CHAPTER IV

RESULTS

Retrospective Results

There were 306 patients in the study, 141 were male and 165 were female. Age of the patients ranged from 2 month to 78 years. About one-fourth of the patients were 16-30 years of age (82 cases). Others were less than 15 years of age (66 cases), 31-45 years of age (64 cases), 46-60 years of age (61 cases) and more than 60 years of age (33 cases) (Fig. 1)

Table 1 showed the distribution of age of patients who were treated with CAP in 4 different departments. Sixty-one percent of the patients (186 out of 306) who received CAP during hospitalization were from the Department of Surgery and 20% were from the Department of Pediatrics. In pediatric wards, infant less than one years of age used CAP more often than other age groups. Others were aged 1 to 2 years (6 cases), 2 to 5 years (9 cases), 5 to 10 years (17 cases) and 10 to 15 years (18 cases). (Fig. 2)

Duration of CAP treatment varied from 1 to 42 days as shown in table 2. One hundred and forty out of 306 patients (45.8%) were treated with CAP for 8 to 14 days. But 130 (42.5%), 24 (7.8%), 10 (3.3%) and 2 (0.7%) cases were treated with CAP for a period of 1 to 7 days, 15 to 21 days, 22 to 35 days and more than 35 days (5 weeks), respectively.

There were 3 methods of CAP administration. They were intravenous infusion alone, intravenous infusion followed by oral ingestion and oral route alone. The duration and percentage of patients in various routes of administration were shown in Fig. 3,4. Fifty percent of the patients received CAP by intravenous route followed by oral with total duration ranged from 4-42 days. Intravenous route alone were used in 37.4% of cases. The range of treatment varied from 1-29 days. Only 12.6% were treated with oral route alone, for the period varied from 3-21 days.

Doses of CAP in adults were given in g/day in 4 divided doses, but doses in infant and children were calculated in mg/kg/day, in 4 divided doses. Table 3 showed the doses per day of CAP and number of patients in each dosage from four departments. The dose of 2 g/day (500 mg every 6 hours) was most commonly used (71.6%) in adult patients. But in pediatric ward, the dose of 75-100 mg/kg/day was most commonly used (31 out of 47 cases). The dose of 2 g/day, or approximately 25-50 mg/kg/day, was mostly used in Ramathibodi Hospital (71.6%). (Fig. 5)

Table 4 showed the indication of CAP treatment by systems. Central nervous system infections were the most common indication for using CAP (47.4%); they included miningitis and prophylactic treatment for craniectomy, meningocelectomy and others. The second indication involved gastro-intestinal system (28.4%); which included appendicitis, cholecystectomy and others, most of them needed surgery. The third indication involved dermatologic system (10.1%). Most of them were

suspected to have anaerobic infection, such as; gangrene, bed sore, cellulitis, etc. The other indications were genitourinary system (3.3%), pulmonary system (1.6%), skeleton system (1.6%) and others (7.5%).

The total suspected incidences of ADR from CAP was 11.11% (34 out of 306 patients), 15 of them were female and 19 were male. There was no significant difference between sex and ADR as analyzed by chi-square test. ($P > 0.05$)

Table 5, 6 showed 41 incidences of ADR that occurred during CAP therapy in 34 patients. In table 5, 5 cases (patient no. 15, 16, 18, 21, 23) had more than one type of ADR. Ten cases (patient no. 1, 6, 9, 11, 18 22, 23, 25, 29, 34) had elevated SGOT before CAP treatment, the cause of increased transaminase enzymes probably dued to liver impairment. Thirteen cases (patient no. 4, 5, 7, 8, 15, 16, 20, 25, 26, 27, 31, 32, 33) developed slightly anemic before CAP treatment which might be caused by iron deficiency, nutritional anemia or hemolysis.

Patient no. 9 had slightly elevated BUN before CAP treatment but cause of this problem was not known. Patient no. 10, 25 had elevated BUN before CAP treatment probably due to aminoglycoside therapy (amikacin, dibekacin, gentamicin).

