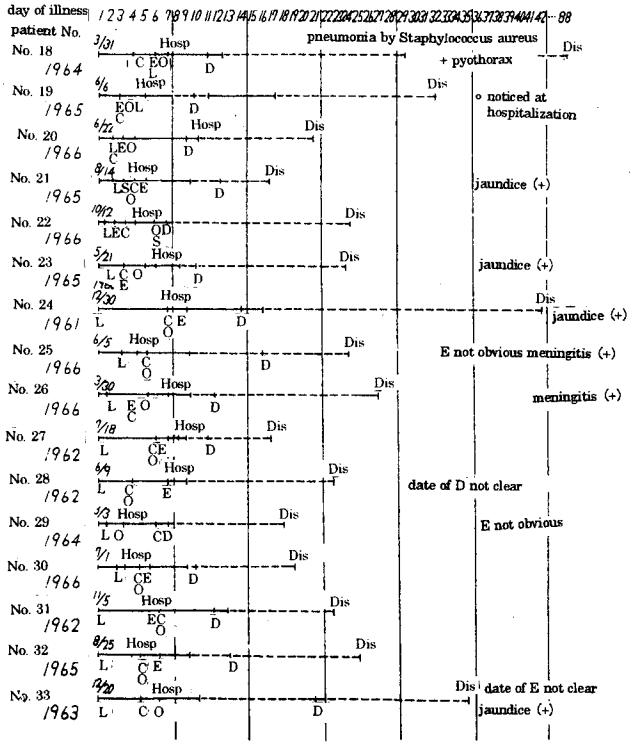


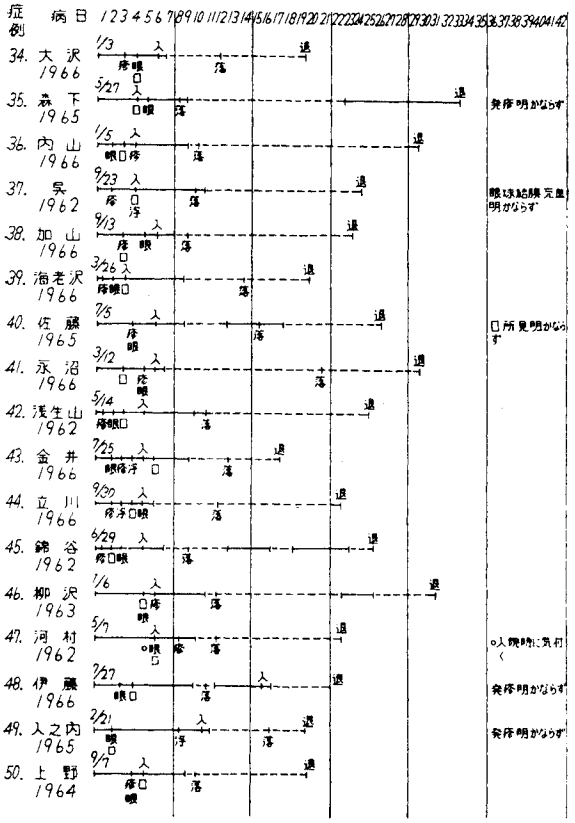
Table 27. Sequence of development of major symptoms for each patient (No. 2 of 3) Patient Nos. 18 - 33



note for Tables 26-28

L: Swollen cervical lymph node C: Hyperemia of bulbar conjunctivae
E: Skin eruptions O: Symptoms on lips and oral mucosa
D: Desquamation beginning at the fingertips
S: Edematous swelling of the hands and feet

表28　症例毎の主症状出現順序（その3）
症例No. 34—50



では粃糖状の落屑が僅かに臀部その他にみることがあるが，膜様に落屑した例は1例もなかつた．即ち，本症候群の膜様落屑は指，趾，手，足に限局し，腕関節より越えない点が特徴的である．特に指先のみの落屑では容易に見落す可能性があるから，下熱後も充分注意して観察する必要がある．この様な落屑様式の小児を下熱後に診察した時は，前述の主症状をよくきき出すことによつて，retrospective に診断することが可能である．

以上7つの主症状はいずれも本症候群には重要な所見であるが，表26，27，28は之等の諸症状発現時期の相互関係を示したものである（頚部淋巴腺腫脹は淋，両側眼球粘膜充血は眼，発疹は疹，口唇，口腔所見は口，落屑は落，手足の浮腫は浮及び38℃以上の発熱は実線——で示した）．一般に淋，眼，疹，口浮及び発熱は第7病日迄に出現し，各々同時に現われることもあるし，多少相互にずれている場合もあつて，一定していない．落屑は大部分が第2病週中（第7～14病日）にはじまり，明かに他の症状とは時期的な差を示している．故に，落屑は恢復期の，他の諸症状は急性期の症候といえよう．

8）特異な症状又は所見を呈した症例

ここでは余り定型的でない症状又は所見を呈した症例について述べる．

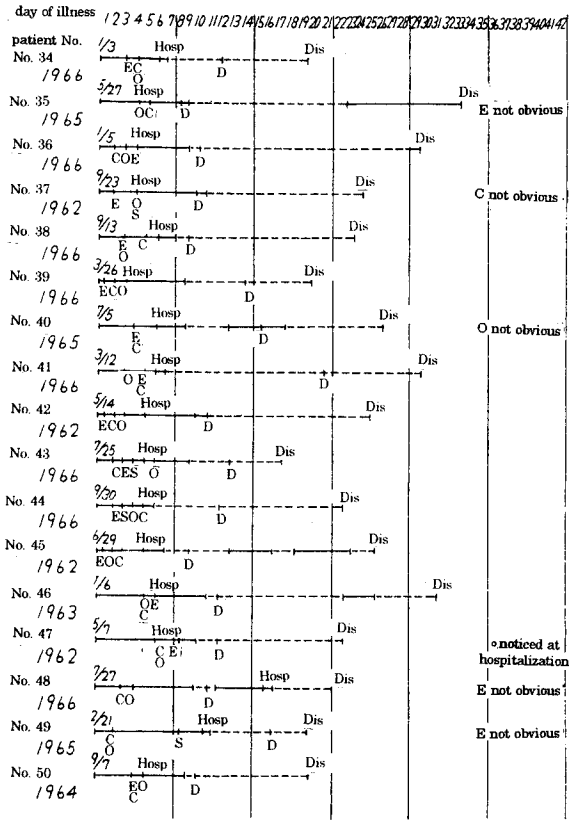
イ）黄疸を認めた症例（4例）表29．

表は各症例の黄疸指数及び肝機能検査の経過を表にしたものであるが（症例番号No. 24山添，No. 33中坪，No. 23岩淵，及びNo. 21高橋），いずれも余り黄疸が高度ではなく，且比較的早く治癒する様であつた．肝機能も

表29　黄疸を伴つた4例の黄疸指数及び肝機能の推移

症例	年令	性別	病日	I.I.	T.B.	DIR.	IND.	高田	TTT	C.C.F.	Gros	SGOT	SGOP	Kunkel
山添	4才3月	男	13	20.0	2.6	1.5	1.1	—	2.8 Mu	±	±			
(1961)			17	26.7	4.8	2.6	2.2	—	4.0 〃	—	+			
			19	20.0	2.8	1.2	1.6	±	3.15〃	+	±			
			27	11.0	1.0	0.3	0.7	—	2.7 〃	±	±			
			33	11.4	1.2	0.4	0.8	—	2.5 〃	—				
			38	8.0				—	2.0 〃	—	—			
中坪	9才1月	男	7	60	8.1	4.7	3.4		1.2 〃	++		54	68	8.4k.u.
(1963)			22	15	1.3	0.3	1.0				—			
岩淵	4才2月	女	8	55	6.0	5.6	0.4		2.0 〃			49		3.0〃
(1965)			11	15	1.3	1.2	0.1							
			15	8	0.8	0.6	0.2		3.0 〃			19		5.0〃
			22	7	0.6	0.2	0.4							
高橋	3才9月	女	5	22				—	1.0 〃					
(1965)			7	25								64	80	4.0〃

Table 28. Sequence of development of major symptoms for each patient (No. 3 of 3) Patient Nos. 34 - 50



afebrile child who presents with this particular pattern of desquamation, detailed inquiries may be made about the aforementioned symptoms, and may arrive at this diagnosis retrospectively.

These 7 major symptoms described above are important in diagnosing this syndrome. Tables 26, 27, and 28 show the interrelations among timing of the development of these symptoms. (In the tables 26-28, the major symptoms are abbreviated as follows: Cervical lymph node swelling (L), congestion of bulbar conjunctivae in both eyes (C), skin eruptions (E), findings of the lips and oral cavity (O), desquamation (D), edema of the hands and feet (S), and fever exceeding 38 ℃ a solid line, respectively.) In general, the symptoms L, C, E, O, S and fever are found by the illness day 7. The appearance times of these symptoms are variable: They may appear simultaneously or more or less sequentially. Desquamation starts mostly during the second week of illness (between days 7 and 14), which is clearly different from the other symptoms. It may be said that desquamation is a symptom of the recovery stage while others appear in the acute stage.

8) Cases with unique symptoms or signs

Atypical symptoms or findings are described below.

a) Patients with jaundice (4 cases): Table 29

The icteric index and the results of liver function tests for each case are shown in this table (patients No.24, 33, 23, and 21). In each case, the jaundice was mild and the patients recovered relatively rapidly. The hepatic functions were not affected severely.

b) Patients with aseptic meningitis (5 cases): Table 30

The table shows the cerebrospinal fluid findings in each patient (patients No.5, 7, 26, 25, and 1)

No. 5 developed a mild pleocytosis, and presented meningitis-like symptoms. He was included in this category. He and the other 4 patients recovered rapidly from menningitic symptoms.

These 9 patients — those with jaundice and meningitis — all belong to the CLA (+) group and none in the CLA (-) group. It was suspected that there may be some etiological difference between these two groups.

Table 29. Icteric index and changes in liver functions for 4 cases with jaundice

patient No.	age	sex	days of illness	I.I.	T.B.	DIR	IND	Takada reaction	TTT	C.C.F.	Gros	SGOT	SGOP	Kunkel
24	4y3m	M	13	20.0	2.6	1.5	1.1	-	2.8 Mu	±	±			
(1961)			17	26.7	4.8	2.6	2.2	-	4.0	-	+			
			19	20.0	2.8	1.2	1.6	±	3.15	+	±			
			27	11.0	1.0	0.3	0.7	-	2.7	±	±			
			33	11.4	1.2	0.4	0.8	-	2.5	-				
			38	8.0				-	2.0	-	-			
33	9y1m	M	7	60	8.1	4.7	3.4		1.2	++		54	68	8.4 k.u.
(1963)			22	15	1.3	0.3	1.0				-			
23	4y2m	F	8	55	6.0	5.6	0.4		2.0			49		3.0
(1965)			11	15	1.3	1.2	0.1							
			15	8	0.8	0.6	0.2		3.0			19		5.0
			22	7	0.6	0.2	0.4							
21	3y9m	F	5	22				-	1.0					
(1965)			7	25								64	80	4.0

余り犯されてない．

ロ）無菌性髄膜炎を伴つた症例（5例）表30

表は各症例のリコール所見の経過を示している（症例番号No. 5松田，No. 7小川，No. 26加藤，No. 25松本及びNo. 1原）

松田例は軽度の細胞増多症をみたのみであるが，臨床的に髄膜炎症状を呈していたので，この分類の中に入れたが，他の4例共々，比較的早く髄膜炎症状は消失している．

表30　無菌性髄膜炎を伴つた5例のリコール所見

症例	年　令	性別	病日	Pandy	Nonne-Apelt	細胞数	糖 mg/dl
松田	8　月	男	5	＋	＋	42／3	59.2
(1962)			7	±		43／3	80.3
小川	1　才	女	17	＋＋	＋	495／3	47.8
(1963)			21	＋		74／3	68.7
			41	＋		38／3	66.1
加藤	5才1月	男	7	＋		254／3	65.3
(1966)			13	＋		25／3	56.6
松本	4才7月	男	6	＋＋	＋	338／3	37.4
(1966)			9	＋	＋	34／3	69.6
			13	＋	＋	34／3	52.2
原	4　月	男	5	＋		248／3	
(1966)			8	＋		82／3	59.2
			22	＋		24／3	

上記の黄疸例と髄膜炎例計9例はいずれもＣＬＡ(＋)群に属し，ＣＬＡ（－）群には1例もない点はＣＬＡ（＋）群とＣＬＡ（－）群との間には，何等かの相異が病因的に存在しているのかも知れない．

ハ）急性中耳炎を伴つた症例

当院耳鼻科に診察を依頼した13例中7例に急性中耳炎の診断をうけたが，いずれも両側の鼓膜充血で，切開しても膿汁はなく，化膿した例は1例もなかつた（当院耳鼻科小倉部長）．

ニ）関節痛を訴えた症例（7例）

症例番号No. 19田部井，No. 21高橋，No. 27桑原，No. 28飯島，No. 49入之内，No. 48伊藤及びNo. 30矢島の7例で，いずれも2才以上であつた．

このうち整形外科的及び　線学的に明かに関節炎と診断された例は1例もなかつた．関節痛はいずれも発熱中の訴えであるので，整外では“熱発に伴う Arthralgie であろう．”との事であったが，本症候群が上述の様に全身性の急性熱性疾患であるから，他の部位と同様に関節にも，一過性の炎症が起ることは当然考えられることである．関節痛とＡＳＬＯ値との関係は，表31の様に関節痛を訴えた7例のうち田部井例及び伊藤例をのぞく他の5例は，いずれも本症候群の一般的なＡＳＬＯ値即ち

表31　関節痛，咽頭分離菌及びＡＳＬＯ値との相互関係

No.	氏　名	年　令	関節痛	咽頭分離菌	ＡＳＬＯ値	検査病日
1	田部井	3才 6月	＋	β溶連菌，緑連菌，ナイセリヤ，黄色ブ菌	12単位—12—12単位	5—16—23病日
2	飯　島	5才10月	＋	β溶連菌，ナイセリヤ．α〃〃〃	333— 250	8—18
3	入之内	2才 7月	＋	ナイセリヤ	2,500— 2,500	12—17
4	桑　原	5才 8月	＋	α溶連菌．ナイセリヤ	50	9
5	高　橋	3才 9月	＋	Staphyl. epidev.	100— 100	3— 9—16
6	伊　藤	2才 3月	＋	ナイセリヤ　緑連菌	12	17
7	矢　島	6才 9月	＋	ナイセリヤ，緑連菌　黄色ブ菌，β溶連菌	50— 166— 125—50	4—11—18—61
8	上　野	3才 4月	—	緑連菌，ナイセリヤ	50— 100	6—12
9	内　山	6　月	—	緑連菌　黄色ブ菌	100—12	6—12
10	中　坪	9才 1月	—	緑連菌	333— 625	7—20—29
11	東　川	8才 7月	—	ナイセリヤ	100— 125	4—14—20
12	梅　本	6才 4月	—	ナイセリヤ　緑連菌	1,250— 2,500	4—10—17
13	高　柳	1才 8月	—	β溶連菌　α〃〃〃．ナイセリヤ	50—12— 125	10—17—28
14	原	4　月	—	緑連菌　ナイセリヤ	50—12	6—22
15	高　山	3才 7月	—	—	100—50	10—17
16	竹　浪	4才 1月	—		50— 166— 100	6—13—24

c) Patients with acute otitis media

Of the 13 patients who were referred to the Otorhinology Department in our hospital, 7 were diagnosed with acute otitis media. All suffered from congestion of the tympanic membrane on both sides, the incision of which yielded no pus. None was found to suffer from suppuration (according to Dr. Ogura, Chief of the Department of Otorhinology).

Table 30. Cerebrospinal fluid findings for 5 cases with aseptic meningitis

patient No.	age	sex	days of illness	Pandy	Nonne-Apelt	cell count	glucose mg/dl
5	8m	M	5	+	+	42/3	59.2
(1962)			7	±		43/3	80.3
7	1y	F	17	++	+	495/3	47.8
(1963)			21	+		74/3	68.7
			41	+		38/3	66.1
26	5y1m	M	7	+		254/3	65.3
(1966)			13	+		25/3	56.6
25	4y7m	M	6	++	+	338/3	37.4
(1966)			9	+	+	34/3	69.6
			13	+	+	34/3	52.2
1	4m	M	5	+		248/3	
(1966)			8	+		82/3	59.2
			22	+		24/3	

d) Patients complaining of arthralgia (7 cases)

They were patients No.19, 21, 27, 28, 49, 48, and 30. All were over 2 years of age.

Based on an orthopedic or histological examination, none were found to be suffering from arthritis. Arthralgia was reported by all during the time when they had a fever and the prevailing opinion of the orthopedic department was that this was "arthralgia secondary to fever." Because this syndrome is an acute systemic febrile condition, as stated earlier, it is likely that the joints, like the other organs, were affected by a transient inflammation. With the exception of patients 1 and 6, 5 of the 7 patients who complained about arthralgia showed ASLO values that were slightly higher than the usual for this syndrome (i.e., 12 units). The significance of this finding is unclear. It has dubious relationship with organisms isolated from pharyngeal swabs, especially hemolytic streptococci.

e) Pneumonia-like image recognized on thoracic radiograms

Patient No. 17 suffered from severe coughing about one week after hospital admission and his chest radiogram indicated a suspicious shadow. No abnormalities were noted in the 28 other patients who received chest radiography.

f) The patient who developed *Staphylococcus aureus*-pneumonia and pyothorax while hospitalized

Patient No. 18 is a monozygotic twin. Her twin sister was completely healthy only this patient was

Table 31. Relationship between arthralgia, pharyngeal isolates, and ASLO level

No.	patient No.	age	arthralgia	pharyngeal isolates	ASLO level	days of illness
1	19	3y6m	+	β-hemolytic streptococci, Streptococcus viridans, Neisseria, Staphylococcus aureus	12 units - 12 - 12 units	5-16-23 dasy
2	28	5y10m	+	β-hemolytic streptococci, Neisseria, α-hemolytic streptococci	333-250	8-18
3	49	2y7m	+	Neisseria	2,500-2,500	12-17
4	27	5y8m	+	α-hemolytic streptococci, Neisseria	50	9
5	21	3y9m	+	Staphylococcus epidermidis	100-100	3-9-16
6	48	2y3m	+	Neisseria, Streptococcus viridans	12	17
7	30	6y9m	+	Neisseria, Streptococcus viridans, Staphylococcus aureus, β-hemolytic streptococci	50-166-125-50	4-11-18-61
8	50	3y4m	-	Streptococcus viridans, Neisseria	50-100	6-12
9	36	6m	-	Streptococcus viridans, Staphylococcus aureus	100-12	6-12
10	33	9y1m	-	Streptococcus viridans	333-625	7-20-29
11	32	8y7m	-	Neisseria	100-125	4-14-20
12	29	6y4m	-	Neisseria, Staphylococcus aureus	1,250-2,500	4-10-17
13	11	1y8m	-	α-hemolytic streptococci, β-hemolytic streptococci, Neisseria	50-12-125	10-17-28
14	1	4m	-	Staphylococcus aureus, Neisseria	50-12	6-22
15	20	3y7m	-	.	100-50	10-17
16	22	4y1m	-		50-166-100	6-13-24

12単位より多小とも高かつたが，その意義は明かでない．亦咽頭分離菌，特に　溶連菌との関係は極めてうすいことが判る．

ホ）胸部レ線像に肺炎様陰影を認めた症例

症例No. 17中林例は入院後約1週間してから咳嗽が強くなり，胸部に陰影を認めた．他に胸部のレ線写真を撮つた28例には何等異常をみなかつた．

ヘ）入院中に黄色ブ菌肺炎及び膿胸を合併した例

症例No. 18川田例は一卵性双生児で，他の1人は全く健康で，患児のみが本症に罹患し入院したが，入院中院内感染により，本症がほぼ全治した頃，黄色ブ菌による肺炎及び膿胸を併発した．この症例の如く，3才4カ月にもなつて，黄色ブ菌性肺炎が院内感染で起つた例は今迄に経験がなく，本症候群による，抵抗力の減弱に因るものと思われる．

ト）自己免疫性溶血性貧血及び黄疸を伴つた例

上述の黄疸例中の症例No. 24山添例は，血沈を実施中室温にも拘らず，血沈棒中で赤血球が凝集して沈降し，血沈値が異常に速進したので，クームス試験を実施したところ直接クームスが陽性であつた（本例の精細は症例の項の第1例ですでに述べた）.そこで本例以降35例にクームス試験を実施したが，1例も陽性がなかつた．

チ）ポールバンネル陽性例

症例番号No. 27桑原例は異種血球凝集反応で高値を認めた（後述）.然し，血液像では単核細胞増多症とは云えなかつた．

リ）脾腫及び心炎合併例

現在迄のところ脾腫を認めた例は1例もなかつた．心電図は表47に示す様に12例に実施したが，症例No. 15市木例に病初PQの延長がみられたが，上述した様に（症例の項第7例），特に皮質ホルモンの使用なしに正常化した．その他の例では著変はなかつた．

ヌ）一卵性双生児にみられた症例（2例）

症例No. 15市木例及びNo. 18川田例は共に一卵性双生児の1人であるが，両例共，患児が本症に罹患して入院したにも拘らず，他の1人は共に全く健康であつた．然し，一卵性双生児の罹病率は，水痘，麻疹，百日咳では非常に高いが，赤痢，ヂフテリヤ，肺炎では比較的低いので[8]，この2例から本症が感染に基づく疾患であることを否定する根拠とはなり得ない．

ル）外陰部及び肛門周囲の皮膚粘膜移行部の変化：

陰嚢或は肛門周囲に紅斑が出来ている例は時に認めたが，尿道口や肛門，亀頭或は女子外陰部の粘膜にアフタ形成，偽膜，水疱或は潰瘍をみた例は1例もなかつたし，口唇に於けるが如き糜爛や皺裂のあつた例も1例も気付かなかつた．然しやや充血乃至は発赤していると感じた例は数例みられた．

要するに本症候群は外陰部や肛門が殆んど犯されない点が特徴である．

4. 検査成績の分析

自験50例についての一般検査所見及び特殊な検査（ウイルス学的並びに皮膚及び頸部淋巴腺の組織学的検査）成績についてまとめてみると次の様である．但し，必ずしもすべての検査がすべての症例に行われてないので各検査毎に症例数を（　）内に記することとした．

1)　血沈（50例（表32）

一般的に相当速進し，入院時すでに最高値に達しているものが多い（最高値1時間50㎜以上が35例70%）.

2)CRP（48例）（表33）

陰性は僅かに2例で46例（95.8%）が2（＋）から10（＋）迄の陽性であつた．CRP陰性化と血沈との関係は追求出来た36例について表34に記した．一般にCRPも血沈も3～4病週中に陰性化又は正常近似値となるが，必らずしも両者は一致していないことがわかる．

3)　ASLO値（49例）（表35）

2回以上検べた症例44例，1回のみ検べた症例5例，計49例で検査しなかつた例は1例にすぎなかつた．このうち2回以上12単位であつたもの31例（63.3%）1回の

表32　血沈1時間値（入院時及び最高時）と症例数

血沈値 / 症例	10以上	20	30	40	50	60	70	80	90	100	110	120	130	140	150	計
入院時	3	6	5	4	7	4	6	6	5	2	1	0	0	0	1	50例
最高時	3	5	5	2	7	4	5	7	5	4	2	0	0	0	1	50〃

表33　CRP（最高値）と症例数

CRP	0	1＋	2	3	4	5	6	7	8	9	10	計
例数	2	0	6	10	8	10	4	5	1	1	1	48例

affected by the syndrome. When the condition was almost completely cleared, she contracted a nosocomial infection and developed Staphylococcus aureus pneumonia and pyothorax. We have not seen a child in this age (3 years and 4 months) develop nosocomial Staph pneumonia before. Perhaps this could be attributed to the fact that her immunological defense system had been weakened by this syndrome.

g) A case with autoimmune hemolytic anemia and jaundice

During the blood sedimentation test for patient No. 24, listed above among those with jaundice, the erythrocytes agglutinated and precipitated even at ambient, with abnormal acceleration of the sedimentation rate. Coombs' test, conducted subsequently, yielded a positive result in the direct test [details of this case are given in the section entitled Case Studies (Case Study 1)]. Since then, Coombs' test was conducted for subsequent 35 patients but none produced a positive result.

h) A case with a positive reaction to the Paul-Bunnell test

Patient No. 27 indicated an exaggerated result in a heterophile hemagglutination test (to be detailed later) but this patient's hemotologic profile was not conclusive for infectious mononucleosis.

i) Cases accompanied by splenomegaly or myocarditis

Splenomegaly was not detected in any of the patients. As shown in Table 47, electrocardiography was conducted for 12 cases. PQ prolongation was recognized in the early stage of the syndrome in patient No. 15; but as described earlier (for Case 7 of the Case Studies), the condition improved without the use of an adrenocortical hormone. No remarkable changes were noted in the other cases.

j) Monozygotic twins developing the syndrome (2 cases)

Patients Nos. 15 and 18 were both monozygotic twins. Both were hospitalized with this syndrome. (Their twin counterparts remained completely healthy.) The incidence of measles, chickenpox, and whooping cough is very high but for dysentery, diphtheria, and pneumonia it is relatively low among monozygotic twins.[8] Therefore, the findings on these two patients do not necessarily go against the infection-based etiology of this syndrome.

k) Changes in the dermal-mucosal junction of the external genitalia and around the anus

Erythema was occasionally found at the external genitalia or the perianal region but none exhibited aphtha, pseudomenbrane, blister, or ulcer formation at the mucosa of the urinary meatus, anus, glans penis, or female external genitalia. Even those cases with erosion or cracking of the lips, changes in the urogenital mucosa were completely absent. However, a slight congestion or erythematous state was found in several.

It was concluded that another characteristic of this syndrome is that the external genitalia or anus are largely spared.

4. Analysis of the laboratory test results

General laboratory tests and specific tests, including histological examinations of the skin and cervical lymph nodes, and virological tests were performed for the 50 cases. The results are discussed below. Numbers in parentheses indicate the number of patients tested.

1) Erythrocyte sedimentation rate (50 cases) (Table 32)

The results show considerable acceleration in general, and often the patients' sedimentation rates were at a peak when they were admitted to our hospital. Thirty-five cases (70%) showed one-hour peak rate of 50+ mm.

2) CRP (48 cases) (Table 33)

Negative results were obtained in only 2 patients. Positive test result ranging from 2 (+) to 10 (+) were shown in 46 cases (95.8%). Thirty six cases were available for longitudinal comparison between CRP and the erythrocyte sedimentation rate. Both test results returned to either negative or nearly normal values within 3 to 4 weeks after the onset. However, the time course of these 2 tests results did not always agree (Table 34).