Patient no. 13 developed nausea, vomiting during PGS and CAP treatment however it occurred a few days after craniectomy which might cause cerebral edema and vomiting.

Patient no. 15 had increased reticulocyte and developed retinal hemorrhage, which might be due to one of the following reasons: 1) severe vomiting, 2) ADR from CAP and 3) increased intracranial pressure due to

underlying disease.

Patient no. 30 was suspected to develope anemia due to the additive effect of process of lymphoma and CAP treatment. Patient no. 31 developed gentamicin nephritis before CAP treatment.

Among 34 patients who developed suspected ADR due to CAP, 3 patients (no. 4, 25, 29), 3 patients (no. 12, 16, 24) and 6 patients (no. 5, 13, 16, 22, 26, 33) were treated with vitamin K, phenobarbital and paracetamol during CAP treatement, respectively.

The most common ADR found was nausea, vomiting (9 out of 306 or 2.9%) (Table 6). Two out of 9 cases of nausea and vomiting were probably caused by high doses (4 g/day) of CAP (patient no. 15, 18). Three cases (patient no. 10, 12, 17) were possibly and four cases (patient no. 11, 13, 14, 16) were doubtfully casued by either CAP itself or other concomitant drug or the process of underlying diseases.

Hematological side effect was also the common ADR found in this study (8 out of 306 or 2.6%). They were 2 cases of leukopenia (patient no. 29, 30), 1 case of pancytopenia (patient no. 21), 5 cases of anemia (patient no. 15, 18, 31, 32, 33). Four out of 8 cases of hematological side effect (patient no. 18, 21, 29, 30) were probably caused by CAP. But 2 cases (patient no. 15, 31) were possibly related to CAP and underlying diseases, and the other 2 cases (patient no. 32, 33) were doubtfully related to either CAP or process of underlying diseases.

Diarrhea was found in 8 cases (2.6%). Three and five of them were possibly and doubtfully related to either CAP or other concomitant antibiotics.

The other suspected ADR were thrombophlebitis (1.6%), super-infection (1.6%) (three cases of oral moniliasis and 2 cases of urinary tract infection), elevated BUN (1.0%), drug fever (0.3%), rashes (0.7%). It was not clear that these 5 types of ADR were actually due to CAP, but it could be shown that they were possibly and doubtfully caused by either CAP or other concomitant antibiotics and process of underlying diseases.

Data from table 7 suggested that nausea and vomiting were likely to occur in young patients aged less than 15 years (6.1%) and in elder patients aged more than 60 years (6.1%). Nausea and vomiting were more commonly occurred when high dose of CAP (15.6%) of 4 g/day) was given for a prolonged period of time (20% of 22-35 day of treatment). In adult, when CAP was given in low dose (2 g/day), the incidence of gastro-intestinal side effect (nausea, vomiting and diarrhea) was 4.8% (8 out of 166 cases). But when CAP was given in high dose (4 g/day), the incidence was 35.7%. This suggested that gastro-intestinal side effect were likely to occur in adult when CAP was given in high dose rather than in low dose.

Hematological side effect were likely to develop in young patients of less than 15 years of age (6.1%) and old patients of 46-60 years of age (4.9%) rather than in other aged-groups. They usually occurred when CAP was given for 2 weeks or longer. The longer duration of CAP treatment there would be higher chance of developing hematological side effect.

Figure 1 Distribution of age of patients who received CAP in Ramathibodi Hospital, in 1980

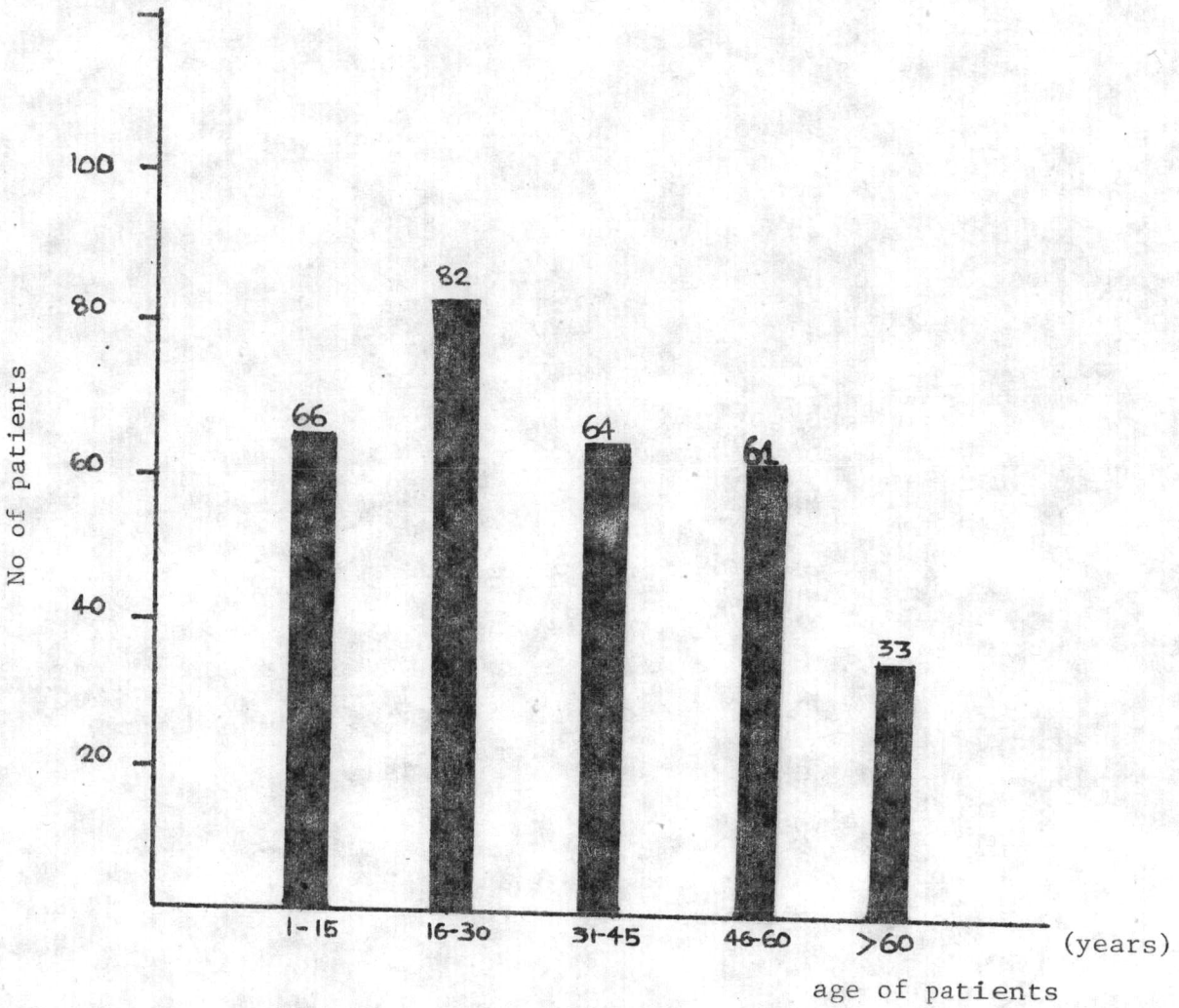

Figure 2 Distribution of patients aged less than 15 years who received CAP in in pediatric ward, Ramathibodi Hospital, 1980