3) ASLO (49 cases) (Table 35)

Out of the total of 49 cases for whom ASLO

Table 32. Erythrocyte sedimentation rate (one hour, at hospitalization and at the maximum) and the number of cases

	ESR															
cases	10+	20	30	40	50	60	70	80	90	100	110	120	130	140	150	total
at hospitalization	3	6	5	4	7	4	6	6	5	2	1	0	0	0	1	50 cases
maximum level	3	5	5	2	7	4	5	7	5	4	2	0	0	0	1	50 cases

Table 33. CRP (maximum) and the number of cases

CRP	0	1+	2	3	4	5	6	7	8	9	10	total
No. of cases	2	0	6	10	8	10	4	5	1	1	1	48 cases

表34　CRP陰性化と血沈値（1時間値）との関係

症例	病日	CRP	血沈	皮質ホルモン使用の有無	症例	病日	CRP	血沈	皮質ホルモン使用の有無	症例	病日	CRP	血沈	皮質ホルモン使用の有無
松本	4 20	8+ —	61 33	—	東川	4 14	4+ —	61 41	+	今田	9 15	— —	11 8	—
高井	8 23	5+ —	96 12	—	中坪	7 20	5+ —	38 17	—	中村	8 25	5+ —	86 17	+
河村	6 18	4+ —	112 70	—	内山	6 20	4+ —	35 10	—	竹内	10 17	2+ —	29 8	—
浅生山	6 15	2+ —	78 32	+	山本	4 25	9+ —	81 25	—	岩淵	11 22	3+ —	11 14	+
松田	6 23	6+ —	36 20	+	竹浪	6 24	6+ —	64 10	—	村田	9 20	3+ —	84 9	+
岡田	7 21	2+ —	40 15	+	立川	5 20	4+ —	63 9	—	高橋	3 16	3+ —	25 16	+
梅本	4 17	10+ —	107 64	—	飯島	8 16	— —	75 15	—	目黒	8 15	4+ —	30 13	+
川田	7 17	7+ —	58 23	—	錦谷	6 11	2+ —	58 21	—	加藤	7 20	5+ —	94 56	+
上野	6 12	3+ —	36 29	+	柳沢	7 23	3+ —	52 13	—	原	6 22	6+ —	18	—
入之内	12 17	4+ —	108 27	+	男沢	7 19	5+ —	86 26	—	市木	10 17	7+ —	85 20	—
田部井	5 23	3+ —	53 19	+	小川	17 41	5+ —	98 20	+	加山	7 18	6+ —	72 27	—
佐藤	6 17	4+ —	25 18	+	奥山	4 14	2+ —	73 18	—	矢島	4 61	7+ —	58 9	+

表35　ASLO値（12単位以上）14例

氏名	年令	病日	ASLO値	氏名	年令	病日	ASLO値	氏名	年令	病日	ASLO値
入之内	2才 7月	12	2,500単位	竹浪	4才 1月	6	50単位	高橋	3才 9月	3	100単位
		17	2,500〃			13	166〃			9	100〃
梅本	6才 4月	4	1,250〃			24	100〃			16	100〃
		10	2,500〃	原	4月	6	50〃	内山	6月	6	100〃
		17	2,500〃			22	12〃			12	12〃
中坪	9才 1月	7	333〃	桑原	5才 8月	9	50〃	矢島	6才 9月	4	50〃
		20	625〃	東川	8才 7月	4	100〃			11	166〃
		29	625〃			14	100〃			18	125〃
飯島	5才10月	8	333〃			20	125〃			61	50〃
		18	250〃	高柳	1才 8月	10	50〃	高山	3才 7月	10	100〃
上野	3才 4月	6	50〃			17	12〃			17	50〃
		12	166〃			28	125〃				

ASLOを2回以上		ASLO値12単位のみ	
検べた症例	44例	2回以上	31例
1回のみ	5例	1回のみ	4例
検せず	1例		

Table 34. Relationship between conversion of CRP negative and erythrocyte sedimentation rate (1 hour)

patient No.	days of illness	CRP	ESR	use of adrenal cortical hormone	patient No.	days of illness	CRP	ESR	use of adrenal cortical hormone	patient No.	days of illness	CRP	ESR	use of adrenal cortical hormone
25	4	8+	61	-	32	4	4+	61	+	13	9	-	11	-
	20	-	33			14	-	41			15	-	8	
16	8	5+	96	-	33	7	5+	38	-	17	8	5+	86	+
	23	-	12			20	-	17			25	-	17	
47	6	4+	112	-	36	6	4+	35	-	10	10	2+	29	-
	18	-	70			20	-	10			17	-	8	
42	6	2+	78	+	6	4	9+	81	-	23	11	3+	11	+
	15	-	32			25	-	25			22	-	14	
5	6	6+	36	+	22	6	6+	64	-	2	9	3+	84	+
	23	-	20			24	-	10			20	-	9	
3	7	2+	40	+	44	5	4+	63	-	21	3	3+	25	+
	21	-	15			20	-	9			16	-	16	
29	4	10+	107	-	28	8	-	75	-	4	8	4+	30	+
	17	-	64			16	-	15			15	-	13	
18	7	7+	58	-	45	6	2+	58	-	26	7	5+	94	+
	17	-	23			11	-	21			20	-	56	
50	6	3+	36	+	46	7	3+	52	-	1	6	6+		-
	12	-	29			23	-	13			22	-	18	
49	12	4+	108	+	8	7	5+	86	-	15	10	7+	85	-
	17	-	27			19	-	26			17	-	20	
19	5	3+	53	+	7	17	5+	98	+	38	7	6+	72	-
	23	-	19			41	-	20			18	-	27	
40	6	4+	25	+	14	4	2+	73	-	30	4	7+	58	+
	17	-	18			14	-	18			61	-	9	

Table 35. 14 cases with ASLO level exceeding 12 units

patient No.	age	days of illness	ASLO level	patient No.	age	days of illness	ASLO level	patient No.	age	days of illness	ASLO level
49	2y7m	12	2,500 units	22	4y1m	6	50 units	21	3y9m	3	100
		17	2,500			13	166			9	100
29	6y4m	4	1,250			24	100			16	100
		10	2,500	1	4m	6	50	36	6m	6	100
		17	2,500			22	12			12	12
33	9y1m	7	333	27	5y8m	9	50	30	6y9m	4	50
		20	625	32	8y7m	4	100			11	166
		29	625			14	100			18	125
28	5y10m	8	333			20	125			61	50
		18	250	11	1y8m	10	50	20	3y7m	10	100
50	3y4m	6	50			17	12			17	50
		12	166			28	125				

		ASLO of 12 units	
ASLO tested twice or more	44 cases	tested twice or more	31 cases
tested only once	5 casee	tested only once	4 cases
not tested	1 case		

み12単位であつたもの4例，計35例（71.4%）であつた．残りの14例は，程度の差こそあれ，12単位以上を示した（表35）．

このうち250単位以上の値を示したものは，4例で（分類番号No. 49入之内，No. 29梅本，No. 28飯島，No. 33中坪），そのうち前より後のＡＳＬＯ値が上昇していたのは2例（梅本及び中坪例）であつた．No. 50上野，No. 32東川，No. 11高柳，No. 22竹浪及びNo. 30矢島例の5例は Titer は低いが，前より後の血清値が上昇していた．扨て，前述の関節痛を訴えた7例とＡＳＬＯ値が12単位以上を示した14例との相互関係及びそれと咽頭分離菌との関係を前述の表31に示した．表の如く，関節痛，咽頭溶連菌及びＡＳＬＯ値の3者間には必ずしも一致した成績を示さないことがわかる．故に本症候群と溶連菌感染症との関係は一部の例を除いては，一般に余り関係がないと云えよう．

4）咽頭分離菌（42例）表36）

表36　咽頭分離菌（42例）

Neisseria	26例
Viridans	23〃
α. Streptococcus	11〃
Staphylococcus aureus	11〃
β. Streptococcus	7〃
Staphlococcus epidermidis	6〃
Escherichia coli	3〃
Klebsiella	2〃
Candida	2〃
Bazillus pyocyaneus	1〃
Diplococcus pneumoniae	1〃

表の如く Neisseria, Viridans が多く，次で α-Streptococcus, Staphylococcus aureus, β-Streptococcusの順で，上述の如く，特に溶連菌が有意義とは云えなかつた．

5）白血球数（50例）（表37）

一般に白血球増多症の傾向がみられた．亦，2才以下27例中15,000以上が8例（30%）であるのに対して，2才以上23例中15,000以上13例（56.5%）で年長児にその傾向が強い．

6）白血球左方核移動（50例）（表38）

50例中41例（82%）に程度の差こそあれ，左方核移動がみられた．

7）好酸球の消長（50例）（表39）

入院時好酸球は一般に減少傾向がみられ，好酸球増多を示すものは，殆んどみられなかつた．

表37　白血球数（入院時）と年令との関係

白血球数＼年令	0才	1	2	3	4	5	6	7	8	9	症例数
5,000>	5	2	1	0	0	1	0	0	0	0	9
10,000>	4	8	1	2	1	1	1	1	1	0	20
15,000>	3	0	1	1	1	0	1	0	0	0	7
20,000>	2	1	2	2	1	1	0	0	0	0	9
25,000>	0	0	0	1	0	0	0	0	0	0	1
30,000>	0	1	0	0	1	0	0	0	0	1	3
40,000>	0	1	0	0	0	0	0	0	0	0	1
例　数	14	13	5	6	4	3	2	1	1	1	50例

表38　白血球左方核移動

白血球種類	前骨髄球	骨髄球	後骨髄球	桿核10%以上	計
症　例	2	13	13	13	41例

表39　好酸球の消長（%）

症例＼%	0	0.5	1	1.5	2	3	4	5	8	10	計
入院時	19	3	12	1	6	4	2	3	0	0	50例
最高時	6	3	11	0	12	7	4	5	1	1	50例

表40　単球の消長（%）

症例＼%	1	2	2.5	3	4	5	6	7	8	23	計
入院時	7	9	1	9	7	6	7	3	0	1	50例
最高時	0	2	0	8	8	7	12	7	5	1	50例

表41　淋巴球（%）入院時及び最高時（　）内

%＼年令	0才	1	2	3	4	5	6	7	8	9	計
0%		1		1	2				1	1	$6_{(0)}$例
10		1	3	3	1		2	$1_{(1)}$			$11_{(1)}$
20	6	$5_{(1)}$	$1_{(2)}$	$2_{(1)}$		1					$15_{(4)}$
30	$4_{(1)}$	$2_{(2)}$	$1_{(1)}$	$_{(2)}$	$1_{(2)}$	$2_{(1)}$			$_{(1)}$		$10_{(10)}$
40	$1_{(3)}$	$2_{(3)}$	$_{(2)}$			$_{(1)}$					$3_{(9)}$
50	$1_{(5)}$	$1_{(1)}$		$_{(2)}$	$_{(1)}$	$_{(1)}$	$_{(2)}$			$_{(1)}$	$2_{(13)}$
60	$1_{(3)}$	$1_{(6)}$			$_{(1)}$						$2_{(10)}$
70				$_{(1)}$							$_{(1)}$
80	$1_{(2)}$										$1_{(2)}$
計	14例	13	5	6	4	3	2	1	1	1	50例 (50)

results are available, 5 received the test once and 44 received it twice. ASLO value of 12 was noted in 33 of 44 (63.3%) in the first group and 4 in the second group of patients. Or 35 of the 49 total cases (71.4%). The remaining 14 patients showed ASLO values in excess of 12 units (Table 35).

Among these 14 patients, 4 cases (patient Nos. 49, 29, 28 and 33) showed levels above 250 units. For patients Nos. 29 and 33, ASLO values rose with time. Even though they had lower titers, patients Nos. 50, 32, 11, 22 and 30 also showed similar trends. Table 31 shows relationships among the 7 patients who complained of joint pain, the 14 who exhibited ASLO over 12 units, and the pharyngeal bacterial isolates. As indicated in the table, there were no apparent correlations among these 3 variables. Thus, we conclude that, in most cases, there is no clear relationship between this syndrome and hemolytic streptococcus infections.

4) Strains isolated from patients' pharynx (42 cases) (Table 36)

Table 36. Pharyngeal isolates (42 cases)

Neisseria	26 cases
Viridans	23
α. Streptococcus	11
Staphylococcus aureus	11
β. Streptococcus	7
Staphylococcus epidermidis	6
Escherichia coli	3
Klebsiella	2
Candida	2
Bazillus pyocyaneus	1
Diplococcus pneumoniae	1

As indicated in the table, Neisseria and Streptococcus viridans were isolated most frequently, followed by α-Streptococcus, Staphylococcus aureus and β-Streptococcus. The presence of hemolytic streptococcus was not significant.

5) Leukocyte count (50 cases)(Table 37)

In general, leukocytosis was one of the major findings. This applies more to older children: 13 of 23 cases (56.5%) over the 2 years of age in contrast to 8 of 27 cases (30%) under 2 years had leukocyte counts exceeding 15,000 .

6) Leukocyte nuclear shift to the left in differential count (50 cases) (Table 38)

Although there were differences in degree, 41 of 50 cases (82%) showed a shift to the left.

7) Eosinophil count (50 cases) (Table 39)

Generally, the eosinophil count tended to decline during admission and a few showed increase in eosinophils.

8) Monocyte count (50 cases) (Table 40)

The monocyte count tended to be either normal or slightly increased.

9) Lymphocyte count (50 cases) (Table 41)

Generally, lymphopenia was observed at the time of admission, and the count tended to become normal in the course of recovery. The table shows numbers of patients subdivided according to age (in years) and

Table 37. Relationship between leukocyte count (at hospitalization) and age

leukocyte count	age 0 y	1	2	3	4	5	6	7	8	9	No. of cases
5,000+	5	2	1	0	0	1	0	0	0	0	9
10,000+	4	8	1	2	1	1	1	1	1	0	20
15,000+	3	0	1	1	1	0	1	0	0	0	7
20,000+	2	1	2	2	1	1	0	0	0	0	9
25,000+	0	0	0	1	0	0	0	0	0	0	1
30,000+	0	1	0	0	1	0	0	0	0	1	3
40,000+	0	1	0	0	0	0	0	0	0	0	1
total	14	13	5	6	4	3	2	1	1	1	50 cases

Table 38. Leukocyte nuclear shift to the left

leukocyte type	promyelocytes	myelocytes	metamyelocyte	10+% rod nuclei	total
No. of cases	2	13	13	13	41 cases

Table 39. Changes in eosinophil count (%)

cases	% 0	0.5	1	1.5	2	3	4	5	8	10	total
at hospitalization	19	3	12	1	6	4	2	3	0	0	50 cases
at maximum	6	3	11	0	12	7	4	5	1	1	50 cases

Table 40. Changes in monocyte count (%)

cases	% 1	2	2.5	3	4	5	6	7	8	23	total
at hospitalization	7	9	1	9	7	6	7	3	0	1	50 cases
at maximum	0	2	0	8	8	7	12	7	5	1	50 cases

Table 41. Lymphocyte count (%) at hospitalization and maximum (in parentheses)

	age 0 year	1	2	3	4	5	6	7	8	9	total
0%		1		1	2				1	1	6(0) cases
10		1	3	3	1		2	1(1)			11(1)
20	6	5(1)	1(2)	2(1)		1					15(4)
30	4(1)	2(2)	1(1)	(2)	1(2)	2(1)			(1)		10(10)
40	1(3)	2(3)	(2)			(1)					3(9)
50	1(5)	1(1)		(2)	(1)	(1)	(2)			(1)	2(13)
60	1(3)	1(6)			(1)						2(10)
70				(1)							(1)
80	1(2)										1(2)
total	14 cases	13	5	6	4	3	2	1	1	1	50(50) cases

表42　ポールバンネル成績（熊谷氏変法による凝集価）　0.5%羊血球使用

		7×		14×	28×	56×	112〃	224×	448×	計
		−	+							
モルモット腎	前	1	1	2	10	18	3	0	1*	36例
臓にて吸収	後	27	7	0	1	0	1*	0	0	36例

*　陽性例

表43　Tiselius（20例）

T. P.	4.5 ～ 5.0	5.1 ～ 5.5	5.6 ～ 6.0	6.1 ～ 6.5	6.6 ～ 7.0						計
	1	6	3	6	4						20例
Al.	30～39	40～49	50～59	60～69	70～79						計
	0	2	14	4	0						20例
α-Gl.	7.0 ～ 7.9	8 ～ 8.9	9 ～ 9.9	10 ～10.9	11 ～11.9	13 ～13.9	15 ～15.9	16 ～16.9	21 ～21.9		計
	1	2	3	5	3	1	2	2	1		20例
β-Gl.	8 ～ 8.9	9 ～ 9.9	10 ～10.9	11 ～11.9	12 ～12.9	13 ～13.9	14 ～14.9	15 ～15.9	16 ～16.9		計
	1	1	5	0	6	1	4	0	2		20例
γ-Gl.	13.0 ～13.9	16.0 ～16.9	17 ～17.9	18 ～18.9	19 ～19.9	20 ～20.9	21 ～21.9	22 ～22.9	24 ～24.9	26 ～26.9	29 ～29.9	計
	1	1	1	2	2	3	4	2	1	2	1	20例

8)　単球の消長（50例）（表40）

単球は正常か，むしろやや増多の傾向がみられた．

9)　淋巴球の消長（50例（表41）

入院時には一般に淋巴球減少傾向がみられるが，改復期には正常化する様である．表は年令別に淋巴球の(%)を入院時及び最高時〔（　）内〕について示したものである．

10)　クームス試験（35例）

35例に実施したが，前述のNo. 24山添例のみが，直接クームス陽性で，他はいずれも陰性であつた．

11)　ポールバンネル試験（36例）（表42）

No. 27桑原例はモルモツト腎臓吸収前に 448倍で，吸収後も 112倍であり，陽性と判定された．他の35例はいずれも陰性であつた．

12)　寒冷凝集反応（24例）

いずれも16倍以下で陰性であつた．

13)　全血培養（12例）

全例陰性であつたが，多くは抗生物質使用中の培養である点を充分考慮する必要があろう．

14)　検尿（39例）

入院時39例中22例（56.4%）が蛋白陽性で，恐らく熱性蛋白尿であろう．沈渣では明かに腎炎或は腎盂炎を疑わせる程著明な変化を伴つた例は1例もなかつた．

15)　Tiselius（20例）（表43）

表の如く，22%以上の γ-Gl 値を示したもの6例（30

表44　Ra. Test CRP, ASLO　（10例）

氏　名	病日	Ra. T	CRP	ASLO
高　橋	16	弱陽性	−	100単位
竹　浪	6	弱陽性	6+	50
	13	−	1+	166
矢　島	18	陽　性	4+	125
	61	陽　性	−	50
田部井	16	−	4+	12
加　藤	20	−	−	12
原	6	−	6+	50
市　木	5	−	−	12
立　川	5	−	4+	12
海老沢	12	−	1+	12
伊　藤	17	−	5+	12

Table 42. Results of Paul-Bunnel test (agglutination according to the modified Kumagaya's method), using 0.5% sheep erythrocytes

		7x		14x	28x	56x	112x	224x	448x	total
		-	+							
absorbed by a guinea pig kidney	pre	1	1	2	10	18	3	0	1*	36 cases
	post	27	7	0	1	0	1*	0	0	36 cases

*:positive

table 43. Tiselius (20 cases)

T.P.	4.5-5.0	5.1-5.5	5.6-6.0	6.1-6.5	6.6-7.0						total
	1	6	3	6	4						20 cases
Al.	30-39	40-49	50-59	60-69	70-79						total
	0	2	14	4	0						20 cases
α-Gl.	7.0-7.9	8-8.9	9-9.9	10-10.9	11-11.9	13-13.9	15-15.9	16-16.9	21-21.9		total
	1	2	3	5	3	1	2	2	1		20 cases
β-Gl.	8-8.9	9-9.9	10-10.9	11-11.9	12-12.9	13-13.9	14-14.9	15-15.9	16-16.9		total
	1	1	5	0	6	1	4	0	2		20 cases
γ-Gl.	13.0-13.9	16.0-16.9	17-17.9	18-18.9	19-19.9	20-20.9	21-21.9	22-22.9	24-24.9	26-26.9	29-29.9	total
	1	1	1	2	2	3	4	2	1	2	1	20 cases

lymphocyte count (%) at the time of admission and at the peak of lymphocyte count [numbers shown in parentheses].

10) Coombs' test (35 cases)

This test was performed in 35 cases. Only one patient, patient No. 24, had a positive result. All others were negative.

11) Paul-Bunnell test (36 cases) (Table 42)

Case No. 27 was considered positive because of agglutination at 1:448 before absorption by guinea pig kidney cells, and 1:112 after the absortption. The other 35 cases were negative.

12) Cold agglutination (24 cases)

All cases were negative, with the values being less than 1:16.

13) Whole blood culture (12 cases)

All samples showed negative results. However, consideration should be given to the fact that most of the cases were under treatment with antibiotic(s).

14) Urinalysis (39 cases)

Of 39 cases, 22 (56.4%) showed proteinuria while in our hospital, which may be interpreted as non-specific febrile albuminuria. As to the sediment examinations not one patient showed enough finding to support nephritis or pyelonephritis.

15) Tiselius test [protein electrophoresis](20 cases) (Table 43)

As seen in the table, there were 6 cases (30%) with γ-Gl fraction equal to or greater than 22%.

16) Ra. Test (10 cases) (Table 44)

Patinet Nos. 21, 22 and 30 showed either positive or weakly positive reactions. In Table 44, the relationships among CRP, ASLO, and the time we examined Ra. T on each patient are shown.

17) LE phenomenon (4 cases) (Table 45)

Patient Nos. 30 (on the 7th day after onset), 22 (15th day), 43 (15th day) and 6 (10th day) were

Table 44. Ra Test, CRP, and ASLO (10 cases)

patient No.	days of illness	Ra. T	CRP	ASLO
21	16	slightly positive	-	100 units
22	6	slightly positive	6+	50
	13	-	1+	166
30	18	positive	4+	125
	61	positive	-	50
19	16	-	4+	12
26	20	-	-	12
1	6	-	6+	50
15	5	-	-	12
44	5	-	4+	12
39	12	-	1+	12
48	17	-	5+	12

%）であつた．

16) Ra. Test (10例) (表44)

症例No. 21高橋，No. 22竹浪及びNo. 30矢島例の3例に陽性又は弱陽性がみられた．

表は，Ra. T 検査時の病日及びCRPとASLO値との関係を示したものである．

17) LE現象（4例）(表45)

症例No. 30矢島例（第7病日），No. 22竹浪例（第15病日），No. 43金井例（第15病日）及びNo. 6山本例（第10病日）の計4例にLE細胞の検査を行つたが，いずれも陰性であつた．

表45　LE細胞検査（4例）

症例	病日	LE細胞
矢島	7	(—)
竹浪	15	(—)
金井	15	(—)
山本	10	(—)

表46　黄疸指数とSGOT，SGPT (14例)

氏名	病日	黄疸指数	SGOT	SGPT	備考
高橋	6	25	64	80	黄疸例
中坪	7	60	54	68	〃
岩淵	8	55	49	—	〃
松本	5	8	19	—	
	7	2	33	19	
	10	1	65	40	髄膜炎例
	13		83	59	
	17	1	39	39	
東川	20	3	31	—	
三上	14	3	29	—	
原	6	1	52	44	髄膜炎例
山本	8	2	37	39	
市木	5	3	76	30	
竹浪	6	3	26	24	
加山	7	3	33	18	
	14		56	31	
金井	5	5	138	141	
	10		37	33	
立川	5	2	37	18	
矢島	7	7	84	166	
	11	5	37	44	

18) SGOT，SGPT値 (14例) (表46)

症例番号No. 21高橋，No. 33中坪，No. 23岩淵の3例は，前述した黄疸例であるが，表の如く，黄疸のない症例でも病初に（症例番号No. 1原，No. 15市木，No. 43金井，No. 30矢島例），或は経過中に（No. 25松本，No. 38加山例），SGOT，SGPTの両者又はSGOTのみの一時的の軽度の上昇がみられた．

19) 心電図 (12例) (表47)

表47　心電図 (12例)

氏名	病日	年月日	分類番号 EKG	所見
内山	20	66. 1—24	No. 197	頻脈
加藤	21	66. 4—19	No. 1075	O. B.
東川	20	65. 9—13	No. 2103	O. B.
高橋	9	65. 8—23	No. 1917	O. B.
中坪	24	64. 1—11	No. 54	頻脈
矢島	16	66. 7—16	No. 2118	呼吸性不整脈
市木	17	66. 9— 6	No. 2566	PQ延長
立川	9	66. 10— 8	No. 2884	O. B.
竹浪	15	66. 10—26	No. 3072	呼吸性不整脈
高山	20	66. 7—16	No. 2122	O. B.
伊藤	18	66. 8—13	No. 2369	頻脈
山本	20	66. 8—13	No. 2376	頻脈

症例番号No. 15市木例にPQの延長がみられたが，皮質ホルモン使用せずに経過を観察し，3カ月後の昭和41年12月8日に再検したところ，正常化していた．心音は病初から異常はなかつた．他の11例は特記すべき異常所見は見られなかつた．

20) B.C.G 接種と本症 (表48)

表の如く，カルテから検べ得た本症候群発症前にB.C.G接種をうけた症例は19例でそのうち接種時期の明らかな例は16例であつた．この表から考察すると，本症とB.C.G. との間には余り関係があるとは考えられない．他の予防注射との関係は大部分が接種時期不明のため，明らかでなかつた．

表48　B.C.G接種と発病との関係

	B.C.G接種後													接種したが時期不明	接種したかどうか不明	未接種	計
	1カ月	2	3	5	6	7	9	10	11カ月	1年半	2年	4年					
例数	1	1	1	1	2	2	1	1	1	1	3	1		3	14	17	50 例

examined for the presence of LE cells. All were negative.

18) SGOT and SGPT (14 cases) (Table 46)

Patinet Nos. 21, 33 and 23 were icteric, as noted previously. As indicated in the table, those patients without jaundice also showed mild elevations of both SGOT and SGPT, or transient rise only of SGOT, during the early stage of disease (patinet Nos. 1, 15, 43, and 30) or the middle of the clinical course (patinet Nos. 25 and 38).

19) Electrocardiography (12 cases) (Table 47)

Although P-Q interval prolongation was detected for patinet No. 15, she was not treated with adrenocortical hormones. When she was re-examined 3 months later (December 8,1966). The ECG pattern had been normalized by this time. No abnormal cardiac sounds had been detected since early onset.

Table 45. Test for LE cells (4 cases)

patient No.	days of illness	LE cells
30	7	(-)
22	15	(-)
43	15	(-)
6	10	(-)

Table 46. Icterus index, SGOT, and SGPT (14 cases)

patient No.	days of illness	icterus index	SGOT	SGPT	remarks
21	6	25	64	80	jaundice +
33	7	60	54	68	jaundice +
23	8	55	49		jaundice +
25	5	8	19		meningitis +
	7	2	33	19	
	10	1	65	40	
	13		83	59	
	17	1	39	39	
32	20	3	31		
9	14	3	29		
1	6	1	52	44	meningitis +
6	8	2	37	39	
15	5	3	76	30	
22	6	3	26	24	
38	7	3	33	18	
	14		56	31	
43	5	5	138	141	
	10		37	33	
44	5	2	37	18	
30	7	7	84	166	
	11	5	37	44	

Table 47. Electrocardiographic findings (12 cases)

patient No.	days of illness	date	No.	findings
36	20	01/24/1966	197	tachycardia
26	21	04/19/1966	1075	n.p.
32	20	09/13/1965	2103	n.p.
21	9	08/23/1965	1917	n.p.
33	24	01/11/1964	54	tachycardia
30	16	07/16/1966	2118	respiratory phasic arrhythmia
15	17	09/06/1966	2566	PQ prolongation
44	9	10/08/1966	2884	n.p.
22	15	10/26/1966	3072	respiratory phasic arrhythmia
20	20	07/16/1966	2122	n.p.
48	18	08/13/1966	2369	tachycardia
6	20	08/13/1966	2376	tachycardia

The other 11 patients did not exhibit any remarkable ECG abnormalities.