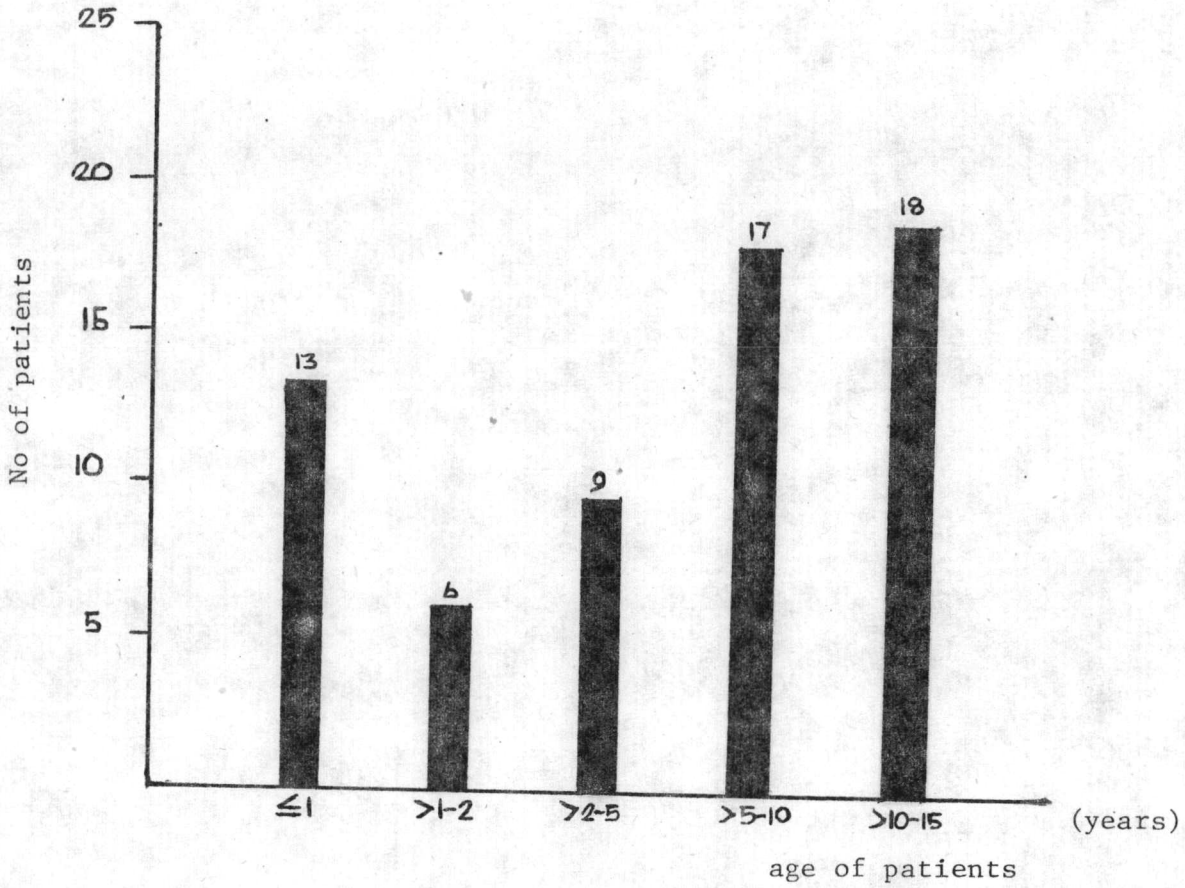

Figure 3 . Percentage of patients received CAP in 3 types of administration

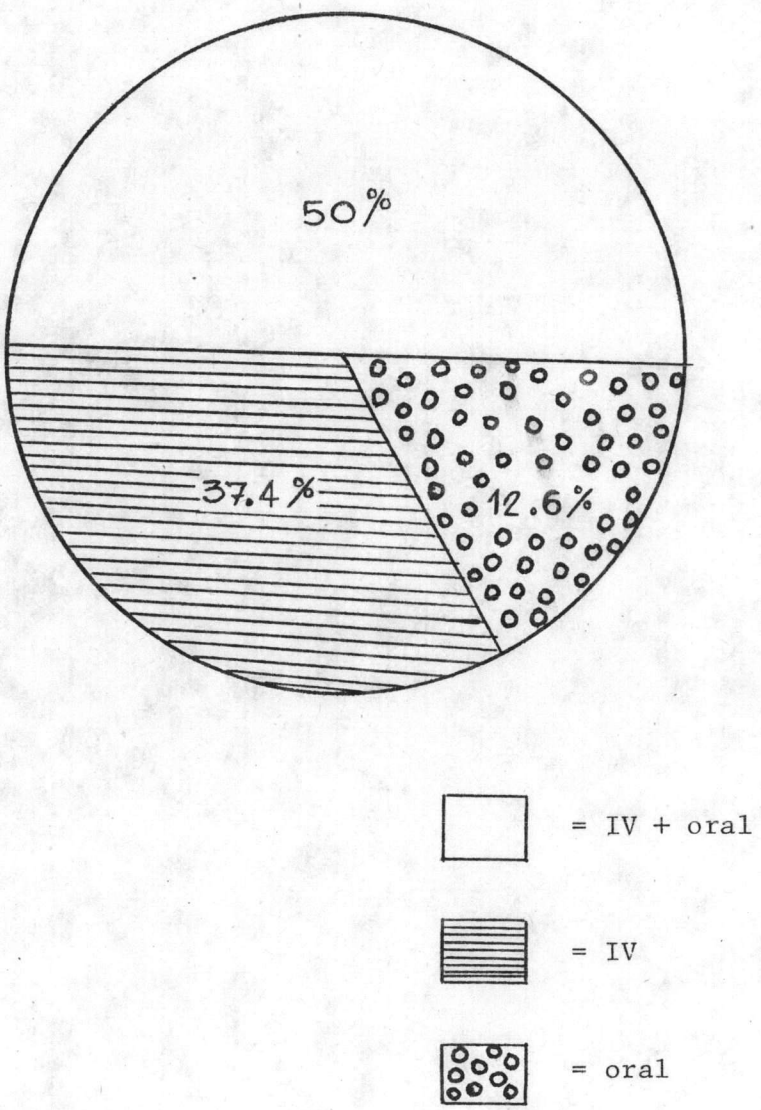