20) BCG vaccination (Table 48)

As seen in the table, 19 cases were inoculated with BCG prior to onset of this syndrome. In 16 of them, the exact dates of inoculation could be identified. According to the data in this table, there is no correlation between BCG vaccination and the onset of symptoms. Because the patients could not provide us with exact records for other major vaccinations, it was not possible to ascertain the exact relationship of other vaccinations with this syndrome.

21) Virological tests (Tables 49-51)

To isolate the specific viral strains, lymph nodes (patinet No. 26), pharyngeal or nasal swabs, fecal specimens or cerebrospinal fluid samples were collected from 14 patients (patinet Nos. 2, 4, 9, 19,

Table 48. Relationship between B.C.G. vaccination and the disease onset

	after B.C.G. vaccination												vaccination but date unknown	unknown	not yet	total
	1m	2	3	5	6	7	9	10	11	1.5y	2y	4y				
No. of cases	1	1	1	1	2	2	1	1	1	1	3	1	3	14	17	50 cases

表49　ウイルス分離（予研芦原博士に依頼）
1965～1966

症例	採取病日	材料	HeLa	MK	HEL	SM
岩淵	第6病日 5/26	K.T.N	—	—	—	
森下	12. 6/7	K.T.N	—	—	—	
入之内	12. 3/4	K.T.	—	—	—	
田部井	5. 6/10	K.T.	—	—	—	
村田	6. 6/25	K.T.	—	—	—	
佐藤	6. 7/10	K.T.	—	—	—	
海老沢	3. 3/28	K	—	—		—
内山	7. 1/11	K	—	—		—
永沼	7. 3/18	K	—	—		—
三上	8. 10/1	K.T.	—	—		—
目黒	8. 8/30	K	—	—		—
高橋	7. 8/20	K.T.	—	—		—
加藤	7. 4/5	K.L.	—	—		—
東川	6. 8/30	K	—	—		—

注：K（便），T（咽頭ヌグイ液），N（鼻ヌグイ液），L（淋巴腺）．（—）はCPEなしを示す．

表50　CoxA 16 ECHO 11及び Adeno 3に対する補体結合反応

	血清採取年月日	病日	CoxA-16	ECHO11	Adeno 3
内山	Jan 1. 66	7	4<	4<	4<
	Jan 24. 66	20	4<	4<	4<
三上	Oct 1. 65	8	4<	4<	64×
	Oct 20. 65	27	4<	4<	32×
加藤	Apr 4. 66	7	4<	4<	4<
	Apr 22. 66	24	4<	4<	16×
海老沢	Mar28. 66	3	4<	4<	16×
	Apr 11. 66	17	4<	4<	16×
岩淵	May26. 65	6			4<
	Jun 23. 65	34			8×
森下	Jun 7. 65	12			4<
	Jun 25. 65	30			4<
田部井	Jun 6. 65	5			4<
	July 7. 65	35			4<
村田	Jun 25. 65	6			4<
	July 7. 65	18			4<
佐藤	July10. 65	6			4<
	Aug 3. 65	30			4<

（予研芦原博士に依頼）

21）ウイルス学的検査（表49～51）

予研芦原博士に依頼して，症例No. 2，4，9，19，21，23，26，32，35，36，39，40，41，及び49の14例の咽頭又は鼻のヌグイ液，便及び髄液，No. 26加藤例の淋巴腺からのウイルス分離を実施して戴いたが，現在迄のところ，いずれの症例及び材料からもウイルスの分離に成功していない（表49）．

一部の症例につき Coxsackie A 16，ECHO11，及び Adeno 3に対する補体結合反応が行われたが，表50に示す様に Coxsackie A 16及びECHO11はいずれも陰性であつた．Adeno 3は No. 26加藤及び No. 23岩淵の2例に急性期より恢復期の血清抗体価の上昇がみられた．No. 9三上及びNo. 39海老沢の2例は，以前に Adeno 感染症のあつたことを示していた．

近年PPLOと M.C.O.S. との関係が注目されて来たので[9)10)]，伝研中村博士に依頼して，PPLOに対する補体結合反応を5例に実施して戴いたが，表51の如く，いずれも陰性であつた．

以上の成績のうち，一部の血清学的結果から本症候群と Adeno 感染症との関係は，今後共更に追求する必要

表51　PPLOに対する補体結合反応（伝研中村博士による）

	血清	I.V.B.S.	I.N.A.	血清稀釈 1:4	1:8	1:16	1:32	結果
1. 岩淵	急性期	0	0	0+	0	0	0	?
	恢復期	0	0+	3′	0+	0	0	
2. 森下	急性期	0	0	0	0	0	0	陰性
	恢復期	0	0	0	0	0	0	
3. 田部井	急性期	0	0	0	0	0	0	陰性
	恢復期	0	0	0	0	0	0	
4. 村田	急性期	0	0	0	0	0	0	陰性
	恢復期	0	0	0	0	0	0	
5. 三上	急性期	0	0	0	0	0	0	陰性
	恢復期	0	0	0+	0+	0	0	
6. 対照 PPLO患者血清	恢復期	0	0	4	4	4	3	陽性

Table 49. Viral isolation (conducted by Dr. Ashihara of the National Institute of Infectious Diseases)
1965-1966

patient No.	days of illness and date	sample	HeLa	MK	HEL	SM
23	6 05/26	K.T.N.	-	-	-	
35	12 06/07	K.T.N.	-	-	-	
49	12 03/04	K.T.	-	-	-	
19	5 06/10	K.T.	-	-	-	
2	6 06/25	K.T.	-	-	-	
40	6 07/10	K.T.	-	-	-	
39	3 03/28	K	-	-		-
36	7 01/11	K	-	-		-
41	7 03/18	K	-	-		-
9	8 10/01	K.T.	-	-		-
4	8 08/30	K	-	-		-
21	7 08/20	K.T.	-	-		-
26	7 04/05	K.L.	-	-		-
32	6 08/30	K	-	-		-

notice: K (feces), T (pharyngeal swab), N (nasal swab), L (lymph nodes), (-) no CPE

Table 50. Complement fixation reactions with Cox A16, ECHO 11, and adeno 3

	date	days of illness	CoxA-16	ECHO11	Adeno 3
36	01/01/1966	7	4<	4<	4<
	01/24/1966	20	4<	4<	4<
9	10/01/1965	8	4<	4<	64x
	10/20/1965	27	4<	4<	32x
26	04/04/1966	7	4<	4<	4<
	04/22/1966	24	4<	4<	16x
39	03/28/1966	3	4<	4<	16x
	04/11/1966	17	4<	4<	16x
23	05/26/1965	6			4<
	06/23/1965	34			8x
35	06/07/1965	12			4<
	06/25/1965	30			4<
19	06/06/1965	5			4<
	07/07/1965	35			4<
2	06/25/1965	6			4<
	07/07/1965	18			4<
40	07/10/1965	6			4<
	08/03/1965	30			4<

(conducted by Dr. Ashihara, the National Institute of Infectious Diseases)

21, 23, 26, 32, 35, 36, 39, 40, 41 and 49), and sent to Dr. Ashihara of the National Institute of Infectious Diseases. No virus has been recovered from any of the samples thus far (Table 49).

Complement-fixation reaction tests to Coxsackie A 16, ECHO 11 and Adeno 3 were performed on some samples (Table 50). All serum samples that were employed in these tests produced negative results for Coxsackie A 16 and ECHO 11. Samples from patient Nos. 26 and 23 showed higher antibody titers during the convalescence period than in the acute phase, as shown in the table. In addition, the test results for patinet Nos. 9 and 39 revealed past adenovirus infections.

Because of the recent attention given to the relationship between PPLO [Pleuropneumonia-like organisms] and M.C.O.S. [Muco-Cutaneous-Occular Syndromes], serum samples from 5 of our patients were sent to Dr. Nakamura (Institute of Infectious Diseases, University of Tokyo) to test for an additional complement-fixation reaction to PPLO.[9][10] All samples produced negative results as described in Table 51.

These results from serological tests may suggest some correlations between the adenovirus infection and this syndrome; therefore, further research effort is required.

Table 51. Complement fixation reaction with PPLO
(by Dr. Nakamura, the Institute of Infectious Diseases, University of Tokyo)

	patient No.	stage	I.V.B.S.	I.N.A.	ratio of serum dilution				result
					1:04	1:08	1:16	1:32	
1	23	acute	0	0	0+	0	0	0	?
		convalescent	0	0+	3'	0+	0	0	
2	35	acute	0	0	0	0	0	0	negative
		convalescent	0	0	0	0	0	0	
3	19	acute	0	0	0	0	0	0	negative
		convalescent	0	0	0	0	0	0	
4	2	acute	0	0	0	0	0	0	negative
		convalescent	0	0	0	0	0	0	
5	9	acute	0	0	0	0	0	0	negative
		convalescent	0	0	0+	0+	0	0	
6	control serum from PPLO patient	convalescent	0	0	4	4	4	3	positive

表52　皮膚組織学的検査（7例）

氏名	年令	バイオプシー 年月日	病日	バイオプシー 部位	病理番号	麻酔
1. 内山	6月	S41. 1—12	8	右拇指先，左大腿中央	No. 58060	—
2. 永沼	1才	41. 3—18	7	左拇指先，左膝上	No. 59998	—
3. 海老沢	9月	41. 3—28	3	左第一趾先，右膝上	No. 60261	—
4. 加藤	5才 1月	41. 4— 6	8	右足外側	No. 60494	局所麻酔
5. 矢島	6才 9月	41. 7— 5	5	左第二趾先	No. 63058	伝達麻酔
6. 市木	2才 5月	41. 8—26	6	右第三趾先，臀部	No. 64417	—
7. 原	4月	41. 9—27	7	右第一趾先，左膝上	No. 65482	—

があろう．

22）皮膚の組織学的検査（7例）（表52，写真S（1）～S（12））

上述の如く，皮膚の症状は本症候群に於ける重要な所見であるが，特に爪皮膚移行部の指趾先の部分には何か特徴的な変化がありはしなかと考えられたので，他の部位に於ける紅斑性病変の皮膚と同時に生検を行つて比較した（症例No. 36内山，No. 41永沼，No. 39海老沢，No. 15市木，No. 1原の計5例）

症例No. 26加藤例は局所麻酔で生検を行つたが，内山，永沼，海老沢，市木及び原例では，乳幼児であり，且，出来るだけ自然の組織像を得るために，麻酔しないで生検を施行した．症例No. 30矢島例は学童であつたので，伝達麻酔で趾先の生検を行つた．

以上7例の生検日，病日，部位等は表52に示した．各症例毎の組織像は写真No. S 1～S 12に示した．当院病理主任の田中昇博士によれば，本症候群に共通する皮膚の組織的学変化の特徴は，

1）角質層の生理的に厚い指趾先では角質層は剝脱する．

2）指趾先も含めた，その他の皮膚では，全体的に表皮直下の結合織のかなり顕著な浮腫と一部毛細血管の拡張及び軽度の血管周囲の細胞浸潤（特に淋巴球及び単核球）がある．

3）2)の変化は一般に Erythema の病変に類似している．等々であつた（参考文献[11]）．

22）頚部淋巴腺の組織学的検査（3例）（表53，写真（L 1～6）

本症候群に於ける頚部淋巴腺腫脹は，前述の如く，特徴的であるので，組織学的にも何か特殊な変化がありはしないかと考え，当院外科の太中部長及び梶谷博士の御協力で表53に示す3例に頚部淋巴腺摘出術を実施して戴いた．

表53　頚部淋巴腺の組織学的検査（3例）

症例	年令	バイオプシー 年月日	病日	バイオプシー 部位，大きさ	病理番号
加藤	5才1月	41. 4— 6	8	右，米粒大	No. 60459
山本	11ヵ月	41. 7—30	6	右，米粒大	No. 63726
原	4月	41. 9—28	7	左，拇指頭大	No. 65482

症例No. 26加藤及びNo. 6山本例は手術時に頚部淋巴腺がまた拇指頭大以上に腫脹していたが，最も大きな淋巴腺は胸鎖乳様筋の下にあつて，摘出が大変なので，無理をせずに皮下組織内の米粒大の淋巴腺をとり，組織学的検査を依頼した．症例No. 1原例は幸いにも，目的の拇指頭大に腫大した淋巴腺が，胸鎖乳様筋の前方に存在

表54　入院後自然観察例（3例）

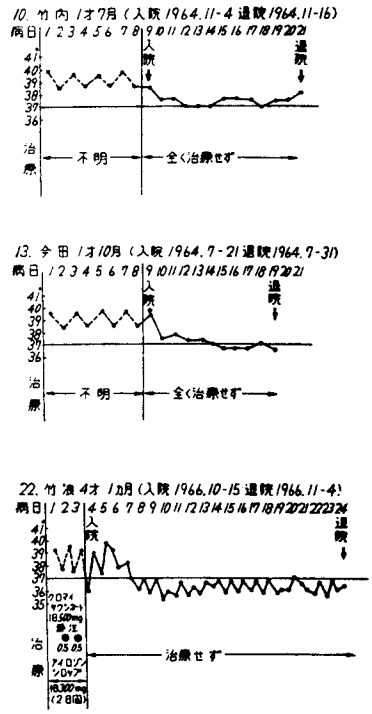


Table 52. Histological examination of the skin (7 cases)

patient No.	age	biopsy date	days of illness	biopsy site	pathological specimen No.	anesthsia
1	36	6m	01/12/1966	8	tip of the right thumb, center of the left thigh	58060	
2	41	1y	03/18/1966	7	tip of the left thumb, upper site of the left knee	59998	
3	39	9m	03/28/1966	3	tip of the left 1st toe, upper site of the right knee	60261	
4	26	5y1m	04/06/1966	8	lateral site of the right foot	60494	local anesthesia
5	30	6y9m	07/05/1966	5	tip of the left 2nd toe	63058	conduction anesthesia
6	15	2y5m	08/26/1966	6	tip of the right 3rd toe, hip	64417	
7	1	4m	09/27/1966	7	tip of the right 1st toe, upper site of the left knee	65482	

22) Histological examination for skin samples (7 cases) (Table 52 and Photo S 1-12)

Dermal manifestation is one of the major findings in this syndrome. Because it was suspected that there might be specific histological patterns at the nail-skin junction of the patients, we conducted biopsies together with samples of other erythematous lesions collected from various parts of the body (patient Nos. 36, 41, 39, 15 and 1).

A skin biopsy sample from patient No. 26 was obtained under local anesthesia, while samples from infants (patient Nos.36, 41, 39, 15 and 1) were collected without using any medication because of their tender age and our preference to observe a natural histological condition as much as possible. patient No.30 was a school-age child and the sample was obtained from a toe under nerve-block anesthesia.

The information concerning sampling is presented in Table 52, as well as images provided in Photos S1 and S12. Dr. Noboru Tanaka, the chief pathologist at our hospital, reported that the dermal manifestations in this syndrome have the following characteristics:

1) Excoriation occurred at the ends of the digits where the corneal layer is naturally thickened.

2) Marked edema was observed in the dermis throughout the affected skin, as well as capillary dilatations and mild perivascular infiltrations (lymphocytes and monocytes in particular).

3) Pathological changes described in 2) that are usually seen in erythema (reference[11]).

22) Histological examinations of samples from cervical lymph nodes (3 cases) (Table 53 and Photos L 1-6)

As described above, swelling of the cervical lymph nodes was also a characteristic symptom in this syndrome. Lymph node samples from 3 patients (Table 53) were, therefore, surgically removed by Drs. Futonaka and Kajiya of the Department of Surgery in our hospital to identify any histological lesions.

Samples from the rice-grain-size subcutaneous lymph nodes were excised from 2 patients (patient Nos. 26 and 6) because the biggest lymph node (thumb size) was located under the sternocleidomastoid muscle and its excision was

Table 53. Histological examinations of cervical lymph nodes (3 cases)

patient No.	age	biopsy date	days of illness	biopsy site and size	pathological specimen No.
26	5y1m	04/06/1966	8	right, rice-grain sized	60459
6	11m	07/30/1966	6	right, rice-grain sized	63726
1	4m	09/28/1966	7	left, thumb's head sized	65482

difficult. The surgery for patient No. 1 was performed relatively easily because the desired lymph node (thumb size) was fortunately located near the surface of the sternocleidomastoid muscle. The histology of

Table 54. Cases only observed without active treatment after hospitalization (3 cases)

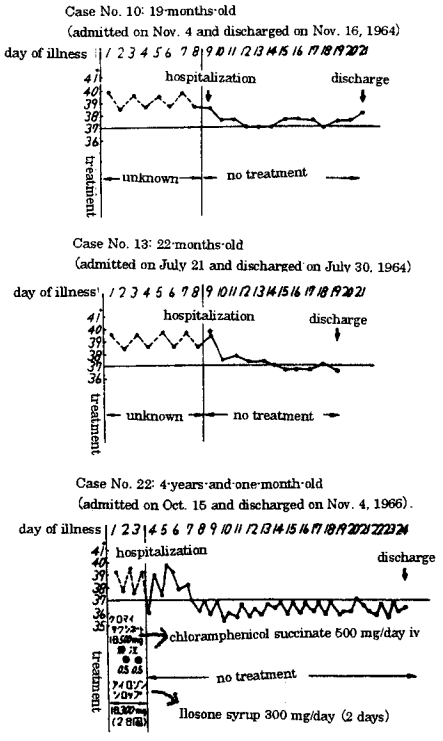
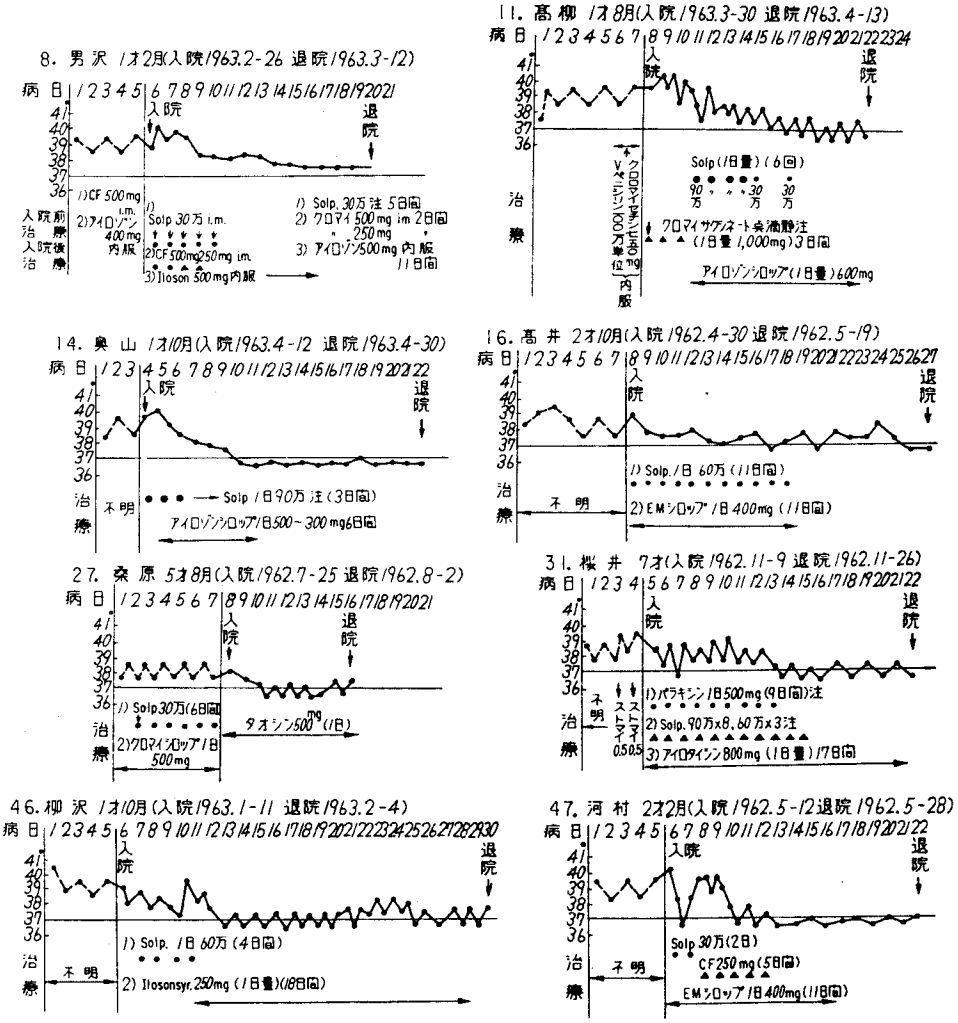


表55　ペニシリン併用例（８例）



したので，比較的容易に摘出出来た．各症例毎の組織像は写真（Ｌ１）～（Ｌ６）に示す如くであるが，山本及び原の２例には，両者共通の，非常に特徴的な病理組織学的変化が，田中博士により指摘された．即ち，強拡大下の写真（Ｌ３）と（Ｌ６）にみられるもので，

1)　Post-Capillary Venule の内皮細胞の異常な腫大．と，

2)　その周囲に於ける細網細胞の増生．とである．

この病変は本症の病因の一端を示唆する重要な所見と考えられるので，更に追求する予定である．

5. 治　　療

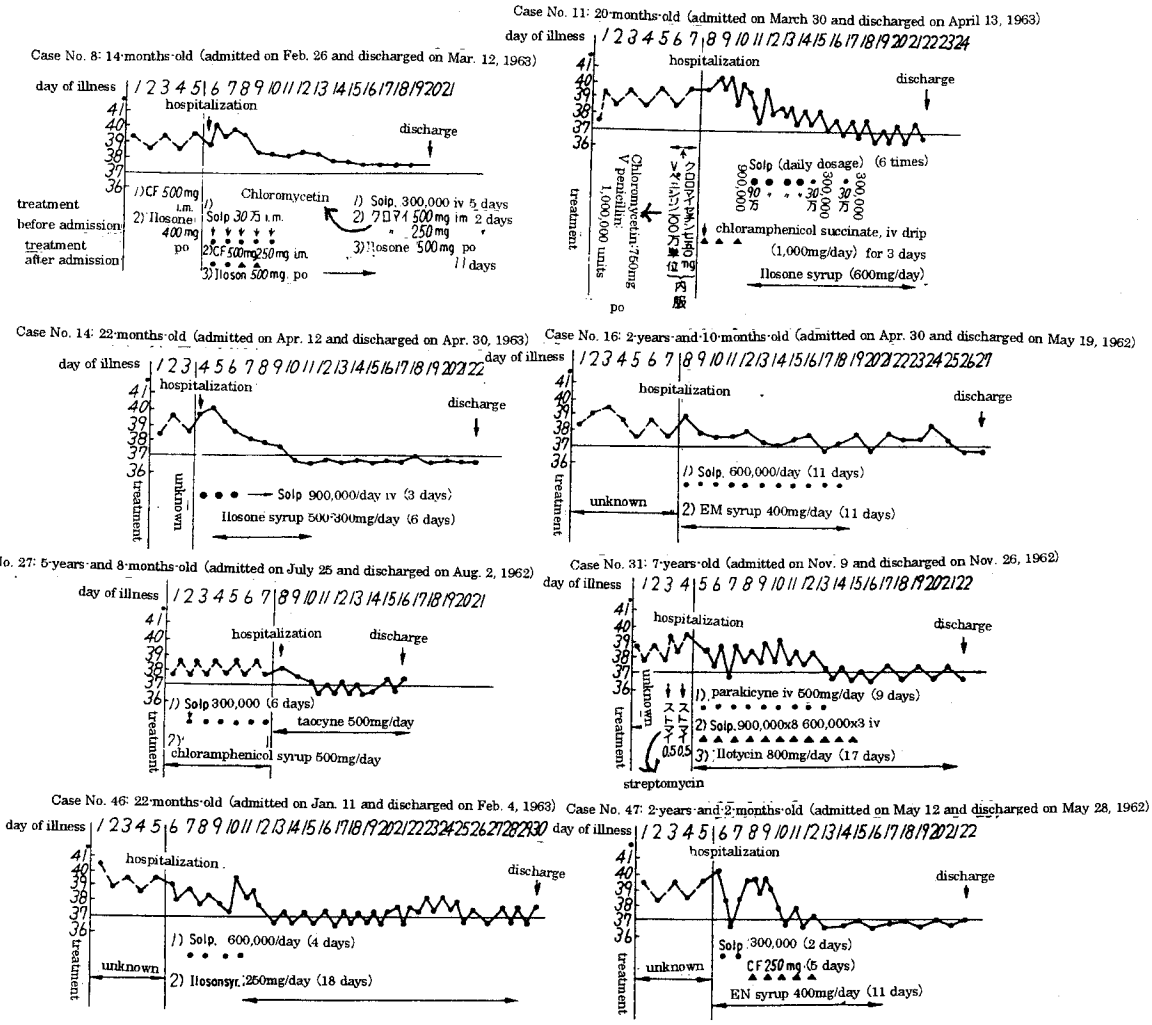
（表54, 55, 56の１と２，57の１と２，58の１と２，59）

上述の如く本症候群の予後は良好で，死亡又は後遺症を残した例は１例もなかつた．然し50例中には相当重症と思われた例もあるれば，入院時すでに恢復期に向つていた例等その症状の程度は様々であつた．前述した臨床像及び検査結果から本症候群が，その本態は未だ不明ではあるが，一応感染に起因する全身性熱性疾患と考えられるので，治療の基本が抗生物質に置かれたのもけだし当然と云えよう．ほぼ全例（例外３例）に入院後各種の抗生物質が投与された．次に使用した薬剤は皮質ホルモンである．約４割の22例に用いられた．依つて我々の50例を主な治療の種類により，次の５つのグループに分けて，観察し，比較した．

1)　入院後自然観察例（３例）（表54）

症例No. 10竹内，No. 13今田及びNo. 22竹浪の３例でそれぞれ第９，第９及び第４病日に入院した．No. 22竹浪例は当院外来で２日間クロマイサクシネート１回 500 mgずつ２回静注され，内服にアイロゾンシロップが１日 300mgずつ２日間投与された後に入院した．他の２例は

Table 55. Cases treated with penicillin combined with other medication (8 cases)



each lymph node sample is shown in Photos L1 through L6. Dr. Tanaka pointed out that the pathology observed in the samples taken from patient Nos.6 and 1 (Photos L3 and L6) was very unique, as defined below:

1) There was an abnormal swelling of the endothelial cells in the post-capillary venules; and

2) Reticulum cell hyperplasia around these lesions.

Because these changes may provide a key to the etiology of this syndrome, we plan to continue research in this area.