Figure 4 Duration of treatment in various types of administration

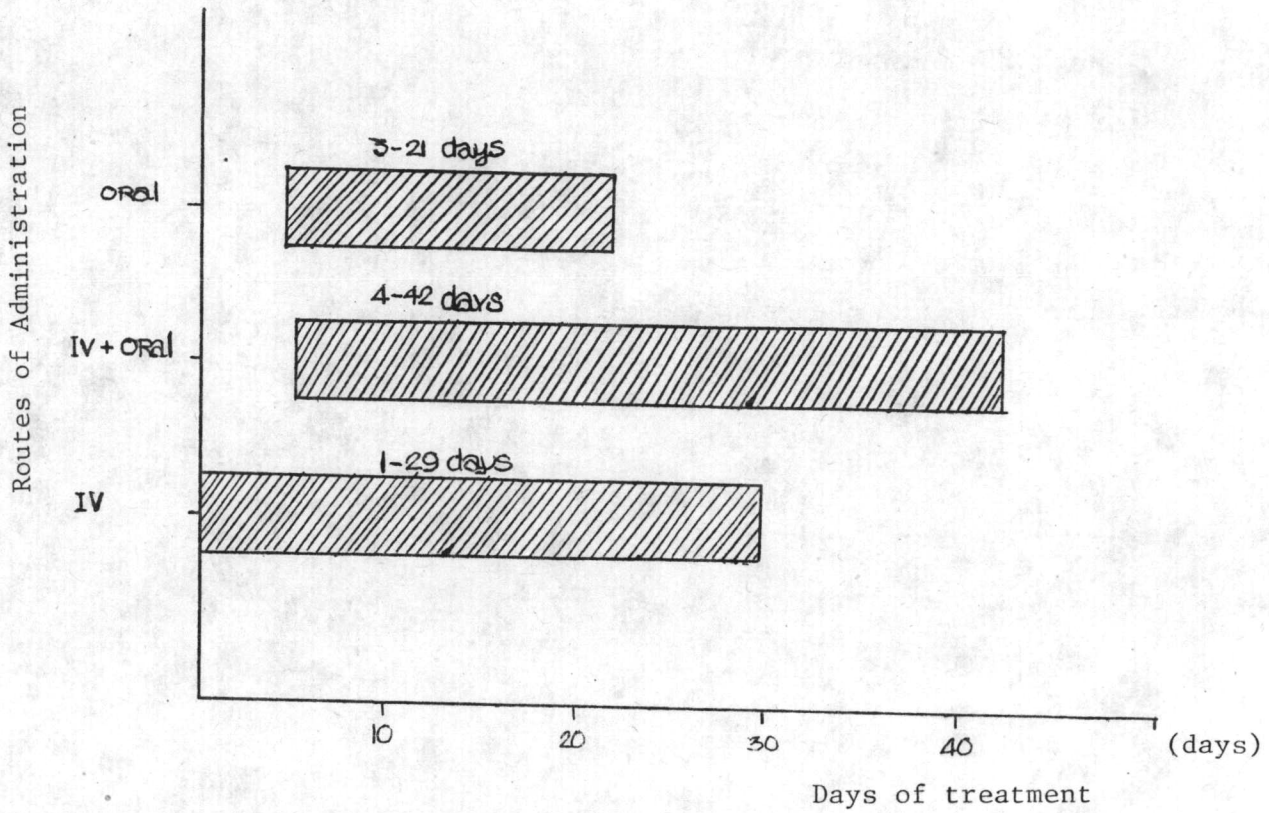

Figure 5 Percentage of doses of CAP used in Ramathibodi Hospital (1980)

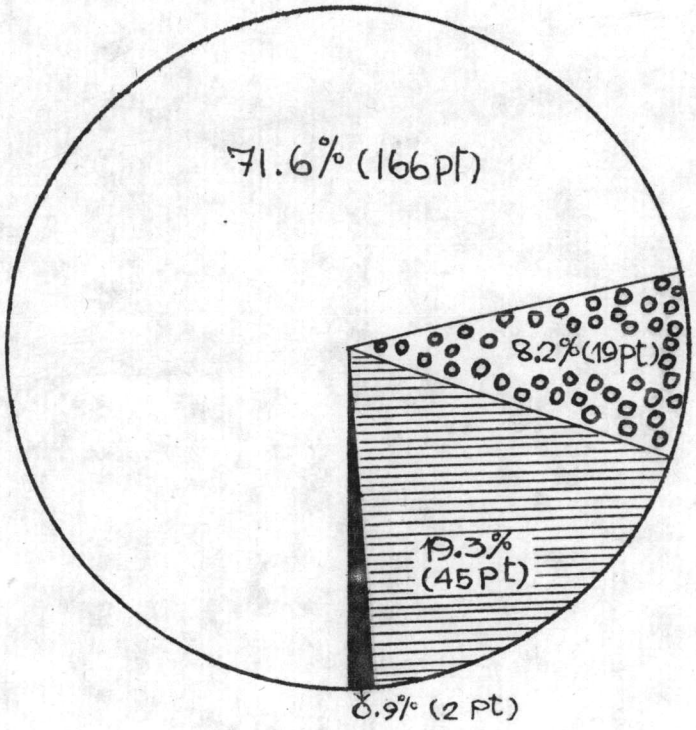

Table 1 Number of patients who received CAP in 4 departments, classified by 5 aged groups