5. Treatment

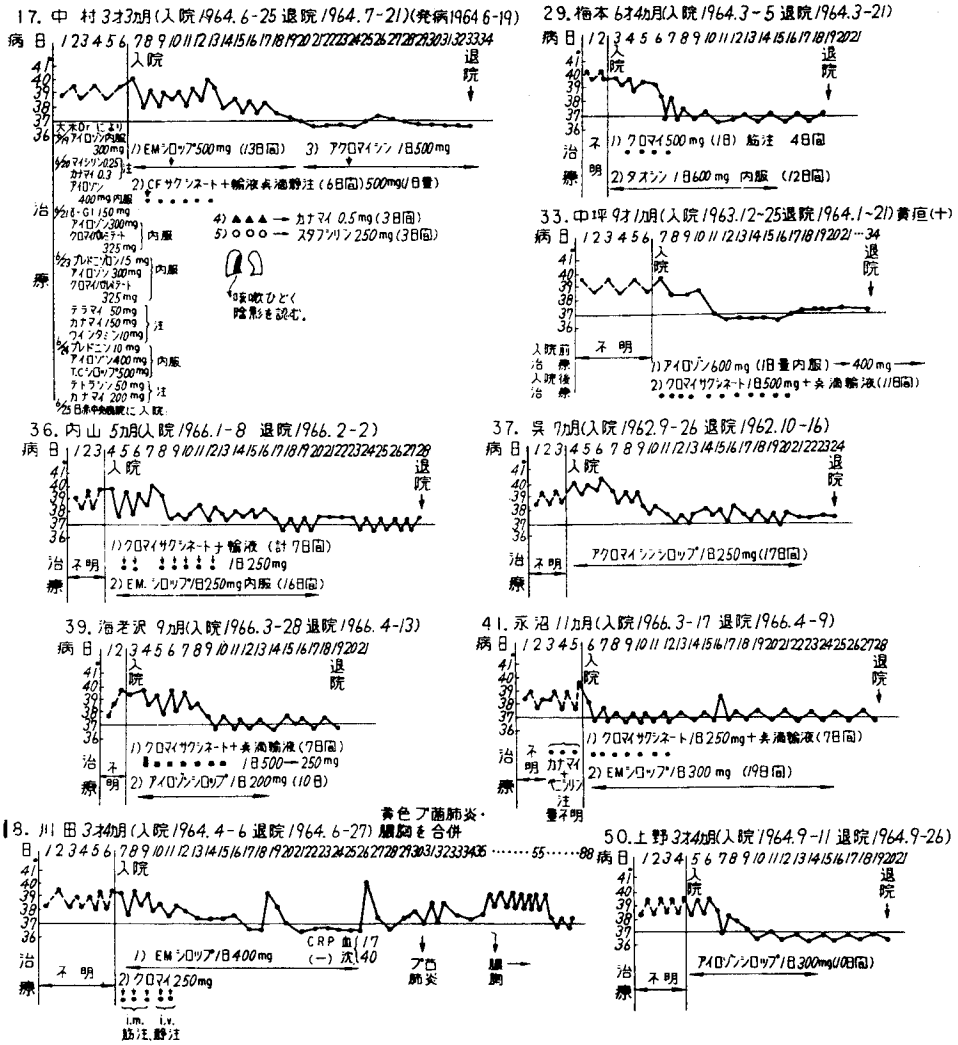
(Tables 54, 55, 56-1 and -2, 57-1 and -2, 58-1 and -2, and 59)

As already described, this syndrome is associated with a favorable outcome. No death or sequelae have been reported. The patients were in diverse stages of the disease when they were admitted to our hospital: some were critically ill and some were already in a recovery period. Although the etiology has not been established according to the clinical symptoms and test results presented above, this syndrome was considered to be a systemic febrile condition caused by some infectious agents. Therefore, as their major therapeutic modality, it was quite reasonable to give the patients antibiotics. All patients (except 3) received antibiotic treatments after being admitted to our hospital. Adrenocortical hormones were also used on approximately 40% (22 cases) of them. For comparison, the 50 patients were categorized into 5 groups according to the medications they received.

1) Observations only (3 cases) (Table 54)

Patient Nos.10, 13 and 22 were admitted to our hospital on days 9, 9 and 4 after onset, respectively. The last was treated with intravenous chloramphenicol succinate (500 mg iv) and Ilosone syrup (300 mg po) orally for 2 days at the outpatient department of our hospital before admission. Medical histories for the other 2 cases were unclear; but they must have been treated with some antibiotics because their temperatures ranged between 38 ℃ and 40 ℃. Following admission they were untreated and were simply placed under observation. All recovered satisfactorily.

表56　（その1）入院後ペニシリン以外の抗生物質使用例（17例）



入院迄の治療経過の精細は不明であつたが，38℃～40℃近くの弛張熱があつたから，抗生物質が投与されていたことはほぼ確実と思われる．入院後はいずれも全く治療せずに観察したが，順調に全治した．

2）　ペニシリン併用例（8例）（表55）

多くの症例は2種類以上の抗生物質が用いられたので，特にペニシリンの使用の有無により，ペニシリン使用（併用）例（8例）と使用しなかつた例（17例）とに分けた．

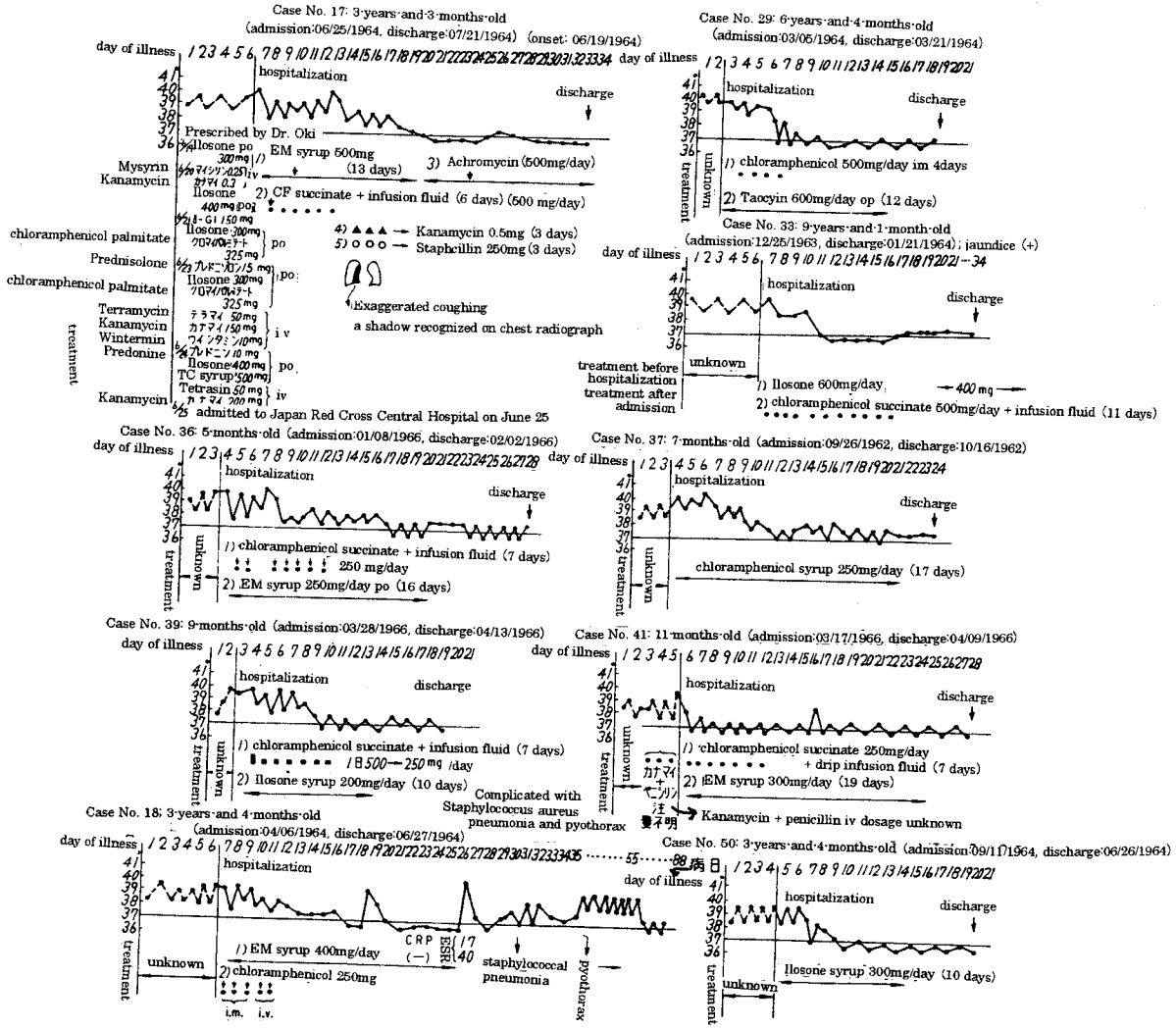
ペニシリン併用例は表に示す如く，8例であつたが，そのうちNo. 27桑原例のみは入院迄外来で病初よりペニシリン治療を行つた例で，他の7例は入院後にペニシリンを使用した例である．個々の体温表に示す様に後述する他の療法群と比較して，特に効果の点に差が見られなかった。

3）　入院後ペニシリン以外の抗生物質の使用例（17例）（表56—その1及びその2）

入院前に使用された薬剤が紹介医師により明かな症例（No. 17中村，No. 41永沼）には，それぞれマイシリン及びペニシリンの注射が行われていたが，入院後には使用しなかつたので，このグループに入れた．症例No. 17中村は肺炎が，No. 18川田は院内感染による黄色ブ菌肺炎及び膿胸の合併例で，すでに前項で述べた．この両者及び症例No. 15，29，33，36，39，41計8例に輸液と共にクロマイサクシネートの点滴静注が行なわれた．No. 1原例にはセボランの点滴静注が，No. 38加山例はアイロタイシンの点滴静注が，No. 43金井例ではロイコマイシン及びアイロタイシンの点滴静注が行われた．

症例No. 37呉例はアクロマイシンシロップの内服のみが，No. 6，20，44，48及び50の5例はエリスロマイシ

Table 56. (part 1) Use of antibiotics other than penicillin after hospital admission (17 cases)



2) Treatment with penicillin with or without other antibiotics. (8 cases) (Table 55)

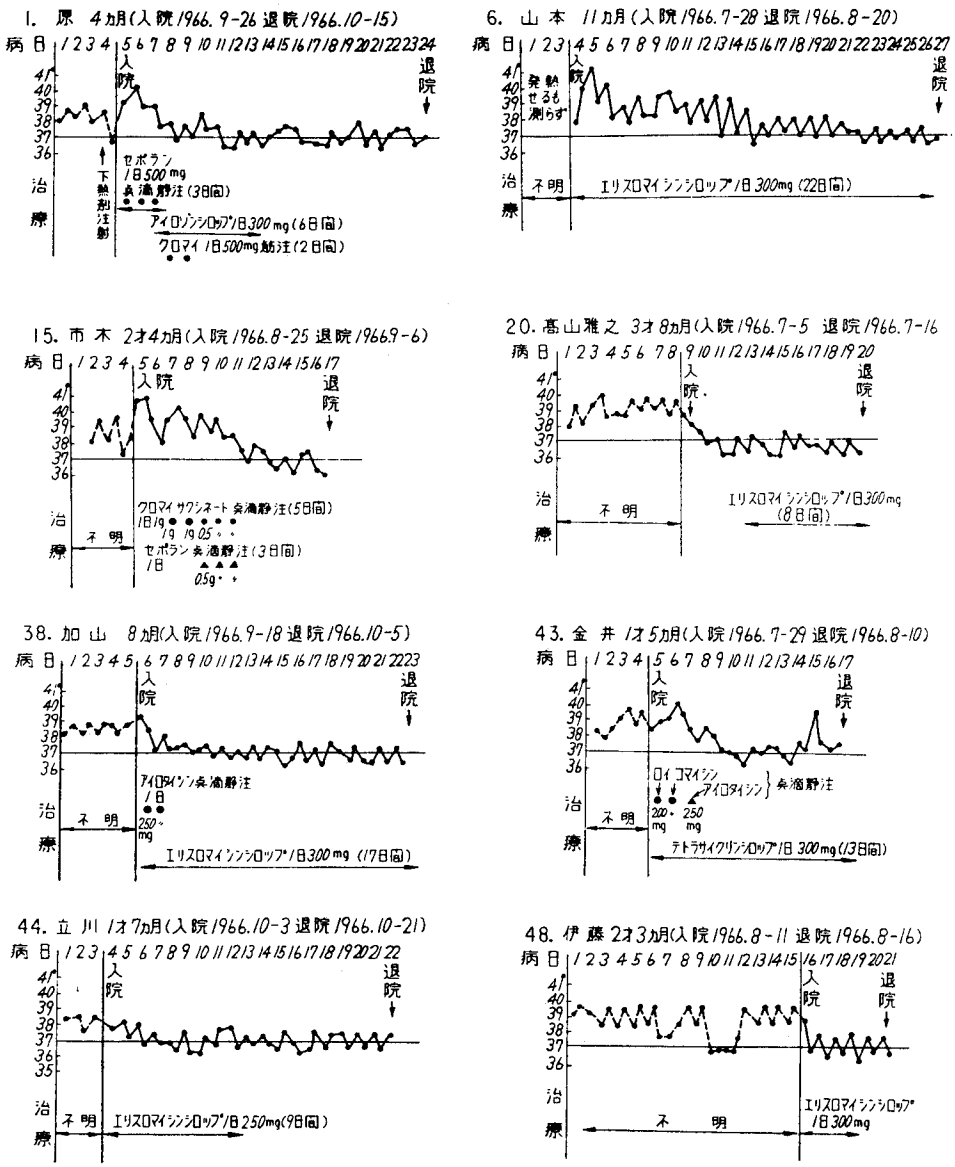
Most cases were treated with more than 2 antibiotics. This group received penicillin alone or in combination with other drugs, in contrast to the non-penicillin group that follows [see 3) below] (17 cases). The patients in the first group were treated with penicillin along with other medications after admission, except patient No. 27, who had already been treated with penicillin at a local clinic. As shown in the temperature chart, no difference was found between this group and others.

3) Antibiotics other than penicillin (17 cases) (Tables 56-1 and -2)

Although patient Nos.17 and 41 had been treated with mycillin and penicillin before being admitted to our hospital, these patients were placed in this group because they were not treated with penicillin after admission. Patient No.17 developed pneumonia, and No.18 deveoped nosocomially acquired *Staphylococcus aureus* pneumonia and pyothorax, as was described previously. These 2 patients, along with patient Nos.15, 29, 33, 36, 39 and 41 were treated with intravenous chloramphenicol succinate. In addition to these treatments, patient Nos.1, 38 and 43 received intravenous Sevoran, Ilotycin and a combination of leucomycin and Ilotycin, respectively.

Patient No.37 received Achromycin syrup only and the other 5 patients in this group (Nos.6, 20, 44, 48 and 50) received erythromycin syrup only. No difference in efficacy was recognized in comparison with the other treatment groups.

表56（その２）



ンシロップのみが投与された．

このグループも全体として，他の治療群との間に効果の点で特に差はみられなかつた．

4） 副腎皮質ホルモン点滴静注例（８例）及び筋注（１例）（表57その１とその２）

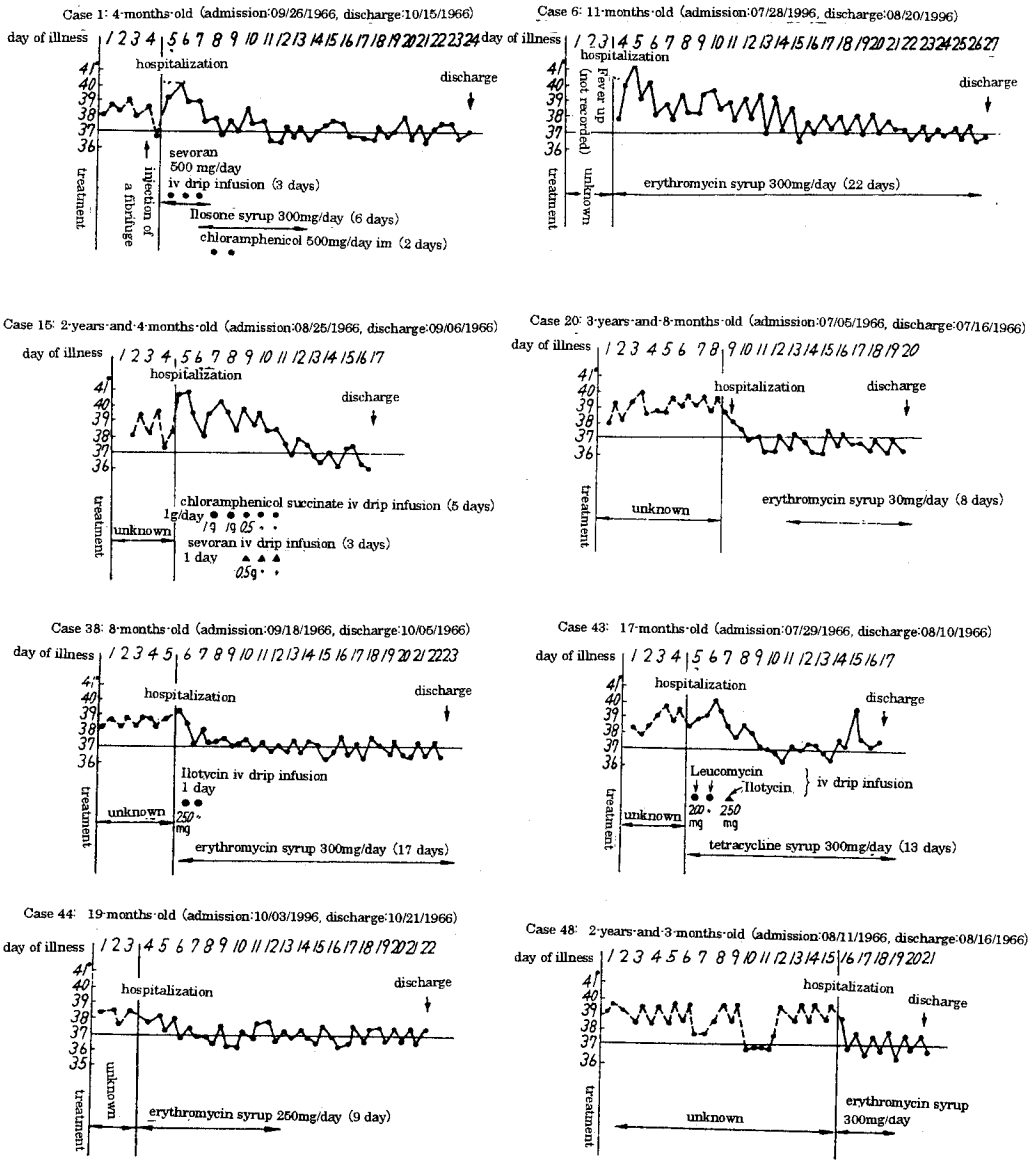
副腎皮質ホルモンは筋注，静注及び内服の３通りの方法で使用した．筋注使用はNo. 24山添例にのみ行われたが，特に有効ではなかつた．

症例No. ２，19，23，25，26，30，32及び40の８例では，プレドニン20～80mg（１日量）が，他の抗生物質及び輸液と共に１～６日間に亘つて，点滴静注された．このうちNo. ２，19，23，30及び40の５例は劇的な解熱効果をみたが，中止すると再び発熱傾向をみた．プレドニンの点滴静注は確かに解熱効果があり，一般状態の改善に役立つ様に思われたが，本症の全経過を短縮する効果があるかどうかは，他の治療群と比較してみて，余り差が見られなかつたので，慎重に判断する必要がある．

5） 副腎皮質ホモン経口投与例（13例）（表58その１とその２）

使用薬剤はプレドニン，パラメゾン及びデカドロンの３種類で，比較的早期に使用された例もあれば，相当日数を経てから投与された例もあるので，その効果の判定は非常に困難であるが，No. ７小川例を除いては，一時的に，点滴静注程ではないが，解熱効果がある様な印象

Table 56. (part 2)



4) Adrenocortical hormones given intravenously (8 cases) or intramuscularly (1 case) (Tables 57-1 and -2)

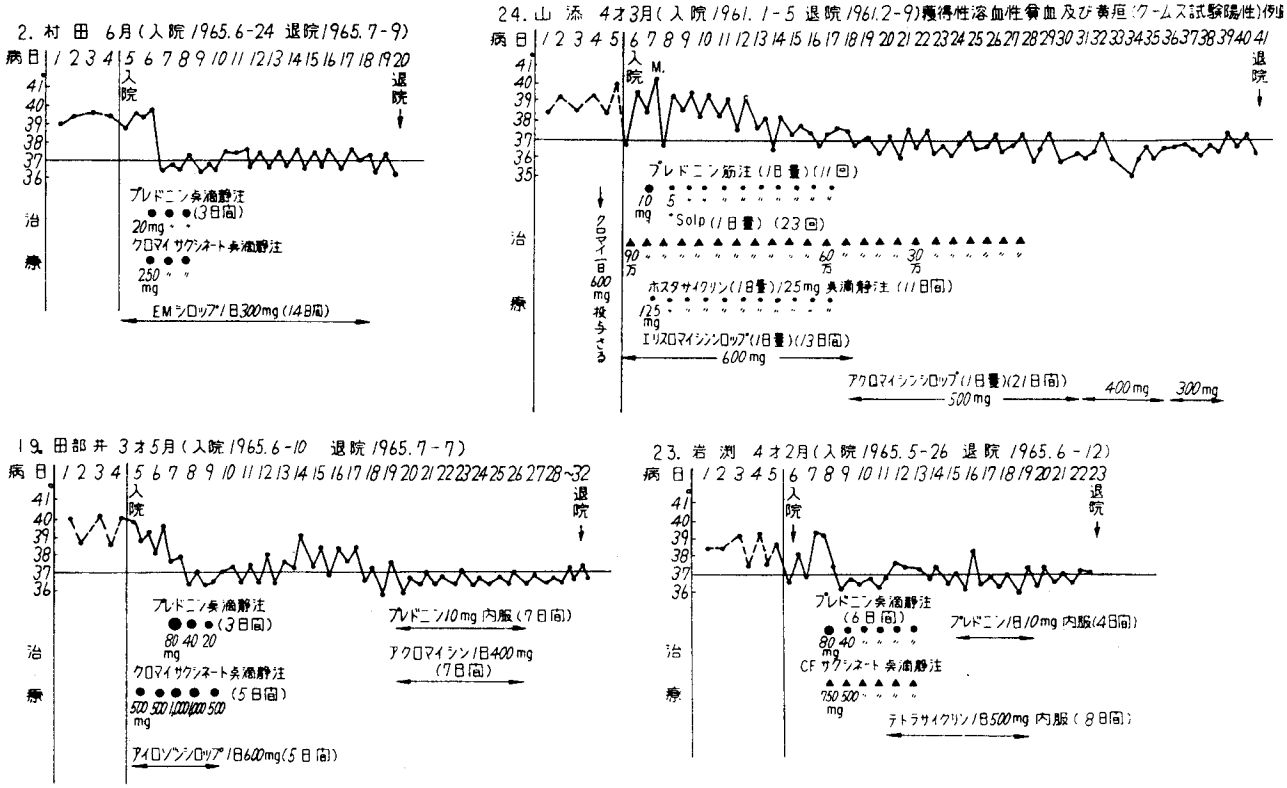
Adrenocortical hormones were administered via 3 different routes intravenous, intramuscular, and oral. Only patient No.24 received the hormone intramuscularly, which produced no significant effect.

Eight patients (patient Nos. 2, 19, 23, 25, 26, 30, 32 and 40) received intravenous Predonine (20-80 mg/day) along with other antibiotics and IV fluids for 1 to 6 days. The antipyretic effect was dramatic in patient Nos. 2, 19, 23, 30 and 40; however, body temperature rose after the treatment was discontinued. Although intravenous Predonine administration may provide a favorable antipyretic effect and it seemed to be useful in improving the patient's general condition, there was little evidence to support the effectiveness of this agent in shortening the overall clinical course of this syndrome when the treatment option was compared to others. This matter must be examined carefully.

5) Oral adrenocortical hormones (13 cases) (Tables 58-1 and -2)

Predonine, Paramesone and Decadron were employed as oral therapeutic agents. Some patients received the medication relatively early in their clinical course and others did not until days after their admission to the hospital. Thus it is again very difficult to evaluate the efficacy of this therapeutic modality. In considering this matter, it seemed that the antipyretic effect of oral administration of this hormone (though not as obvious as its intravenous administration) was observed over the short term in all patients except patient No.7. However, the results indicate that there is no significant difference when compared to other treatment options. The drug efficacy for self-limited disease like this syndrome must be assessed with extreme care.

表57（その1）副腎皮質ホルモン点滴静注例（8例）筋注（1例）



を得た．然し，前述迄の各種の治療群との比較では，いずれも，その間に有意の差があるとは思われないので，本症候群の如き，Self-limited の疾患に於ける薬剤効果の判定は余程慎重でなければならない．

表59（その1とその2）は各症例毎の使用薬剤を表にしたもので．大部分の症例が，2種類以上の薬剤の併用が行われていることがわかる．

本症候群が果して，全く抗生物質を使用しない場合でも，Self-limited でありうるかどうかについては，興味ある問題ではあるが，比較的軽い例ならいざ知らず，高熱の持続する例が多い本症候群では偶然の場合以外，この様な症例をもつことはまず不可能であろう．この問題は偶然例の累積により，時が解決してくれる事であろう．

6. 病　因

本症候群は全身性の急性熱性疾患で，発病が急であり，頸部淋巴腺腫脹を伴う例が多く，且，再発しない点より，感染に基因する疾患と考えられるが，特定の細菌或はウイルスによる感染症であるのか，或は非特異的な感染アレルギー乃至は何等かの自己免疫機序が介在しているものであるのか，今迄上述した様に，種々検索を試みたが，現在の時点に於ては，そのいずれとも判定し難い．

イ）特定のウイルス感染症とする考え方．

我々の症候群では，

1）　血液培養でも，頸部淋巴腺穿刺でも細菌が証明出来ない．

2）　無菌性髄膜炎や肝炎を伴うことのある急性の全身性の非化膿性炎症である．

3）　再発例がなく，凡そ3週間以内に治癒する．

4）　既知のウイルスはまだ証明されない．

以上の点より何か新しいウイルス感染症ではなかろうかと考えて，この方面の検索を目下，予研芦原博士と協同して追求している．

ロ）細菌感染とする考え方．

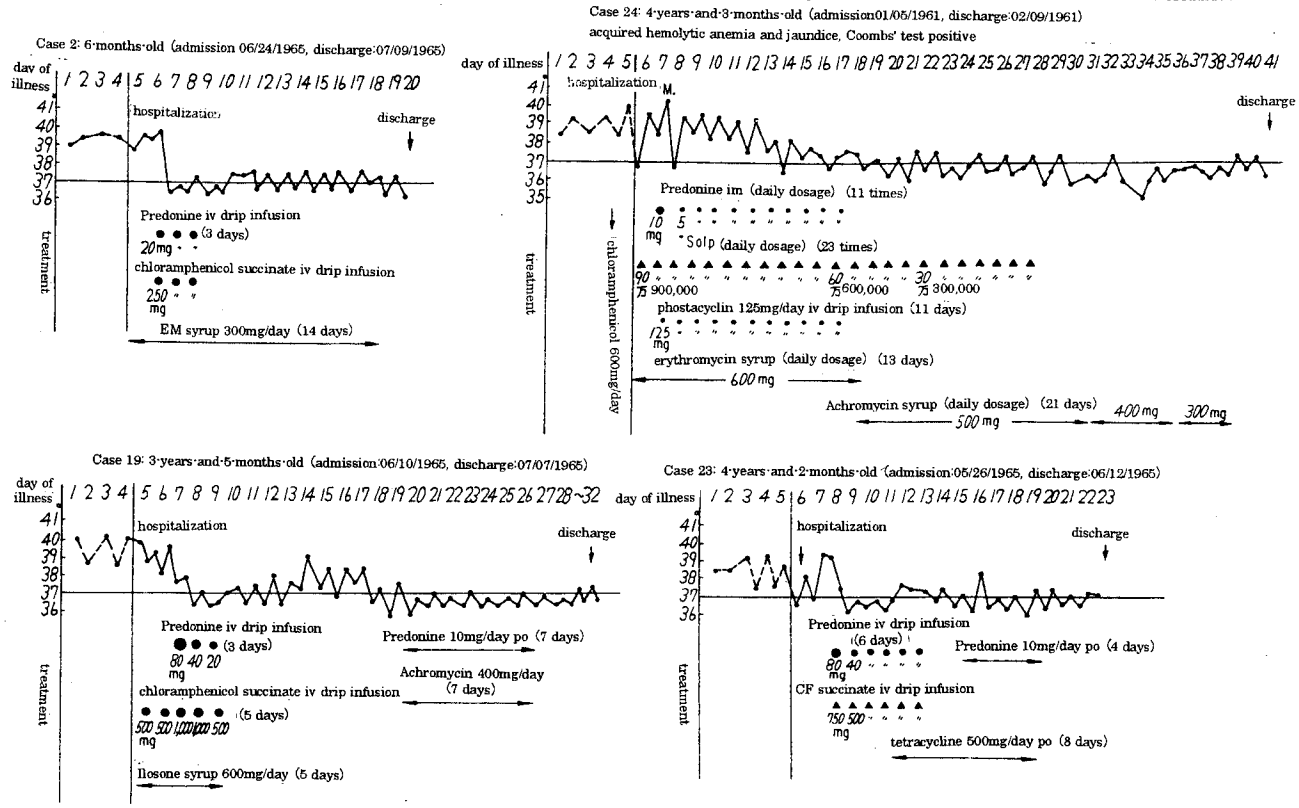
我々の症候群では，

1）　本症にみられる頸部淋巴腺炎は急性で，多くは片側，局在性で，汎発性でないところから，咽頭からの細菌感染が最も考え易い．

2）　白血球増多症，左方核移動，血沈速進等はウイルス感染よりむしろ，細菌感染の方が考え易い．

3）　今迄知られている発疹を伴うウイルス性疾患は，

Table 57. (part 1) Intravenous drip infusion (8 cases) and intramuscular injection (one case) of adrenocortical hormone



The medications administered to all patients are summarized in Tables 59-1 and -2. As seen in these tables, most patients received combinations of more than 2 different agents.