Ward	age (in years)					total	
	≤ 15	16-30	31-45	46-60	≥ 60	no of pt.	%
Gynecology	-	13	12	8	3	36	11.8
Medicine	-	3	7	10	4	24	7.8
Surgery	7	65	45	43	26	186	60.8
Pediatrics	59	1	-	-	-	60	19.6
Total	66	82	64	61	33	306	100
%	21.6	26.8	20.9	19.9	10.8	100	

Table 2 Number of patients who received CAP in 4 departments, classified by 5 periods of treatment

Ward	Duration of treatment (days)					total patients
	1-7	8-14	15-21	22-35	≥ 35	
Gynecology	27	9	-	-	-	36
Medicine	12	8	3	1	-	24
Surgery	67	100	14	3	2	186
Pediatrics	24	23	7	6	-	60
Total	130	140	24	10	2	306
%	42.5	45.8	7.8	3.3	0.7	100

Table 3 Number of patients who received CAP in 4 different doses. (calculated in g/day and mg/kg/day)

Ward	Dose (in g/day and mg/kg/day				total
	* 1	2	3	4	
	▲ 25	25-50	50-75	75-100	
Gynecology	-	11	-	2	13
Medicine	-	16	2	2	20
Surgery	2	139	1	10	152
Pediatrics	-	-	16	31	47
Total	2	166	19	45	232
%	0.9	71.6	8.2	19.3	100

* = dose in g/day

▲ = dose in mg/kg/day

Table 4 Listing of diseases in systems leading to CAP treatment

Disease in systems	no of patients	percentage
Central nervous system	145	47.4
Gastro-intestinal system	87	28.4
Dermatologic system	31	10.1
Genitourinary system	10	3.3
Pulmonary system	5	1.6
Skeletal system	5	1.6
Others	23	7.5
Total	306	100

Table 5 Analysis of data from patients who was suspected to have ADR during CAP treatment.

pt. no.	sex	age (years)	duration of treatment	Dose	Indication for CAP treatment (days)	Concomitant antibiotics at the time of ADR	Onset of ADR after CAP therapy (days)	type of ADR	Remarks
1.	M	70	6	2g/d	Craniectomy	PGS	2	diarrhea	SGOT = 33 (∵ alcohol)
2.	M	33	12	2g/d	Peritonitis	K,A	5	diarrhea	-
3.	F	49	8	4g/d	Peritonitis	PGS,K	5	diarrhea	-
*4.	F	58	8	3g/d	Cellulitis	PGS	2	diarrhea	Slightly anemic before CAP treatment
▲5.	M	2/12	6	100mg/k/d	Meningitis	A	3	diarrhea	Hb, Hct↓before CAP treatment
6.	F	43	5	4g/d	Peritonitis	PGS,K	3	diarrhea	Jaundice
7.	F	27	11	2g/d	Ileocolostomy	Dib.	9	diarrhea	Slightly anemic before CAP treatment
8.	F	45	4	2g/d	Hysterectomy	PGS,K	2	diarrhea	Slightly anemic before CAP treatment
9.	F	63	16	2g/d	Colectomy	PGS,K	2	drug fever	SGOT, BUN↑before CAP treatment
10.	M	62	13	4g/d 2g/d	Cholecystec--tomy	A,Ak	7	nausea, vomiting	BUN (∵ aminoglycoside?)
11.	M	17	7	2g/d	Flap infect--ion	A,K	7	nausea, vomiting	SGOT = 50, SGPT = 44
+12.	M	27	14	4g/d	Peritonitis	-	13	nausea, vomiting	-