It is an intriguing subject to consider whether this syndrome would be self-limited, if the patients had not been treated with antibiotics. However, it would be very difficult to prove this supposition in actual patients because, with exception of a handful of mild cases, most develop a persistent high fever and would inevitably be treated with antibiotics. Perhaps this question might be answered in due time after a sufficient number of non-antibiotic-treated cases have been studied.

6. Etiology

This syndrome is a systemic, acute febrile disease with a sudden onset. It is accompanied by swelling of the cervical lymph node in many. Because it does not recur, it is suspected to be caused by an infection. However, various investigations, such as those described above, have not provided us with a definitive answer to the question of whether it is an infection caused by a specific bacteria or virus or if it is due to a non-specific infectious allergy or some type of autoimmune mechanism.

a) Consideration of a specific virus infection

The following have been established in the study of this syndrome:

1) No bacteria have been identified either in the blood culture or samples taken by puncturing the cervical lymph nodes;

2) The disease is an acute, systemic non-suppurative inflammation that may be accompanied by aseptic meningitis or hepatitis;

3) No recurrence has been noted and patients recover in about 3 weeks; and

4) No known virus has been isolated.

In view of these findings, it was next suspected that the condition is an infection by a new type of virus. Virological investigations are currently underway with the cooperation of Dr. Ashihara of the National Institute of Infectious Diseases.

b) A bacterial infection

This theory is plausible for the following reasons:

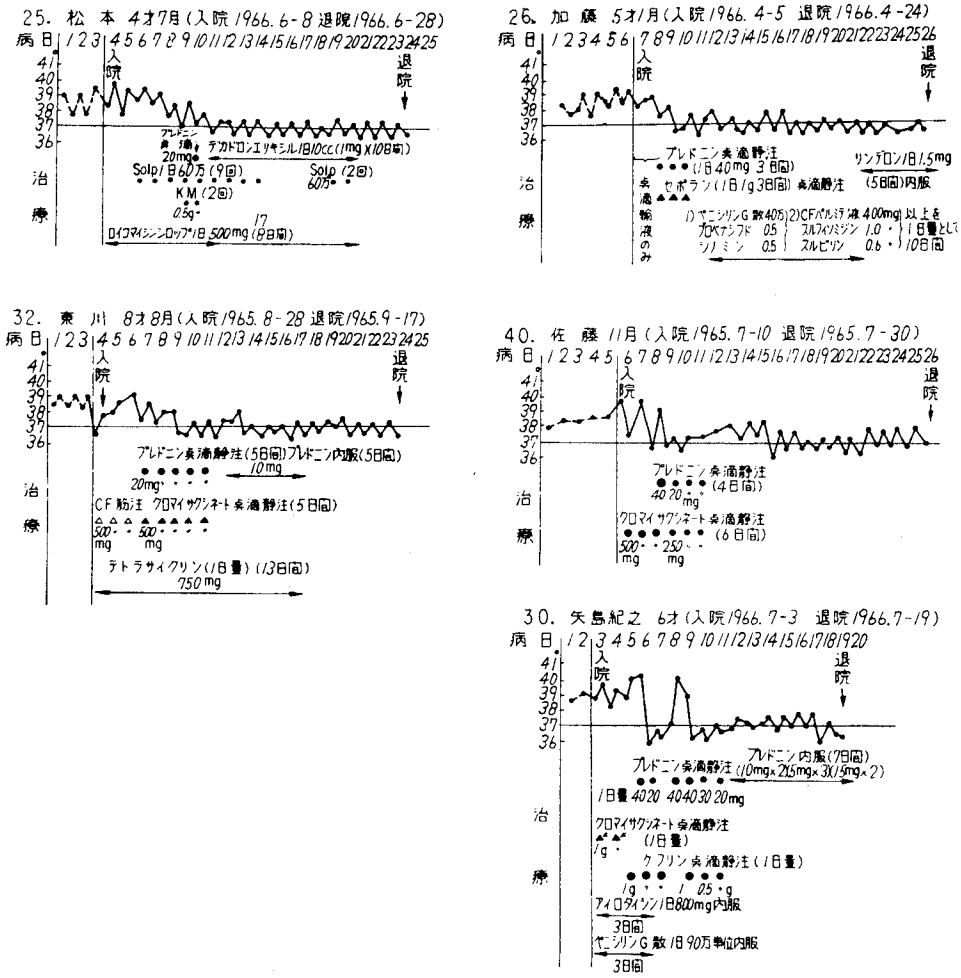
1) Cervical lymphadenitis associated with this syndrome is acute, often unilateral and localized but not widespread. Therefore bacterial invasion through a pharyngeal route is most logical as an etiology;

2) Findings, such as leukocytosis, left nuclear shift, and exaggerated blood sedimentation rates are readily explained by a bacterial infection; and

3) Known virus infections causing skin eruptions are normally associated with a fever that lasts for a week.

However, a simple theory of bacterial infection is not completely accepted because of the following:

表57（その2）



一般に，有熱期間が1週間内外迄である．等の点より，細菌感染の考えも充分成り立つが，

1） 本症は化膿の傾向が全くない．

2） 菌が頸部淋巴腺からも，血液からも証明されない．

3） Focus が特に見当らない．等々．

単なる細菌感染症とするには，根拠が弱い様である．

ハ）非特異性の感染アレルギー乃至は自己免疫性機序の介在を考慮する考え方．

リウマチ熱やＳＬＥ，或は P.N. 等所謂膠原病の成立機序は現在でも正確には不明であるが，一応非特異性の細菌アレルギー或は自己免疫疾患の可能性について，各方面から検索され，且論じられている．

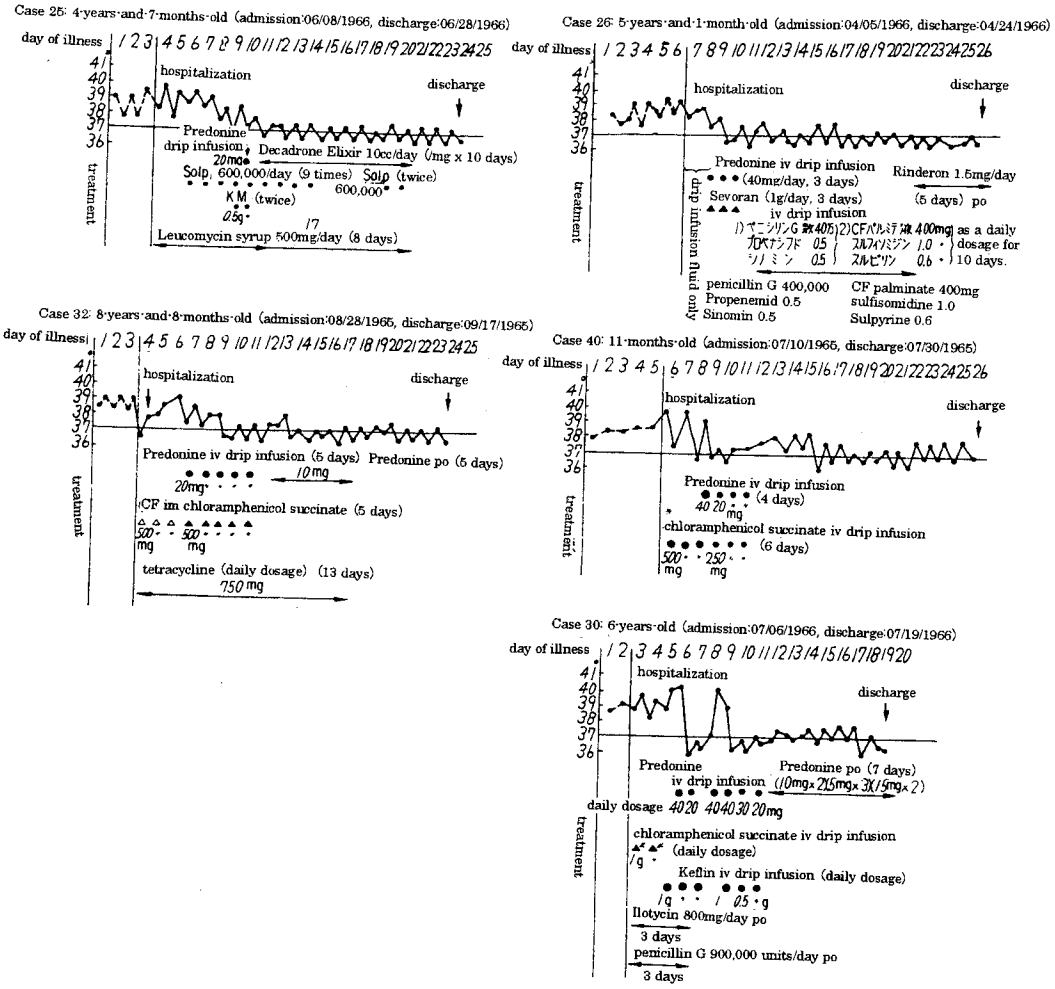
我々の症候群が，ウイルスも，細菌も証明出来ない現時点に於て，膠原病又は，その近縁疾患としての可能性についても考える必要があろう．事実，我々は近年乳児 P.N. の2例を経験し，その臨床的特徴が，本症候群と極めて類似していることを報告した．[53]然し一般的に云つて，膠原病では，1） 臨床経過が長期に亘り，2） 予後も比較的悪く，3） 皮質ホルモン使用が常に要求される点で我々の症候群とは臨床像が相異しているかの如くみえる．然し乍ら，上述の如く，色々な点で膠原病に類似した症状も呈している．且，1） クームス陽性例がある．2） Ra テスト陽性例がある．3） 頸部淋巴腺の組織像に post-capllary venule の内皮細胞の腫大及びその周囲に於ける細網細胞の増生という尋常でない response が見られる．等々，この方面の検索も今後の重要な課題として残されている．

7. 考　按

以上私は過去約6年間に経験した自験例50例の臨床的特徴，検査所見及び治療についてその大要を述べた．扨て，ここで我々の症候群と既知の類似疾患とを比較検討してみる必要がある．

1） 急性全身性熱性疾患

Table 57. (part 2)



1) The syndrome has no tendency for suppuration;

2) No bacteria have been isolated from either cervical lymph nodes or the blood; and

3) No specific infectious foci have been found.

c) Involvement of non-specific hypersensitivity caused by infection or an autoimmune mechanism

The mechanism through which the so-called collagen diseases (e.g., rheumatoid fever, SLE, and PN) develop has not been totally elucidated; but the possibility for a non-specific hypersensitivity caused by the presence of bacteria or an autoimmune disease has been investigated and discussed from several aspects.

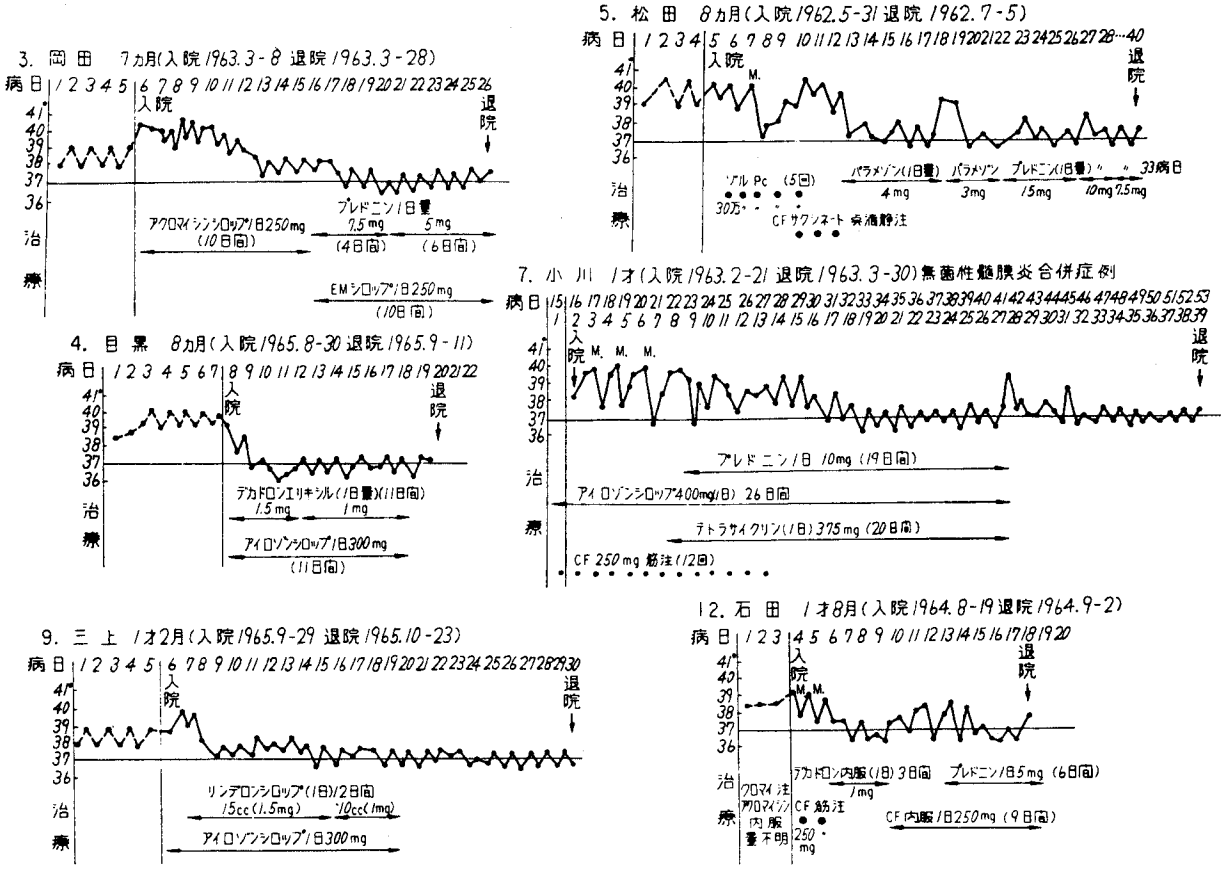
Thus far the presence of a virus or bacteria has not been proven and there is a need to consider the possibility of collagen diseases or related disorders. In fact, we have recently encountered 2 cases of PN involving infants and reported that their conditions simulated those of this syndrome.[53] However, the following clinical symptoms related to collagen disease appear to be contrary to those of this syndrome: 1) a protracted clinical course; 2) a relatively poor prognosis; and 3) a continual need for adrenal cortex hormones. On the other hand, the following symptoms of this syndrome are reminiscent of collagen diseases: 1) the patients respond positively to Coombs' test; 2) some produce positive responses to the Ra test; and 3) unusual responses — enlarged endothelial cells of post-capillary venules and proliferation of the reticuloendothelial cells around them — have been noted in the histological examination of cervical lymph nodes. This is an area that is important for future investigation.

7. Discussion

The clinical characteristics, results of diagnostic tests, and treatment given to 50 cases observed by us over the past 6 years were summarized. At this point, it is appropriate to compare this syndrome with known related diseases.

1) Acute systemic febrile diseases

表58（その1）副腎皮質ホルモン経口投与例（13例）



イ）敗血症……我々の症候群は，

i）流血中から菌が証明されてない．

ii）Focus herd と考えられる頚部淋巴腺からも菌が証明出来ない．

iii）転移病巣がない．等々敗血症を裏付ける positive なデータが1つもなかつた．

ロ）リウマチ熱……我々の症候群は，

i）溶連菌感染と関係がうすい．

ii）心炎合併例がない．亦，所謂 Johns の他の大症状が1つもみられない．

iii）再発例がない．

iv）年令分布が異なる．等の理由から，リウマチ熱も否定出来よう．

ハ）Rheumatoid Arthritis（或は Still 氏病）

我々の症候群は，

i）慢性の経過はとらないし，再発もなく，関節炎の固定もない．

ii）脾腫がない．等の点で異なる．

ニ）Subsepsis allergica Wisslser（S.a.w.と略）

我々の症候群は，

i）月余に亘る間歇熱ではない．

ii）発疹が繰返し出現しない．

iii）指趾先からの特有な落屑がある．

iv）心障害を伴つた例がない．

v）流血中のエオジン細胞が減少しているものが多い．等で S.a.W. とは異なる．

2）発疹を伴うウイルス性疾患群

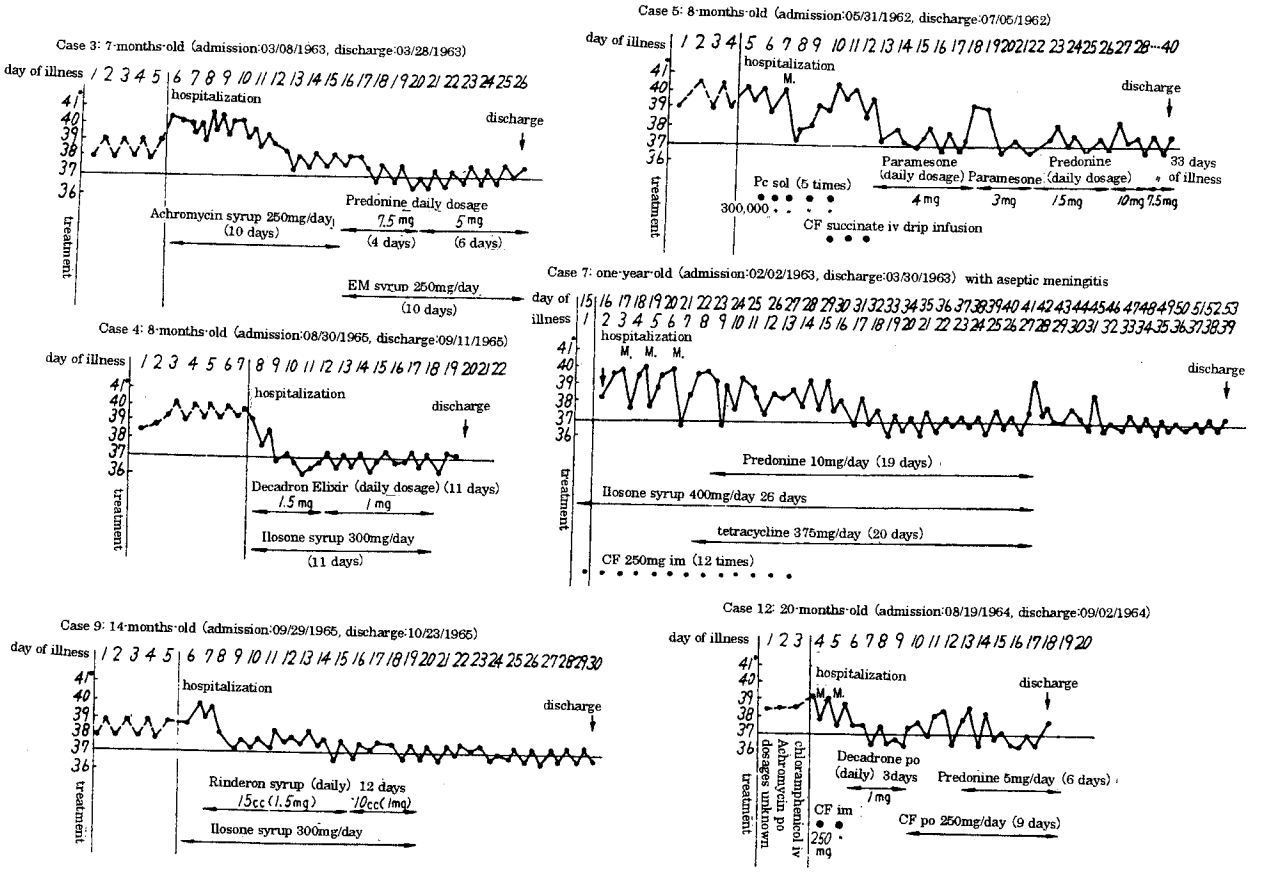
古典的な発疹性ウイルス疾患，即ち麻疹，風疹或は水痘等でないことは明かである．

近年新しいウイルスによる発疹症が次々に報告されて来た．

中尾[13]，渡辺[14]の解説による Coxsackie A 及び B, ECHO, Adeno, 及び Reo ウイルス感染に伴う発疹症は，一般的に，1）発熱期間が短い，2）発疹の性状が多少異なる．3）落屑がない．等の点でいずれにも概当するものがない．ただ，発疹の部位がよく似ている Hand-Foot and Mouth disease[15][16]についてふれる必要があろう．

本症は題名の如く，手や足及び口腔内に，小水疱を形

Table 58. (part 1) Oral administration of adrenocortical hormones (13 cases)



a) Septicemia: this disease is ruled out for the following reasons

i) No bacteria have been isolated from the circulating blood;

ii) The presence of bacteria has not been proven in the cervical lymph nodes, the most probable focus herd; and

iii) There are no metastatic foci.

Thus there is not a single positive bit of data to substantiate the septicemia theory.

b) Rheumatic fever: this entity can be also ruled out for the following reasons:

i) There is no relationship with a streptococcal infection;

ii) There are no inflammatory complications involving the myocardium. Neither is there any of the so-called Jones' major criteria;

iii) There are no instances of a recurrence; and

iv) The age distribution is different.

c) Rheumatoid arthritis (or Still's disease)

This syndrome differs from the above in the following features:

i) The syndrome does not take a chronic course or recur. The associated arthralgia does not progress to fixated arthritis; and

ii) No splenomegaly has been observed.

d) Subsepsis allergica Wisslser (abbreviated to S.a.w.)

This syndrome differs from S.a.w. because of the following:

i) There is no intermittent fever lasting for months;

ii) There is no recurrent skin eruptions;

iii) The characteristic desquamation starts at the ends of the fingers and toes;

iv) There are no incidences of cardiac disorders; and

v) The number of eosinophilic cells is reduced in the circulating blood of many patients.

2) Virus diseases associated with skin eruptions

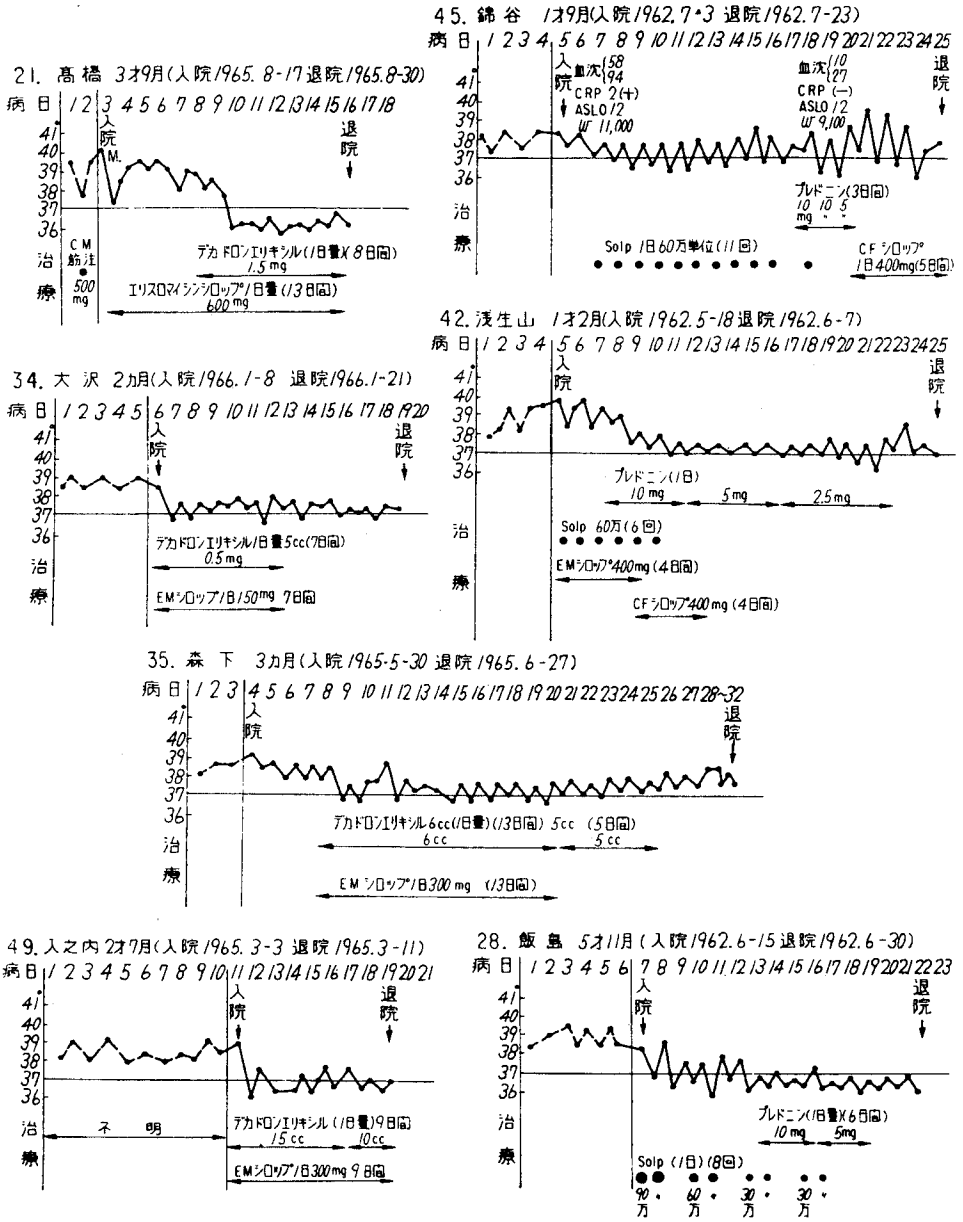
It is evident that this syndrome is not a classical known viral infection with skin eruptions, such as measles, rubella, and chickenpox.

Recently, new virus diseases that cause skin eruptions have been reported.

Coxsackie A and B, ECHO, adeno, and Reo virus infections with skin eruptions that have been explained by Nakao[13] and Watanabe[14] do not fit the description of this syndrome because the former are characterized by 1) a short febrile period; 2) skin eruptions that are different; and 3) absence of the desquamation process. Here it seems reasonable to touch upon the hand-foot-and-mouth disease[15][16] which resembles this syndrome in the sites of eruptions.

As indicated by its name hand-foot-and-mouth disease is unique in that small blisters form on the hands, feet, and in the oral cavity. It has been

表58（その2）



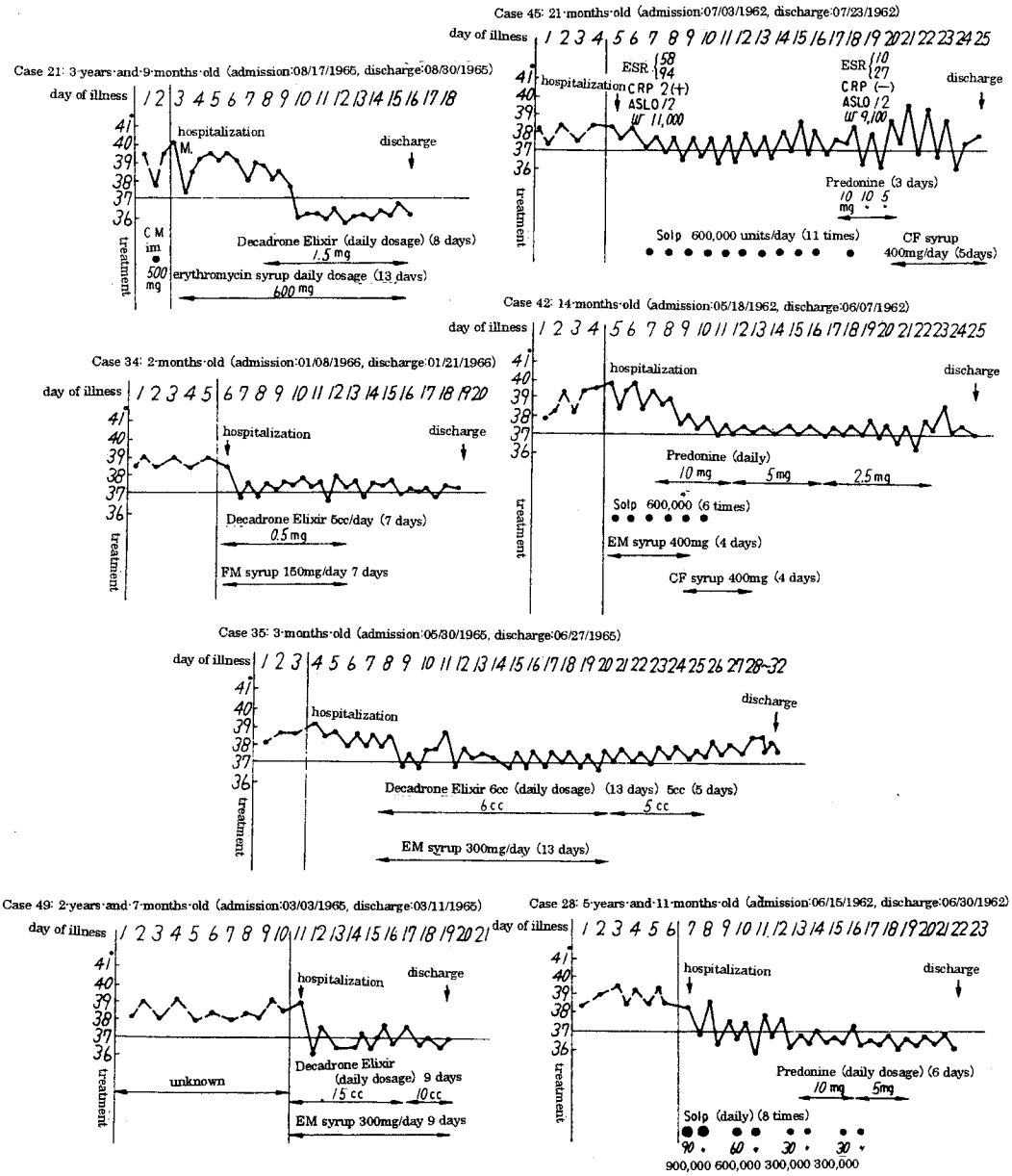
成する特殊な発疹症で，Coxsackie A 16感染症とほぼ確定された疾患である．我々の症候群では，発疹に水疱形成を伴わないことが特徴であるからH.-F.-M.D. とは明かに異るものである．然し，Gohd[17]等は，16カ月の女児で Coxsackie A 16感染症に我々の症候群によく似た症状を伴つた1例を報告している．かりに Gohd 等の症例の如き，特殊な例がECHOや Adeno 感染症でみられたとしても，普遍的なものではない．この点を考慮すると，我々の症候群は既知のウイルス性発疹症とは明かに異つたものであるといえよう．

3) 小児の落屑を伴う疾患群（主なもの）

我々の症候群に於ける落屑は非常に特異的で診断の決め手の1つである．故に，小児にみられる主な落屑疾患と鑑別する必要がある．

イ）猩紅熱……我々の症候群の落屑方式が特有で，必ず指の爪皮膚移行部よりはじまり，膜様の落屑は両手，両足に限られることは前述したが，この様な記載は小児の疾患中猩紅熱の項にしか見られぬ独特のものであつた．即ち，Brennemann[18]の小児科書の猩紅熱の項に，“Desquamation begins on the neck, chest or upperback and not infrequently is first noted on fingers or toes at the junction of nail and skin under the nail.”

Table 58. (part 2)



generally recognized to be an infection by Coxsackie A16. In our syndrome, skin eruptions do not characteristically include blister formation, clearly distinguishing it from the hand-foot-and-mouth disease. However, Gohd, et al[17] reported on a case of Coxsackie A16 infection with symptoms that simulated those of our syndrome in a 16-month-old girl. Even if we assume that a unique case such as this one is included in ECHO or adenovirus infections, it is not a frequently seen situation. Thus it is concluded that this syndrome is evidently different from known virus diseases with skin eruptions.

3) Diseases affecting children that are associated with desquamation (We will discuss a few major diseases in this category)

Desquamation is a unique feature of this syndrome and plays a key role in its diagnosis; therefore it is necessary to distinguish it from other major desquamating diseases.

a) Scarlet fever

It has already been stated that the pattern of desquamation in this syndrome is unique: it always starts at the nail-skin junction of the digits; and membranous desquamation is limited to both hands and feet. Among the diseases of children, such a feature is unique and found only in the description of scarlet fever among the diseases of children, viz., "Desquamation begins on the neck, chest, or upper back and not infrequently is first noted on the fingers or toes at the junction of nail and skin under the nail" as mentioned in the section of scarlet fever in the pediatric textbook by Brennemann.[18] This description matches the desquamation pattern in our syndrome. The section on scarlet fever in the textbook by Pfaundler und Schloßmann[19] and also the

表59（その１）副腎皮質ホルモン使用例とその使用例とその使用薬の種類（22例について）

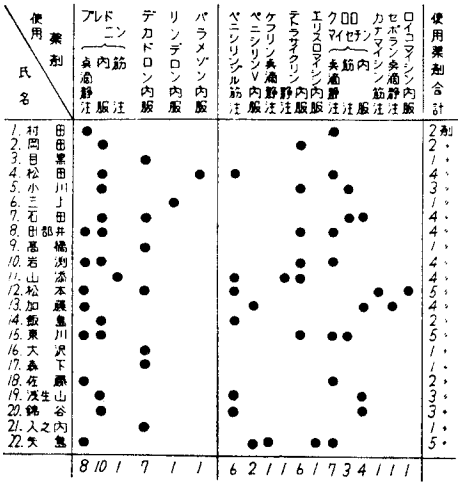


表59（その２）副腎皮質ホルモン不使用例とその使用薬の種類（28例について）

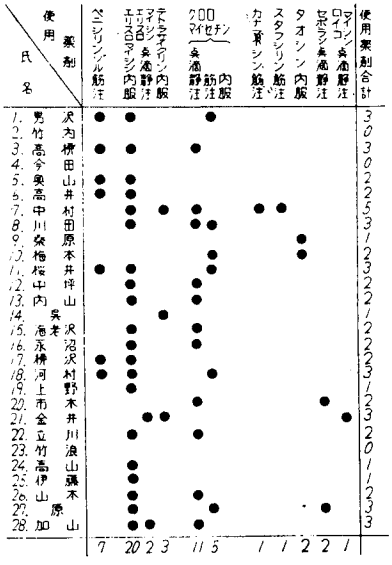


表60　薬物誘発試験（４例）

症　例	投与した病日	投与期間	臨床的反応
海老沢	第14～19病日	6日間	なし
内山	第88～93病日	6日間	〃
三上	第20～24病日	5日間	〃
加藤	第12～20病日	9日間	〃

という全く我々の症候群の落屑様式に一致する記載があつた．又，Pfaundler und Schloßmann[19]及びFanconiの小児科書の猩紅熱の項にも共に，“diagnostisch wichtig ist die Schuppung an den Finger und Zehenspitzen, die auch bei geringer Abschuppung nicht fehlt.”と記されている．以上の如く落屑方式のみをとれば猩紅熱によく一致しているが，我々の症候群は，

i）溶連菌との関係がうすい．

ii）発疹の性状が違う．

iii）Angina を殆んど認めない（入院時）．亦，腎炎の合併もない．

iv）ペニシリンが特に有効とはいえない．

v）年令層が若い．等より猩紅熱は否定出来よう．

ロ）泉熱……我々の症候群は，

i）集団発生をみない．

ii）発疹の性状が異うし，又，二次性発疹を欠く．

iii）年令層も違う．等々泉熱も否定出来よう．

ハ）Erythem scarlatiniforme dsequamativum recidivans 又は Erythema Scarlatiniforme[20]

我々の症候群は，

i）再発性でない．ii）落屑が主に第２病週にはじまる．iii）白血球増多症や苺舌が存在する．等の点で本症とは異る．

ニ）薬疹……我々の症候群が，入院前に使用された薬剤についての精細な情報を多くの症例で欠いているので，薬剤との関係は明かでない．そこで表60に示す様に４例についてペニシリンG散20～40万（１日量），プロベネシツド，シノミン，クロマイパルミテート，スルピリン及びスルフイソミジンの合剤による薬物誘発試験を行つたが，いずれも臨床的には陰性であつた．然も50例の中に再発をみた例が１例も存在しない点より，先ず薬疹の可能性は少ないと思う．

ホ）中毒疹……薬疹といい，中毒疹といい，原因の明かでない場合は一種の想像的又は仮定的診断名で確実なものではない．我々の症例を診て皮膚科の専門家は“若し１例のみを診た場合，発疹に限つていえば，“中毒疹とも診断しうるであろう”．然し，“他の幾つかの主症状の特徴を考慮すれば，“単なる中毒疹ではなくて，一定の臨床像をもつた症候群と考えられる”．との意見であつた．（当院皮膚科垣内部長，関東逓信病院皮膚科西山茂夫博士）

ヘ）Gianotti-Crosti Syndrome[21)22)]……本症は，Acrodermatitis papulosa infantum とも呼ばれ，組織学的には Eine reaktive subakute Reticuloendothelitis とも称される小児特に乳幼児にみられる発疹性落屑性疾患であるが，我々の症候群は，

Table 59 (part 1). Patients treated with adrenal cortical hormones: cases and types of hormones used (22 cases)

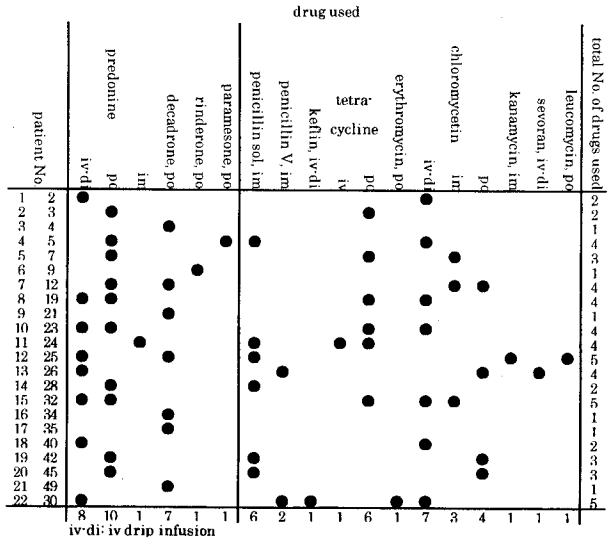


Table 59 (part 2). Patients not treated with adrenal cortical hormones: cases and the types of drugs used (28 cases)

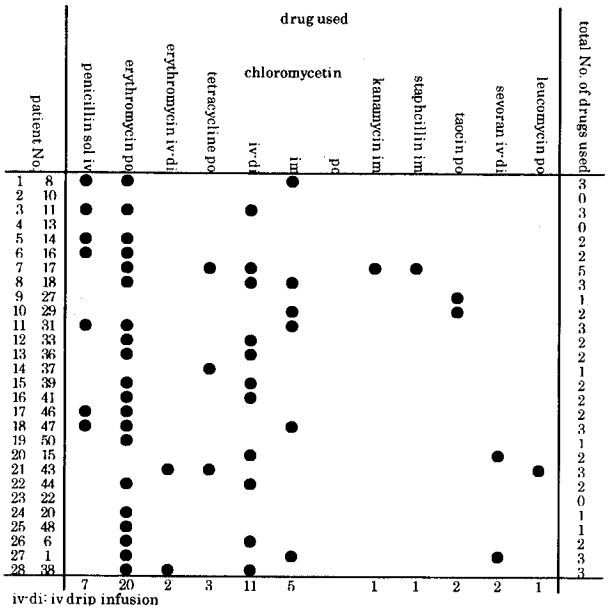


Table 60. Drug provocation test (4 cases)

patient No.	days of illness of drug administration	duration of drug administration	clinical reaction
39	14-19 day	6 days	none
36	88-93 day	6 days	none
9	20-24 day	5 days	none
26	12-20 day	9 days	none

one by Fanconi include the following: "diagnostisch wichtig ist die Schuppung an den Finger und Zehenspitzen, die auch bei geringre Abschuppung nicht fehlt." If one limits his attention to the manner of desquamation, this syndrome matches the description of scarlet fever. However, the syndrome also presents the following characteristics that rule out its being identified with scarlet fever:

i) Its relationship with hemolytic streptococci is doubtful;

ii) The manner by which skin eruptions develop is different;

iii) *Angina* [old term for sore throat] is rarely recognized (at hospital admission); and the syndrome is not associated with nephritis;

iv) The efficacy of penicillin as a therapeutic agent is generally ruled out; and

v) The age of the patients is younger.

b) Izumi fever

This clinical entity is also ruled out in identifying this syndrome for the following reasons:

i) There have been no mass outbreaks;

ii) The characteristics of eruptions are different and there is no incidence of secondary eruptions; and

iii) The age levels of the patients are different.

c) Erythem scarlatiniforme desquamativum recidivans or erythema scarlatiniforme[20]

Our syndrome differs from (c) above because:

i) It does not recur;

ii) The desquamation process starts mainly in the second week after onset; and

iii) It is associated with leukocytosis or a strawberry tongue.

d) Drug-induced eruptions

The relationship of this syndrome with drugs used prior to hospitalization is uncertain because precise information is not always available. Therefore as shown in Table 60, drug provocation (using a combination of 200 to 400/day of penicillin G powder, probenecid, Sinomin, chloramphenicol palmitate, Sulpyrine, and sulfisomidine) was conducted on 4 patients. Subsequently, all 4 had negative reactions. In addition, no recurrence of the eruption was noted in any of the original 50 patients. Therefore a possibility of drugs inducing eruptions was deemed highly unlikely.

e) Skin eruption caused by intoxication

Whether one calls it drug-induced eruption or toxic eruption in the absence of an identifiable causative agent, it becomes a mere supposition or a hypothetical diagnosis, and it is by no means definitive. Upon examining our patients, a dermatological specialist commented as follows: "If the examination is limited to one patient and the diagnosis is based on skin eruptions only, the condition may be called a toxic eruption. If one takes into account several other major symptoms, it can be now considered a syndrome with definitive clinical features rather than a simple toxic eruption." (a statement by Dr. Kakiuchi, Chief, Department of Dermatology, Japan Red Cross Hospital and Dr. Shigeo Nishiyama, Department of Dermatology, Kanto Teishin Hospital).

f) Gianotti-Crosti syndrome[21)22)]

This disease is also called acrodermatitis papulosa infantum or eine reaktive subakute Reticuloendothelitis, based on its histological features. It is an eruptive desquamating condition that affects children, especially infants. Our syndrome differs from this entity for the following reasons:

i）発疹の性状が異う．

ii）皮膚組織所見に，Gianotti-Crosti 症候群の如き特有な変化がない．

等の点で本症とは異う．

4） 眼皮膚粘膜症候群（M.C.O.S と略す）

1948年，Proppe は Dermatostomatitis (Baader), Ektodermosis erosiva pluriorificialis (Fiessinger und Rendu), Stevens-Johnson' sches Syndrom 及び Conjunctivitiset Stomatitis pseudomembranacea を同一の範疇に入れて，"Syndroma muco-cutaneo-oculare acutum Fuchs,, と呼び，Hebra[23] (1860) の所謂粘膜変化のない，多形滲出性紅斑 (E.e.m. と略) と区別した．この論文で同時に Ophthalmia lente (Gilbert[24]1920), Trisymptomenkomplex (Behçet[25]1937) を "periodisch rezidivierendes muco-cuatneo-oculares Syndrom" として区別している．然し，Proppe によると，この呼び方はすでに Franceschetti et Valerio (1939～1940) が，Fuchs'sches Syndrom に対して，"Gilbert'sches muco-cutaneo-oculares Syndrom" と名付けていたことを述べている．

恐らく"眼皮膚粘膜症候群"という名称は，Franceschetti et Valerio により1939～1940年にはじめて名付けられたものであろう．歴史的にみて，之等の疾患群は，Hebra (1866), Fuchs (1876), Duhring[26] (1896), Rendu[27] et Fiessinger[28] (1916, 1923), Stevens and Johnson[29] (1922), Baader[30] (1925) そして Proppe (1948) に至る，所謂多形滲出性紅斑の亜型と見做されるグループと，Bietisch[31] (1879), Neumann (1894), Gilbert (1920), Behçet (1937) 及び Franceschetti et Valerio (1939～1940) に至る所謂 Behçet 氏病及びその近縁疾患グループとに分けられる．之は1954年 Schreck[32] が眼科的な立場から，この両グループを分析して，前者を外胚葉系，即ち結膜や角膜等の Ektodermale Deckschicht が primär に犯されるので，Cutaneo-muco-oculoepitheliale Syndrome と呼び，後者は中胚葉系，即ち Mesodermale Tunica vasculosa des Auges (Uvea) が primär に犯されるのを特徴として，Cutaneo-muco-uveale Syndrome として区別した．この Schreck の分類は，病変の一部にもせよ，発生学的根拠を与えた論理的なもので，両者の相異点を明確にしたものと云えよう．

1950年 Robinson[33] が自験11例と共に文献的考察を行い，Behçet's disease, Stevens-Johnson disease, Reiter's disease[34] 及び Ectodermosis erosiva pluriorificialis (E.o.p と略す) の4疾患を muco-cutaneous ocular syndremes として分析し，Reiter's disease 以外は，E.e.m. の variants であろうと解釈した．然しこの解釈は，上記の Schreck の論文にまつまでもなく必ずしも当を得たものとは云えない．

この様に M.C.O.S の名称ははなはだ便利ではあるが，明かに臨床的には別の疾患をも同一の名称の下に包括したという欠点があつた．

日本の報告でも，小林[35]，西原[36]，佐方[37]等は，M.C.O.S の名称下で E.e.m.S を報告し，古沢[38]等は M.C.O.S の題名で実は Behçet 氏病を取り扱つているという具合で，その欠点が現われている．

1958年，文部省綜合研究班が"皮膚粘膜眼症候群の研究"を発足するに当り，先ず第1段階としてこの症候群の整理から取りかかつたのも，けだし当然と云えよう．その結果 M.C.O.S を，

1） 多形滲出性紅斑症候群

2)Behçet 病

3)Reiter 病

の3群に大別することになつた．西山[39]氏は，その研究結果から，Behçet 病を独立疾患として E.e.m.S. と明確に一線を引くべきことを強調している．

我々の症候群を若しこの分類に当てはめれば，E.e.m.S. に最も類似しているといえよう．

教科書では E.e.m.S. をどの様に解釈しているかというと，Fanconi[40]は，1) Die pluriorificielle Ektodermose と，2) Erythema exsudativum multiforme に2大別し，前者を更に，E.e.m mit Schleimhautbeteiligung, Ubergangsform 及び Pluriorificielle Ektodermose の3つに分けている．Nelson[41]では，Erythema multiforme exudativum (Stevens-Johnson syndrome) として1つの表題にまとめ，特に一部の重症型で開口部に変化のあるものを E.m.e. pluriorificialis と呼んでいる．Ormsby[42]は Erythema multiforme と Ectodermosis erosiva pluriorificialis とに分け，Sutton[43]は Erythema multiforme と Bullous, malignant Erythema multiforme とに，Handbuch der Haut-und Geschlechtskrankheiten[44]には Erythema exsudativum multiforme を，

a） Das idiopathische E.e.m. と，

i) The eruptions develop in a different pattern; and

ii) The histological findings lack the changes that are unique to the Gianotti-Costi syndrome.

4) Muco-cutaneous-ocular syndrome (M.C.O.S.)

In 1948, Proppe placed dermatostomatitis (Baader), Ektodermosis erosiva pluriorificialis (Fiessinger und Rendu), Stevens-Johnson'sches Syndrom and Conjunctivitiset Stomatitis pseudomembranacea in a single category of "Syndroma muco-cutaneo-oculare acutum Fuchs" and distinguished it from Hebra's (1860) so-called multiform exudative erythema (E.e.m.) without mucosal changes.[23] In the same study, Proppe distinguished Ophthalmia lente (Gilbert,[24] 1920) and Trisymptomenkomplex (Behçet[25] 1937) as "periodisch rezidivierendes muco-cutaneo-oculares Syndrom."[3] However, according to Proppe, this clinical entity had already been called "Gilbert'sches muco-cutaneo-oculares Syndrom" by Franceschetti et Valerio (1939-1940) to differentiate it from Fuschs'sches Syndrom.

Perhaps the term, "muco-cutaneous-ocular syndrome," was originally coined by Franceschetti et Valerio between 1939 and 1940. When historically traced, these syndromes may be divided into to a subtype of the so-called multiform exudative erythema proposed by a group of researchers, such as Hebra (1866), Fuchs (1876), Duhring[26] (1896), Rendu[27] et Fissinger[28] (1916, 1923), Stevens and Johnson[29] (1922), Baader[30] (1925), and Proppe (1948); and to Behçet's disease or related diseases suggested by a group that included Bietisch[31] (1879), Neumann (1894), Gilbert (1920), Behçet (1937), and Franceschetti et Valerio (1939-1940). In 1954, Schreck[32] analyzed the aforementioned categorizations from an ophthalmological viewpoint and called the former (multiform exudative erythema) cutaneo-muco-oculoepitheliale Syndrome [because the ectodermal system (Ektodermale Deckschicht), such as the conjunctiva and cornea, is primarily affected]; and he named the latter cutaneo-muco-uveale syndrome because the mesodermal system [Mesodermale Tunica vasculosa des Auges (uvea)] is primarily involved. It is believed that this classification by Schreck adds a logical basis for describing the embryological distinction of the disease (although it focuses on only part of the syndrome) and clearly distinguishes the difference between the two conditions.

In 1950, Robinson[33] reported 11 cases that he had observed, together with a review of the literature. He analyzed 4 conditions — Behçet's disease, Stevens-Johnson disease, Reiter's disease,[34] and Ectodermosis erosiva pluriorificialis (abbreviated to E.o.p.) — as a single entity of muco-cutaneous ocular syndrome and came to a conclusion that all except Reiter's disease are variants of E.e.m. However, this interpretation is not altogether convincing, even without reference to the thesis presented by Schreck.

The term, M.C.O.S. is a very convenient acronym but it is also associated with a shortcoming: it also includes other clinically different diseases.

Among Japanese researchers, Kobayashi,[35] Nishihara,[36] and Sakata[37] reported E.e.m.S. with an acronym of M.C.O.S., while Furusawa, et al[38] pointed out that a condition that is de facto Behçet's disease is included in the category of M.C.O.S. The inconsistency in nomenclature is also evident here.

In 1958, when the Comprehensive Research Group organized by the Ministry of Education launched a "Study of Muco-cutaneous-ocular syndrome," the group's first step was an effort to classify this syndrome in a more logical manner. Subsequently, M.C.O.S. was subdivided into the following 3 categories:

1) Multiform exudative erythema syndrome
2) Behçet's disease
3) Reiter disease

Based on the results of his study, Nishiyama[39] emphasized that Behçet's disease should be treated as an independent entity and clearly distinguished from E.e.m.S.

If this classification system is to be applied to our syndrome, it will come closest to E.e.m.S.

In perusing textbooks, one finds that E.e.m.S. has been interpreted variously: Fanconi[40] categorized the condition into 2 groups 1) Die pluriorifcielle Ektodermose, and 2) Erythema exudativum multiforme and further divided the former into E.e.m mit Schleimhautbeteiligung, Ubergangsform, and Pluriorificielle Ektodermose. Nelson[41] placed erythema multiforme exudativum (Stenvens-Johnson syndrome) into a single category and called its severe type with changes in the oral region E.m.e. pluriorificialis. Ormsby[42] divided the condition into two categories, erythema multiforme and ectodermosis erosiva pluriorificialis; and Sutton[43] divided the same condition into erythema multiforme and bullous malignant erythema multiforme. According to Handbuch der Haut-und Geschlechtskrankheiten,[44] erythema exudativum multiforme is roughly divided into the following two:

a) Das idiopathische E.e.m.

b) Die muco-cutaneo-ocularen Syndrome.

As described above, the classification varies widely, indicating that E.e.m.S has been described in various manners.

Yet its ambiguity (in being differentiated from the others) and uniqueness are amply exemplified in representative studies (e.g., Fuchs, Duhring, Rendu et Fiessinger, Stevens-Johnson, and Baader) since the

b) Die muco-cutaneo-ocularen Syndrome
に2大別している.

以上の如く，各自まちまちで，如何に E.e.m.S が，多種多様に解釈されているかが伺えよう.

之も Hebra 以降 Fuchs, Duhring, Rendu et Fiessinger, Stevens-Johnson, 及び Baader 等の代表的な個々の報告に，それぞれの類似性と独自性とが存するが故であろう.

然も今日，その病因が未だに解明されてないところに混乱の源がある様に思う.

以上の文献や教科書の記載と，我々の症例とを比較検討すると，どれも完全に一致すると思われるものはなかつた. 特に年令的分布では，1947年 Soll[45]は文献上の21例で2～9才が11例を占めていたが，乳児例は1例もなかつた.

1951年 Ashby[46]は81例の症例分析で，3才以下が僅か2例で，乳児例は1例もなかつた.

1957年桂[47]は，M.C.O.S. 119例中 E.e.m.S. が54例で，そのうち1才未満が2例，1～5才9例，6～11才4例で，小児特に乳幼児が少かつた.

1959年井手等[48]は，M.C.O.S. 200例以上の中で，2才以下は4例であつた.

1961年高橋[59]等は，M.C.O.S 200例中 E.e.m.S. が100例で，10才以下約20例，そのうち2才以下は3例にすぎなかつた. と，

1963年 Clexton[50]は2才から72才迄の31例の報告で，9才迄の小児例が11例含まれているが，乳児例の記載はなかつた.

前述の Fanconi の教科書の Pluriorificielle Ektodermose の記載の中では，spätere Kleinkindesalter に多いと記されている.

以上の点から従来の M.C.O.S 乃至は E.e.m.S. の概念では2才以下の乳幼児には極めて頻度が低いことが伺える.

1960年糸賀，山岸氏[51]は，“小児の粘膜，皮膚，眼症候群の下垂体副腎皮質ホルモンによる治療経験”と題する報告で，その症例20例中2才未満が14例（70%）を占め，“従来の文献と較べ，特徴的と言える”. とその年令層の特徴を記している. 私が検べたところでは，内外の文献中2才未満を主体とした M.C.O.S. の報告は，氏等の報告しか見当らなかつた.

氏等の報告例は，色々な点で，我々の症例とよく類似しているが，然しよく検討すると，重要な症状上の相異点がいくつかみられる. 即ち，

1) 皮膚症状……氏等は“全例に全経過を通じ紅斑，丘疹，水疱，落屑等が略々全身に，時として新旧雑然と相混在した”. と記している.

我々の例では，紅斑の存在中に落屑の始まつた例はあるが，水疱を形成した例は1例もなかつた. この点は極めて重要な皮膚所見上の相異点である. 落屑について氏等は，“新たな発疹出現停止と同時に全例で，程度に応じた落屑を数日～20日以上みた”. と記している. 我々の症候群の落屑は極めて特徴的で，“爪皮膚移行部から始まり両手，両足以外には膜様落屑を見ない”. ことである.

2) 眼症状……氏等は“全例に結膜炎乃至は結膜炎様の所見を認めた”. と記しているが，我々の例では単なる結膜炎というよりは，全身の血管結合織反応の一部分現象と思われる. 両側の眼球結膜の充血（実際は毛細血管拡張と呼ぶべきか）が特徴である.

3) 粘膜症状……氏等は“口腔粘膜で特記されたのは，偽膜1例，アフタ糜爛，出血，潰瘍，鵞口瘡等10例である”. と述べている. 我々の症例では，口唇の乾燥，発赤，糜爛，皺裂，口腔粘膜全体の瀰蔓性の充血で，アフタ，潰瘍或は偽膜の形成のない点が特徴である.

4) 頸部淋巴腺腫脹……氏等の症例では，“7例（35%）に認められた”. と記されているが，我々の症例では33例（66%）と約倍近い頻度にみられた.

以上我々の症例と糸賀，山岸氏の症例とを比較し，その特徴の相異点を指摘した.

今迄色々と我々の症候群と M.C.O.S. 乃至は E.e.m.S-との関係について述べて来たが，ここで，1954年 Wechselberg[52]が Glanzmann 及び Fanconi の分類を基にした “Polymorphe Ektodermose” の表をみてみる必要があろう. この表にある，Glanzmann の Ectodermose érosive pluriorificielle Typus 1, Fanconi の Übergangsform 及び Wechselberg の Leichte-mittelschwere Übergangsform の概念は，我々の症候群の帰属の将来に重要な意義を持つかも知れない.

然し乍ら，私はこの特殊な年令層にみられる，一定の特有な臨床像をもつた症候群を，現在の時点では無理に既存の疾患乃至は症候群の概念に当てはめないで，上述の如く，その臨床的観察のままを報告した次第であ

days of Hebra.

It appears that the current confusion concerning this syndrome stems from a lack of a valid etiological explanation.

When our syndrome was compared with the descriptions in the literature and textbooks cited above, there was no clear concurrence with any of them. Concerning the age distribution in particular, Soll[45] in 1947 stated that 11 of the 21 cases cited in the literature were of ages ranging from 2 to 9 years; but this group of patients did not include a single infant.

In 1951, Ashby[46] conducted an analysis of 81 cases and reported that only 2 were under the age of 3 years and there were no infants.

Katsura,[47] in his 1957 study, stated that of 119 cases of M.C.O.S., 54 in the following age range were affected by E.e.m.S.: 2 under 1 year, 9 between 1 and 5, and 4 between 6 and 11. Young children, especially infants, were conspicuously rare.

Ide, et al[48] reporting in 1959, stated that there were only 4 under the age of 2 years among 200 patients with M.C.O.S.

In 1961, Takahashi, et al[59] stated that among 200 patients with M.C.O.S., 100 suffered from E.e.m.S.; and of these 100, about 20 were under 10 years of age and only 3 of these were under 2.

A 1963 study conducted by Clexon[50] on 31 cases involving individuals between the ages of 2 and 72 included 11 children but there was no description of any infants.

In the description on Pluriorificielle Ektodermose that appears in Fanconi's textbook cited above, it is stated that the condition occurs frequently in spätere Kleinkindesalter.

From all these descriptions of M.C.O.S. or E.e.m.S., their occurrence among infants under 2 years of age appear very low.

A 1960 report entitled "Experience in the use of pituitary adrenocortical hormones for muco-cutaneous-ocular syndrome in young children" by Itoga and Yamagishi[51] found that 14 of the 20 patients observed (70%) were under 2 years. They stated that this age distribution was "unique compared with what has been reported." From the current author's search of the literature, this is the sole reference to M.C.O.S. that focused on incidences among those under 2 years of age.

The cases described by Itoga and Yamagishi closely resemble ours in many aspects. However on closer examination, there are several disparities in important symptoms, such as those listed below:

1) Skin symptoms:

Itoga and Yamagishi described the symptoms as: "erythema, papules, blisters, and desquamation, which are in the total body, affecting all patients, and present throughout the clinical course, with occasional co-existence of new and old lesions."

Among our cases, some developed desquamation while the skin was still erythematous but none of the patients developed blisters. This appears to be an extremely important difference in dermatological findings. For desquamation, Itoga and Yamagishi stated that "all developed the desquamation process (its extent corresponding to the severity of skin conditions) within several to 20 days when eruptions ceased to develop anew." We found that desquamation in our syndrome is extremely unique, "starting at the nail-skin junction but no membranous desquamation seen at sites other than the hands or feet."

2) Ocular symptoms:

Itoga and Yamagishi stated that "conjunctivitis or conjunctivitis-like symptoms were found in all." The ocular characteristic found in our cases was congestion of both bulbar conjunctivae (perhaps dilatation of the capillaries), which was suspected to be part of the response of the systemic vascular connective tissue.

3) Mucosal symptoms:

According to Itoga and Yamagishi, "the findings on the oral mucosa included pseudomembrane formation in one, aphthous erosion, hemorrhage, ulcer formation, thrush, and others in 10." Our patients developed dryness, erythema, erosion, and cracking of the lips and diffuse hyperemia affecting the entire oral mucosa. The absence of aphtha, ulcers, or pseudomenbranes was characteristic of our syndrome.

4) Cervical lymph node swelling:

Among the cases observed by Itoga and Yamagishi, "7 (35%) developed this condition." The incidence of this lymphatic symptom was almost double (33 cases or 66%) among our patients.

Thus one cannot deny that there are some outstanding differences between the cases observed by Itoga and Yamagishi and those described here.

The relationship between our syndrome and M.C.O.S. or E.e.m.S. has been discussed. It would be meaningful here to examine the table of "Polymorphe Ektodermose" prepared in 1954 by Wechselberg[52] on the classification by Glanzmann and Fanconi. The concepts of Glanzmann's Ectodermose érosive pluriorificielle Typus 1, Fanconi's Übergangsform, and Wechselberg's Leichte-mitelschwere Übergangsform expressed in this table may have a significant bearing on the future classification of this syndrome.

This syndrome — with its specific and unique clinical features that develop only in a certain age group — has been presented as clinical observations, without forcing it to fit into the concepts of pre-existing diseases or syndromes.

Photo legends (page 213-217)

Photo [1] (page 213, upper left) patient No. 15: Lymph node swelling on the right side of the neck; hyperemia of bilateral bulbar conjunctivae; and erythema, drying, erosiveness, and cracking in part of the lips.

Photo [2] (page 213, upper right) patient No. 26: Hyperemia of bilateral bulbar conjunctivae; and erythema, drying, erosion, and cracking of the lips.

Photo [3] (page 213, middle left) patient No. 14: Erythema, erosiveness, and cracking of the lips; and eruptions on bilateral cheeks, chin, and anterior thorax.

Photo [4] (page 213, middle right) patient No. 22: Lymph node swelling on the left side of the neck; and hyperemia of lips and bilateral ear lobes.

Photo [5] (page 213, lower left) patient No. 15: Typical erythema on a palm.

Photo [6] (page 213, lower right) patient No. 15: Erythema of the dorsa of the hands, particularly notable on the fingers and borders.

Photo [7] (page 214, upper left) patient No. 15: Typical erythema of the soles of the feet.

Photo [8] (page 214, upper right) patient No. 15: Erythema of the dorsa of the feet, particularly notable on the heels and the edges.

Photo [9] (page 214, middle left) patient No. 15: Skin eruptions involving the anterior thorax and abdomen.

Photo [10] (page 214, middle right) patient No. 15: Skin eruptions on the neck and axillary regions.

Photo [11] (page 214, lower left) patient No. 15: Skin eruptions on the nape and back.

Photo [12] (page 214, lower right) patient No. 15: Skin eruptions on the lumbar region and buttocks.

Photo [13] (page 215, upper left) patient No. 15: Typical start of the desquamation process at the nail-skin junction of the fingers.

Photo [14] (page 215, upper right) patient No. 15: Typical membranous desquamation starting at the nail-skin junction of a finger.

Photo [15] (page 215, middle left) patient No. 30: Membranous desquamation at a toe: note a biopsy scar on the left second toe.

Photo [16] (page 215, middle right) patient No. 26: Hyperemia of the bulbar conjunctiva.

Photo [17] (page 215, lower left) patient No. 11: Swelling of a lymph node at the left side of the neck; drying, and cracking of the lips; and hyperemia of bilateral bulbar conjunctivae.

Photo [18] (page 215, lower right) patient No. 39: Hyperemia of bilateral bulbar conjunctivae; and erythematous eruptions involving the thoraco-abdominal region and arms.

Photo [19] (page 216, upper left) patient No. 26: Hyperemia of the bulbar conjunctiva (limited to the right side) and catarrhal change of the nares.

Photo [20] (page 216, upper right) patient No. 37: Erythematous eruptions involving the back and buttocks.

Photo [21] (page 216, middle left) patient No. 37: Skin eruptions on the face, trunk, and extremities (especially, diffuse erythema of the right hand).

Photo [22] (page 216, middle right) patient No. 22: Angioneurotic edema-like swelling of the dorsa of bilateral hands and all fingers.

Photo [23] (page 216, lower left) Patient No. 22: Angioneurotic edema-like swelling of the palms of bilateral hands and all fingers.

Photo [24] (page 216, lower right) patient No. 22: Angioneurotic edema-like swelling of the dorsa of bilateral feet and toes.

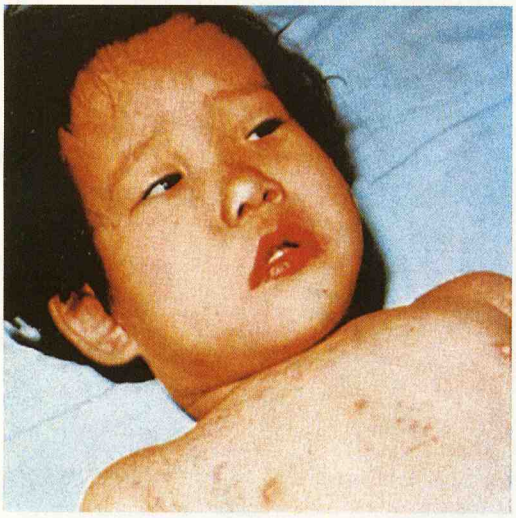
Photo [25] (page 217, upper left) patient No. 22: Angioneurotic edema-like swelling of the soles of bilateral feet and entire back of the toes.

Photo [26] (page 217, upper right) patient No. 15: Typical desquamation of all fingertips.

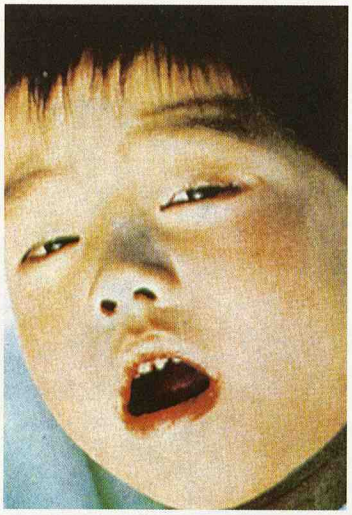
Photo [27] (page 217 middle left) patient No. 37: Membranous desquamation of the fingertips.

Photo [28] (page 217, middle right) patient No. 11: Membranous desquamation of the ends of the toes.

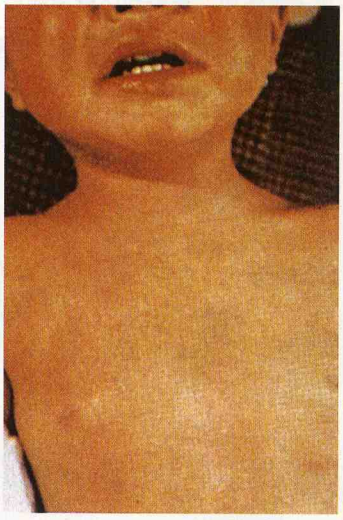
写真〔1〕症例No. 15市木例　右頚部淋巴腺腫脹両側眼球結膜充血口唇発赤，乾燥，糜爛及び一部皺裂



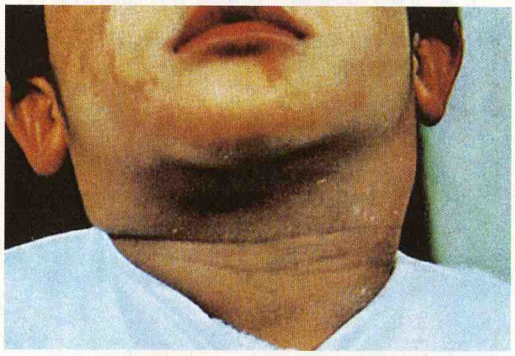
写真〔2〕症例No. 26加藤例　両側眼球結膜充血口唇発赤，乾燥，糜爛及び皺裂



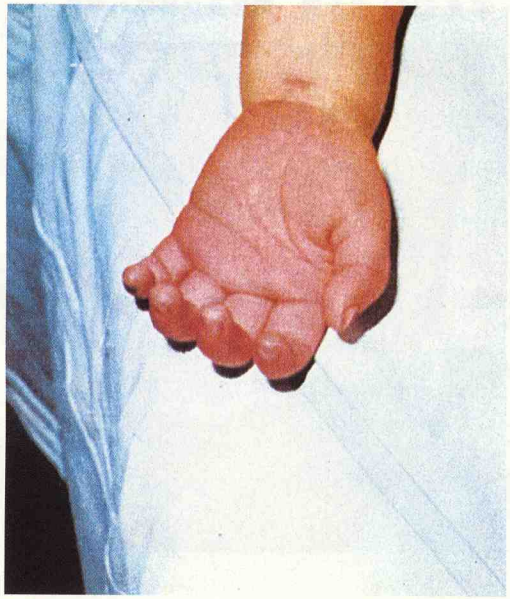
写真〔3〕症例No. 14奥山例口唇発赤，糜爛，皺裂両頬，頤，前胸部の発疹



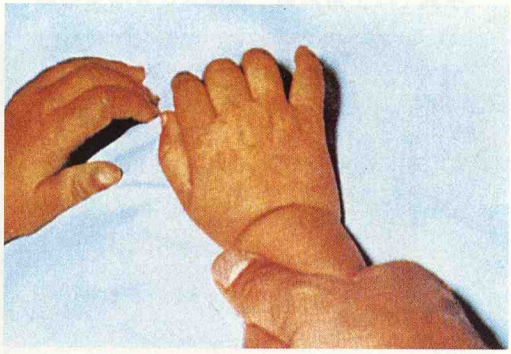
写真〔4〕症例No. 22竹浪例　左頚部淋巴腺腫脹口唇充血両側耳介充血



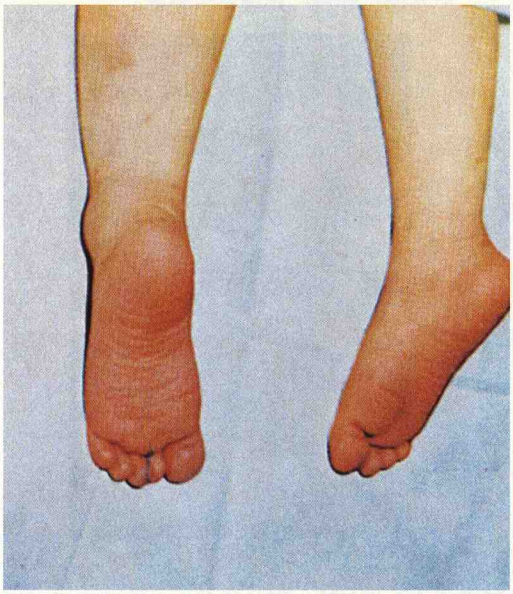
写真〔5〕市木例　定型的な手掌の紅斑



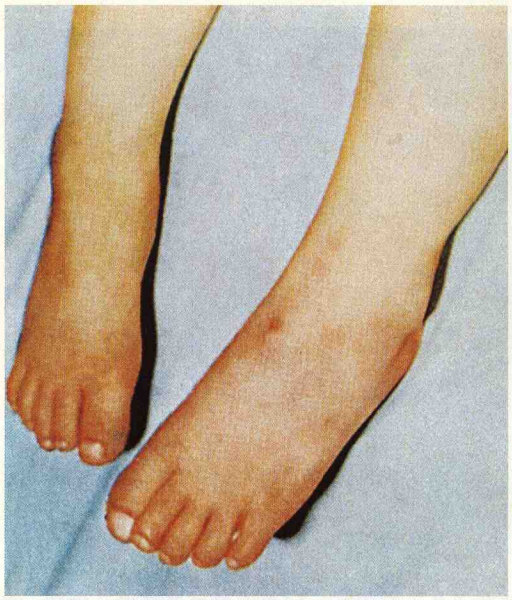
写真〔6〕市木例　手甲の紅斑特に指及び辺縁部に顕著



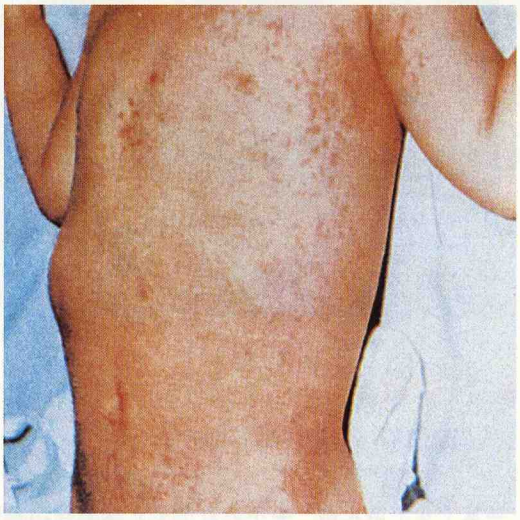
写真〔7〕市木例　定型的な足蹠の紅斑



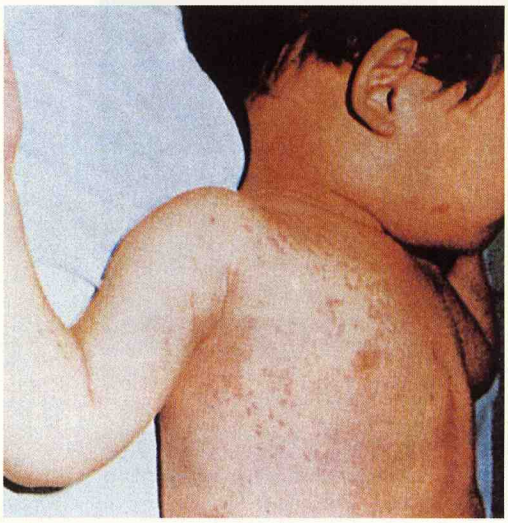
写真〔8〕市木例足背の紅斑特に趾及び辺縁部にみられる



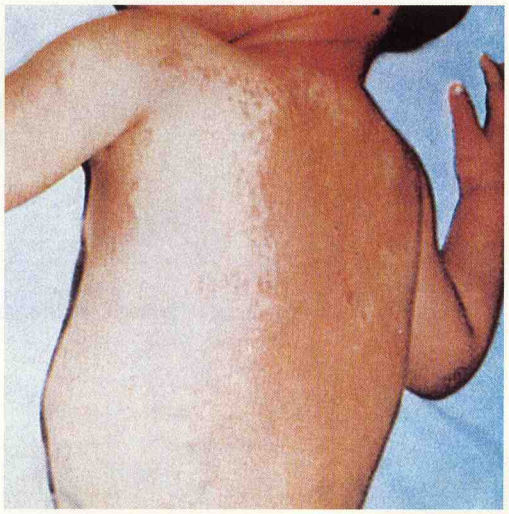
写真〔9〕市木例　前胸部及び腹部の発疹



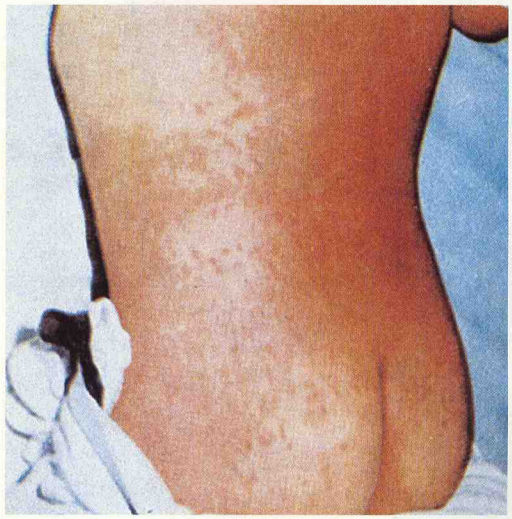
写真〔10〕市木例　頚部及び腋窩部の発疹



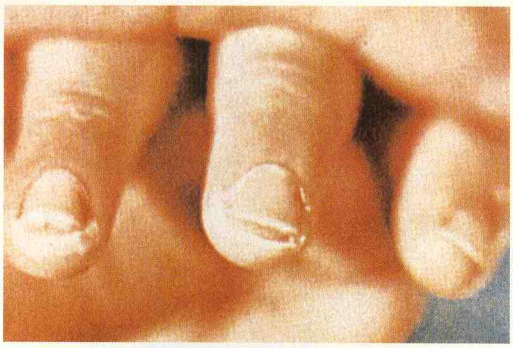
写真〔11〕市木例　項部及び背部の発疹



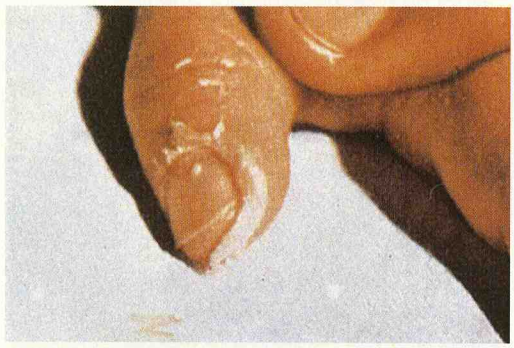
写真〔12〕市木例　腰部及び臀部の発疹



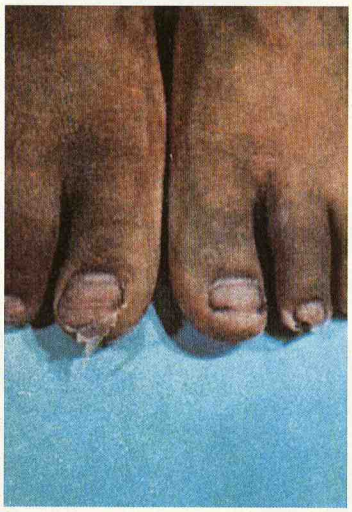
写真〔13〕市木例　定型的な指先の爪皮膚移行部よりの膜様落屑のはじまり



写真〔14〕市木例　拇指先の爪皮膚移行部よりの定型的な膜様落屑

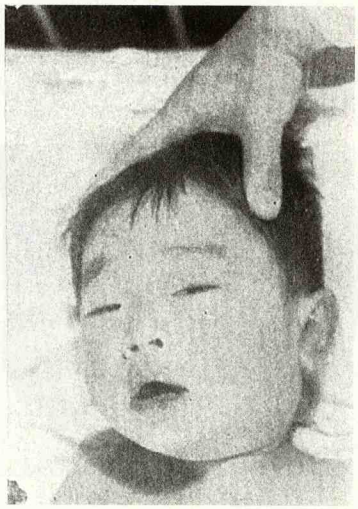


写真〔15〕症例No. 30矢島例　趾先の膜様落屑左第二趾先に生検の痕跡あり

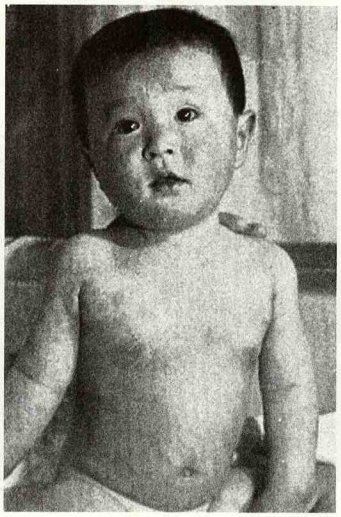


写真〔16〕症例No. 26加藤例　眼球結膜充血

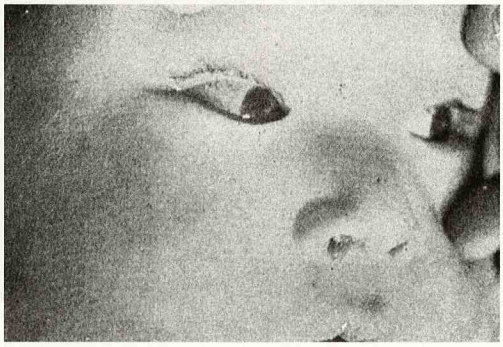
写真〔18〕症例No. 39海老沢例両側眼球結膜充血胸部，腹部　上肢の紅斑様発疹



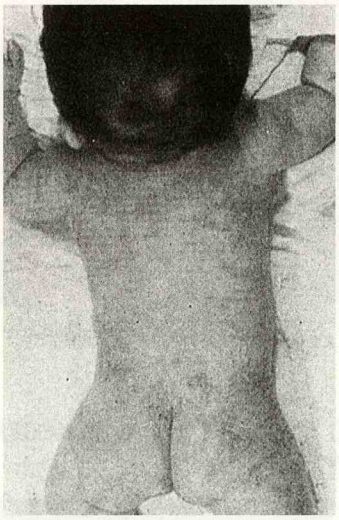
写真〔18〕症例No. 39海老沢例両側眼球結膜充血胸部，腹部　上肢の紅斑様発疹



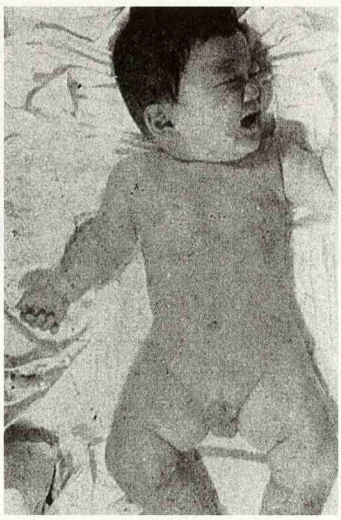
写真〔19〕症例No. 26加藤例　眼球結膜充血（右側のみ）及び鼻入口のカタル性変化



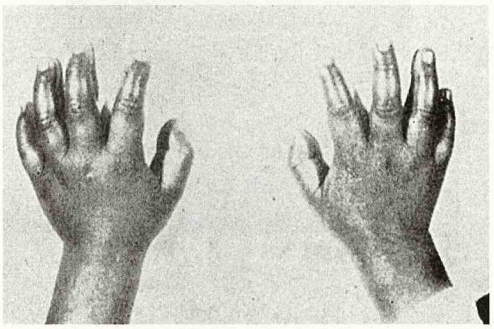
写真〔20〕症例No. 37呉例　背部　臀部の紅斑様発疹



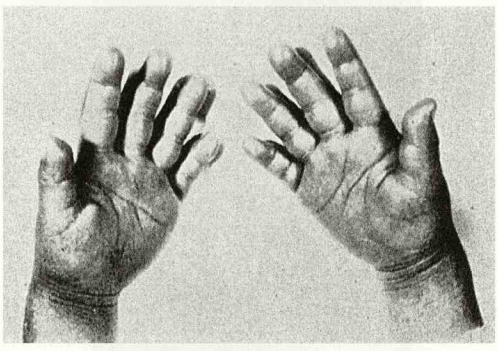
写真〔21〕呉例　顔，躯幹，四肢の発疹（特に右手の瀰蔓性紅斑）



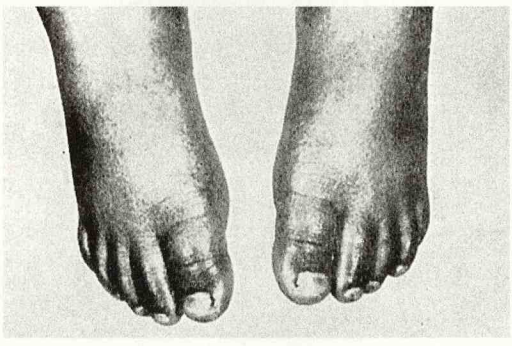
写真〔22〕症例No. 22竹浪例両手甲及び全指の血管神経性浮腫様腫脹



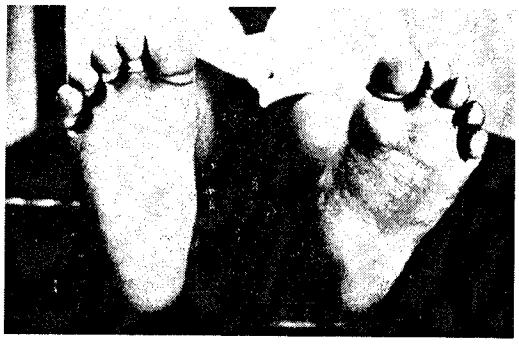
写真〔23〕竹浪例　両手掌，全指裏の血管神経性浮腫様腫脹



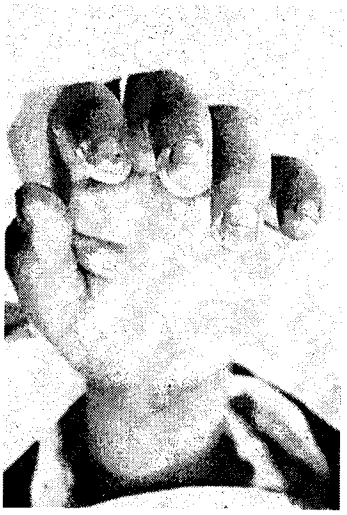
写真〔24〕竹浪例　両足背，全趾の血管神経性浮腫様腫脹



写真〔25〕竹浪例　両足蹠及び全趾裏の血管神経性浮腫様腫脹

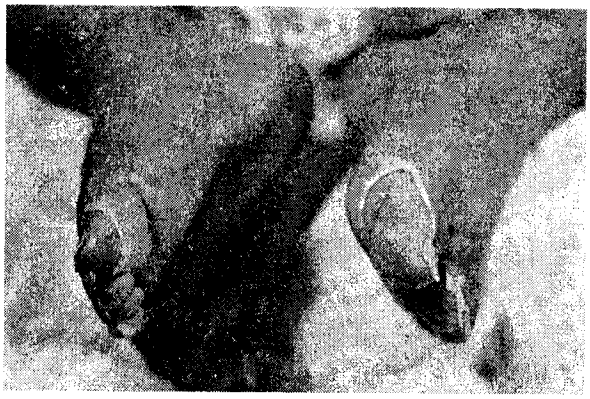


写真〔26〕市木例　全指先の定型的落屑



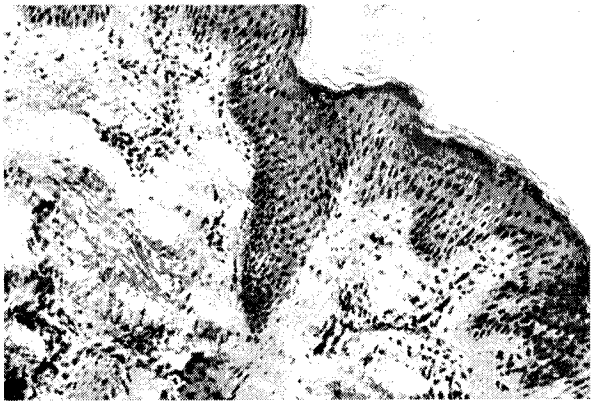
写真〔27〕症例No. 37具例　指先の膜様落屑

写真〔28〕高柳例　趾先の膜様落屑

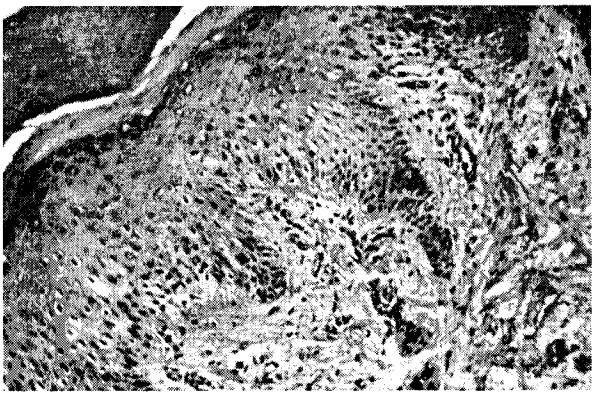


皮膚組織顕微鏡写真

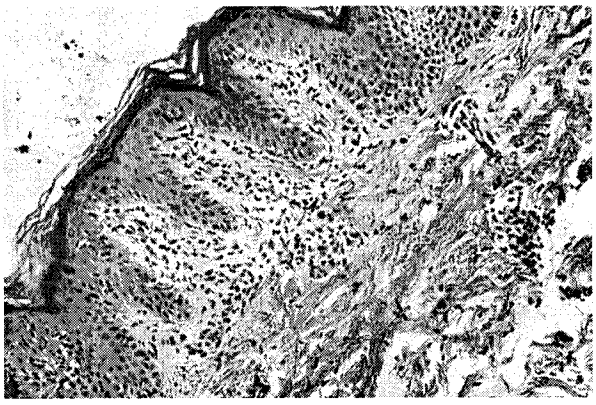
S－1　内山例　表皮直下の浮腫と毛細血管周囲の細胞浸潤



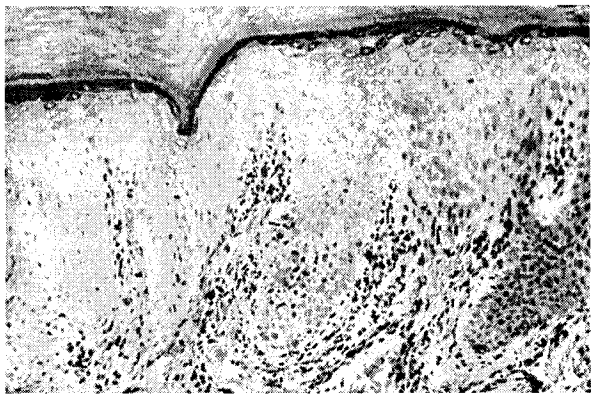
S－2　内山例　爪－皮膚接際部：角質層の剝脱と表皮直下の浮腫と毛細血管周囲の軽度の淋巴球，白血球浸潤



S－3　永沼例　表皮直下の浮腫と毛細血管周囲のかなり著しい細胞浸潤

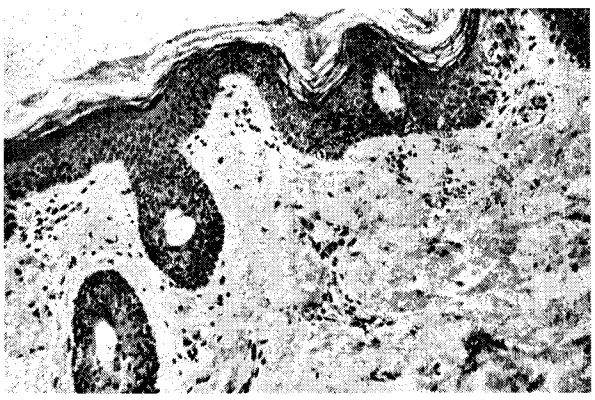


S－4　永沼例　爪－皮膚接際部：表皮直下のかなり顕著な毛細血管周囲細胞浸潤（淋巴球，単球，白血球）

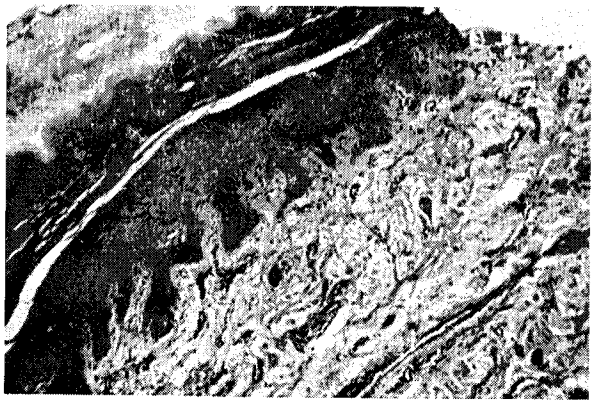


S－5　加藤例　角質層よりの剝脱

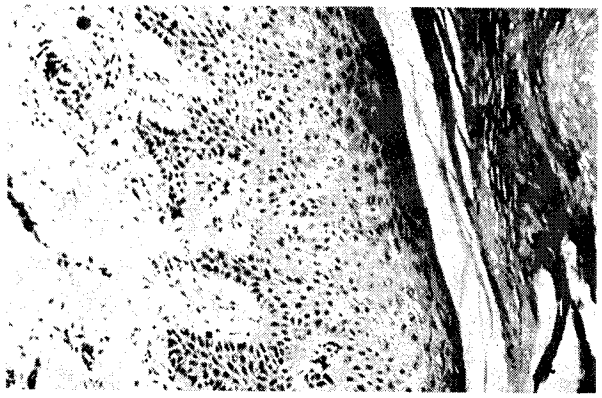
S－6　海老沢例　表皮直下の著しい浮腫，毛細血管拡張及び軽度の血管周囲細胞浸潤



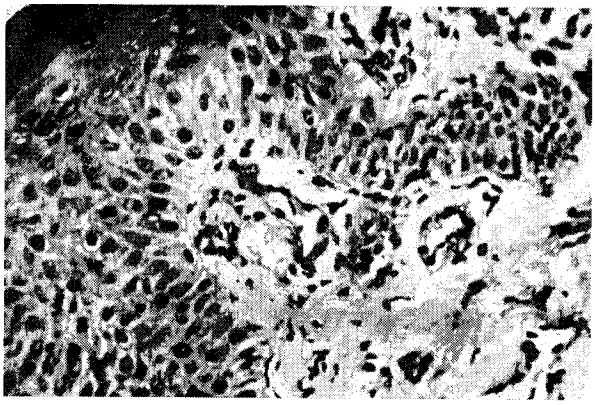
S－7　矢島例　爪—皮膚接際部：角質層よりの剝脱



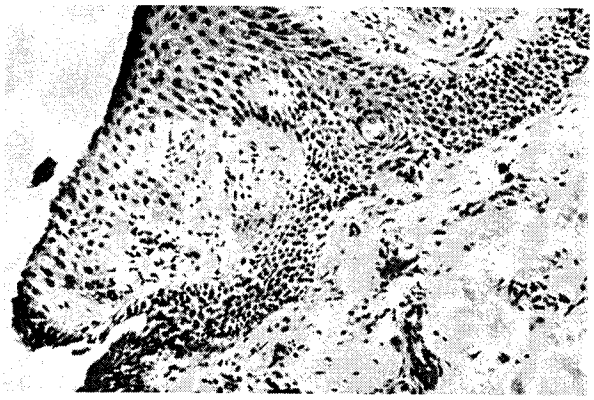
S－8　矢島例　角質層の剝脱と表皮直下の浮腫軽度の血管周囲細胞浸潤



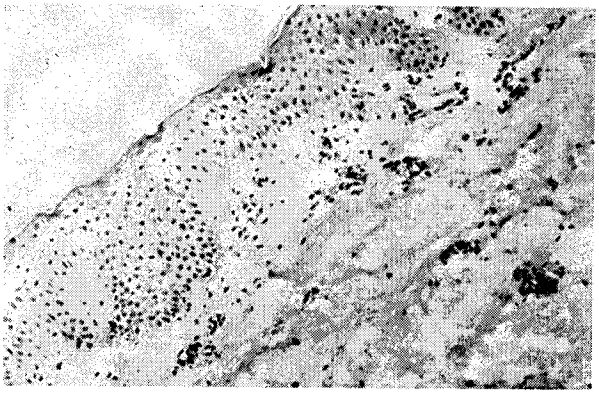
S－9　矢島例：強拡大表皮直下の浮腫，毛細血管拡張及び軽度の血管周囲細胞浸潤



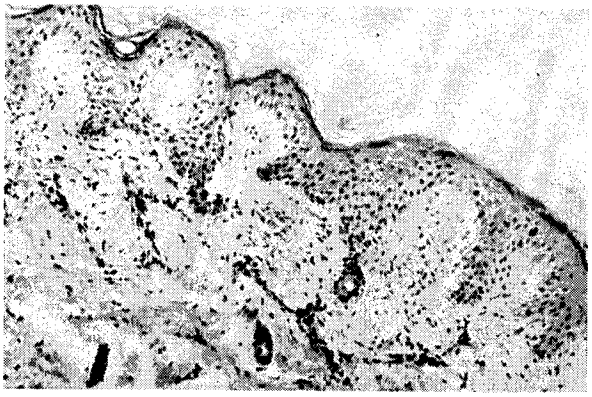
S—10　市木例　表皮角質層は完全に剝脱，表皮直下の浮腫と軽度の血管周囲細胞浸潤



S—11　市木例　皮下組織特に表皮直下の浮腫が著しい．

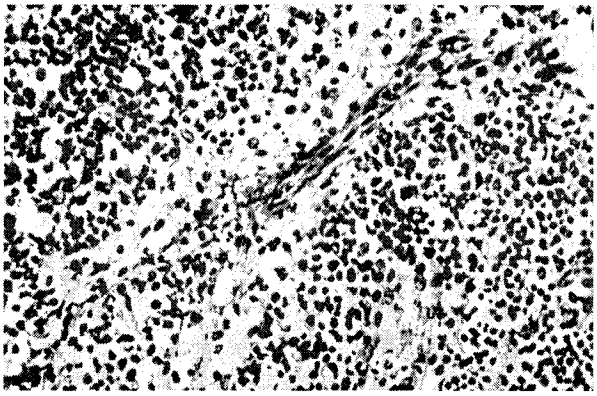


S—12　原例　表皮直下の水疱形成，表皮の剝脱及び表皮直下の浮腫著明，軽度の血管周囲細胞浸潤

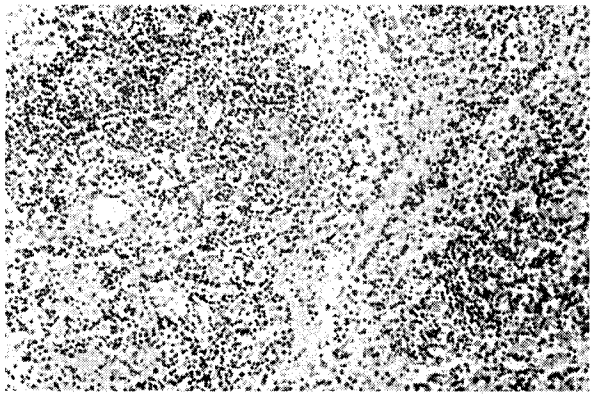


頸部淋巴腺組織顕微鏡写真

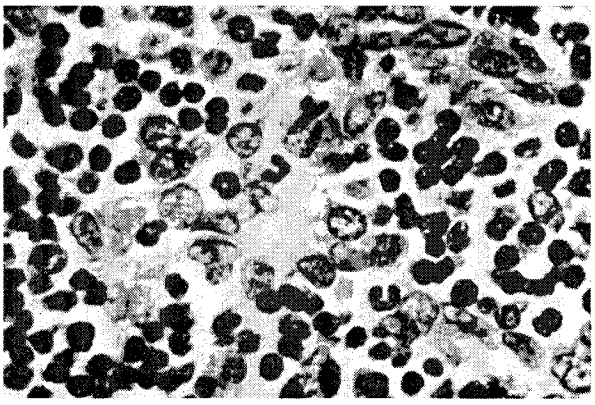
L—1　加藤例：リンパ節洞カタルを主体とする非特異性慢性淋巴腺炎小節の白血球浸潤



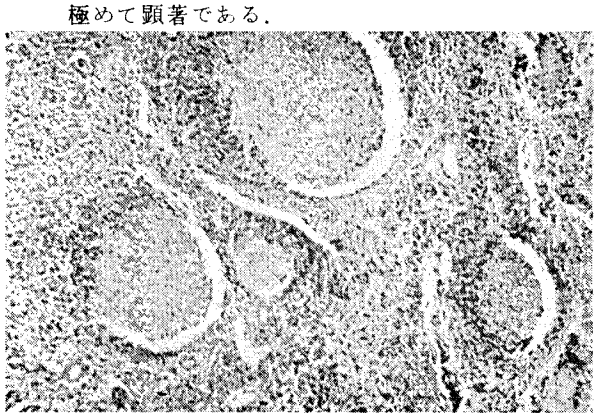
L—2　山本例：リンパ節洞カタル，post-capillary venule の異常な増殖，濾胞腫大を欠く



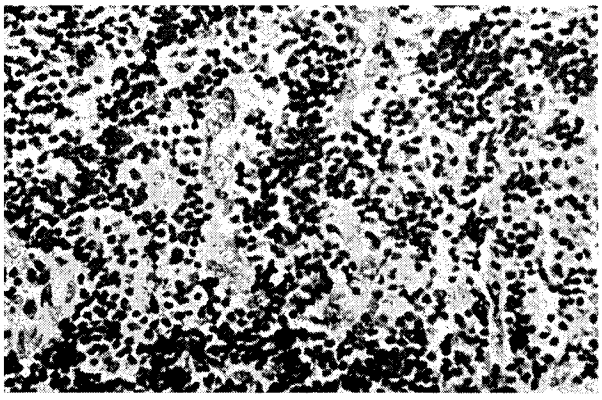
L—3　山本例：強拡大 post-capillary venule の内皮細胞の異常な腫大及びその周囲における細網細胞増生



L—4　原例：リンパ節二次小節（濾胞）の発達が極めて顕著である．



L—5　原例　実質内の post-capillary venule の著明な発達及びその内皮細胞の著しい腫大



L—6　原例：強拡大 post-capillary venule の内皮細胞腫大と白血球を混ずる炎症細胞浸潤及びその周囲の細網細胞増生

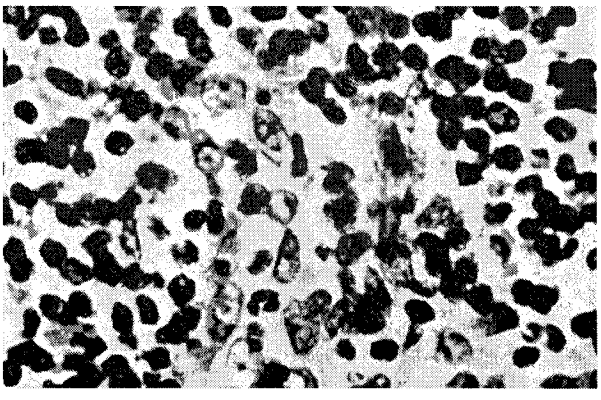


Photo legends (page 218-220)

Photomicrography of the skin

S-1 (page 218, upper left) patient No. 36: Edema and perivascular infiltrate of leukocytes in the upper dermis.

S-2 (page 218, upper right) patient No. 36: The nail-skin junction: Desquamation of the horny layer in the epidermis, edema and mild perivascular infiltrate of leukocytes in the upper dermis.

S-3 (page 218, middle left) patient No. 41: Edema and marked perivascular infiltrate of leukocytes in the upper dermis.

S-4 (page 218, middle right) patient No. 41: The nail-skin junction: Prominent perivascular infiltrate of lymphocytes and monocytes in the upper dermis.

S-5 (page 218, lower left) patient No. 26: Desquamation of the horny layer in the epidermis.

S-6 (page 218, lower right) patient No. 39: Prominent edema, capillary dilatation and mild perivascular cellular infiltrate in the upper dermis.

S-7 (page 219, upper left) patient No. 30: The nail-skin junction. Desquamated horny layer in the epidermis.

S-8 (page 219, upper right) patient No. 30: Detachment of the horny layer from the epidermis, edema and mild perivascular infiltrate in the upper dermis.

S-9 (page 219, middle left) patient No. 30: Edema, capillary dilatation and mild perivascular cellular infiltrate in the papillary dermis.

S-10 (page 219 middle right) patient No. 15: Complete desquamation of the horny layer, edema and mild perivascular infiltrate in the upper dermis.

S-11 (page 219, lower left) patient No. 15: Marked edema of the dermis, especially prominent in immediately beneath the epidermis.

S-12 (page 219, lower right) patient No. 1: Blister formation immediately beneath the epidermis, marked edema in the upper dermis, and slight perivascular infiltrate.

Photomicrography of the cervical lymph nodes

L-1 (page 220, upper left) patient No. 26: Non-specific chronic lymph-adenitis showing sinus catarrh with leukocyte infiltration.

L-2 (page 220, upper right) patient No. 6: Lymph-node sinus catarrh, distended sinus with histiocytes and lymphocytes, proliferation of the post-capillary venules without lymphoid follicle hyperplasia.

L-3 (page 220, middle left) patient No. 6: Marked swelling of the endothelial cells of post-capillary venule and hyperplasia of reticulum cells around the lesion.

L-4 (page 220, middle right) patient No. 1: Prominent enlargement of the reactive germinal centers.

L-5 (page 220, lower left) patient No. 1: Prominent proliferation of post-capillary venules and swollen endothelial cells in the parenchyma.

L-6 (page 220, lower right) patient No. 1: The endothelial cell swelling, intermingling leukocytes of the post-capillary venules, hyperplasia of reticulum cells around the lesion.

る.

本症候群の原因については，目下検索中なので，いずれ第2報として報告する予定である.

8. 結 語

私は，頸部淋巴腺腫脹，両側眼球結膜充血，口唇の乾燥，発赤，糜爛，皸裂，口腔粘膜の瀰蔓性充血及び指趾先の爪皮膚移行部よりの膜様落屑を特徴とする，主として乳幼児にみられる，急性熱性紅斑性疾患群の自験例50例について，その臨床的特徴，検査所見及び治療成績の概要を述べ，文献的考察の結果，本症候群は従来迄に報告されたどの疾患にも属さない症候群としての可能性について言及した.

稿を終るに当り，終始御懇篤なる御指導，御鞭撻をして戴き，御校閲の労を賜つた部長神前先生に深甚なる謝意を表します.

亦ウイルス学的検索に絶大なる御協力を戴きつつある予研芦原義守先生，ＰＰＬＯの検査をお願いした伝研中村先生，皮膚科学的立場から種々有益な示唆を賜つた関東逓信病院皮膚科西山茂夫先生，東大皮膚科笹川正二先生，小児科学的立場から種々御教示を賜つた愛育病院内藤寿七郎先生，関東逓信病院中村兼次先生，貴重な症例を数多くお送り戴いた小久保裕先生，井口正美先生，木島英夫先生居谷健吾先生，大木輝代恵先生，実際の症例につき種々御教示戴いた当院皮膚科垣内先生，宮本先生，内科松井先生，耳鼻科小倉先生，眼科梶先生，外科的立場から御協力戴いた外科太中先生，梶谷先生，病理学的立場から種々御教示及び御協力を戴いた病理田中先生，並に終始症例につき御協力を戴いた医局の麻生，坂田，青木，久保，窪田，清水，竹内，吉野の諸先生方に深謝致します.

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2のb) Franceschetti A, and Valerio, M.: L'uveite recidivante (ad ipopion) manifestazione parziale di una sindrome muco-cutaneous-oculare, Rassegna ital. dottal, 9: 1 (1940). ……33) Robinson より引用.
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For the etiology of this syndrome, studies are underway and the results will be presented as a second report.

8. Conclusion

We described our personal experience with 50 patients with an acute febrile erythematous syndrome, which occurs mainly in infants and is characterized by swelling of the cervical lymph node, hyperemia of both bulbar conjunctivae, dryness, erythema, erosion, and cracking of the lips, diffuse congestion of the oral mucosa, and desquamation that starts at the nail-skin junction of the fingers and toes, including outlines of their clinical features, results of their laboratory tests and their treatment results. From the literature search, one may infer that this is possibly a syndrome which does not belong to any of the diseases that have been reported.

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