Table 5 (Continued)

pt. no.	sex	age (years)	duration of treatment (days)	Dose	Indication for CAP treatment	Concomitant antibiotics at the time of ADR	Onset of ADR after CAP therapy (days)	type of ADR	Remarks
▲13.	F	16	12,11	2g/d	Brain tumor	PGS	3	nausea, vomiting	occurred after surgery 2-3 days
14.	M	73	10	4g/d	Craniectomy	Am.	6	nausea, vomiting	BUN ↑ during PGS,CAP treatment
15.	F	10	30	80mg/k/d	Meningitis	G	6	-nausea, vomiting	Iron deficiency anemia
						A	9	-thrombophlebitis	Abnormal platelets
						-	30	-anemia	
						A	9	-Retinal hemorrhage	
▲‡16.	M	9	35	100mg/k/d	Brain abscess	PGS	12	-Thrombophlebitis	Slightly anemic (Hb ↓) before CAP treatment
							25	-nausea, vomiting	
17.	M	$1\frac{10}{12}$	13	100mg/k/d	gangrene	Ak.	8	nausea, vomiting	-
18.	M	$\frac{25}{12}$	14	100mg/k/d	Meningitis	PGS	9	nausea, vomiting	Jaundice
							13	anemia	
19.	M	46	30	2g/d	Appendicitis	PGS,K	7	rash	-
20.	M	7	30	100mg/k/d	Peritonitis	PGS,K	7	rash	Hb, Hct ↓ before and after CAP treatment

Table 5 (Continued)

pt. no.	sex	age (years)	duration of treatment (days)	Dose	Indication for CAP treatment	Concomitant antibiotics at the time of ADR	Onset of ADR after CAP therapy (days)	type of ADR	Remarks
21.	M	9	29	80mg/k/d	Meningitis	PGS,MTZ	8 27	-Oral moniliasis -Pancytopenia	-
▲22.	M	12	12	100mg/k/d	Craniectomy	PGS	11	Oral moniliasis	hepatomegaly (Enzyme ↑)
23.	M	6	9	100mg/k/d	Ventriculostomy	PGS	6	Oral moniliasis	SGOT = 50 (during PGS, CAP treatment)
+24.	M	36	8	2g/d	Craniectomy	PGS	4	fungal UTI	-
*25.	M	60	14	2g/d	Bed sore	G	2	fungal UTI	SGOT ↑ (∵ alcohol), anemia BUN ↑ (∵ amikacin)
▲26.	F	78	8	2g/d	Cholecystectomy	PGS,G	6	thrombophlebitis	hemoglobulinemia
27.	F	39	6	2g/d	Craniectomy	PGS	5	thrombophlebitis	platelet, Hb, Hct ↓
28.	F	1	6	100mg/k/d	Meningocoele	PGS	5	thrombophlebitis	-
*29.	M	32	21	2g/d	Suture of Ileum	PGS,G	20	leukopenia	jaundice
30.	F	56	4	2g/d	Cellulitis & Lymphoma	CMZ,Tb	4	leukopenia	ADR due to process of lymphoma
31.	F	56	21	2g/d	Gangrene	G,DCC	21	anemia	Gentamicin nephritis

Table 5 (Continued)

pt. no.	sex	age (years)	duration of treatment	Dose	Indication for CAP treatment (days)	Concomitant antibiotics at the time of ADR	Onset of ADR after CAP therapy (days)	type of ADR	Remarks
32.	F	14	21	100mg/k/d	Meningitis	PGS,G	10	anemia	Iron dificiency anemia
▲33.	M	47	13	2g/d	Craniectomy	PGS , Actinomycin	1 3	- anemia - BUN ↑	Hb,Hct ↓ during CAP treatment
34.	M	54	17	2g/d	Peritomitis	PGS,K	2	BUN ↑	Liver impairment (from alcohol)

F = Female
M = Male
UTI = Urinary Tract Infection
A = Ampicillin
Ak = Amikacin
Am = Amoxicillin
CMZ = Cefamezin
DCC = Diclocil
Dib = Dibekacin
G = Gentamicin
K = Kanamycin
MTZ = Metronidazole
PGS = Penicillin G Sodium
Tb = Tobramycin

▲ = received paracetamol (pt. no. 5, 13, 16, 22, 33, 26)

* = received vitamin K (pt. no. 4, 25, 29)

\+ = received phenobarbital (pt. no. 12, 16, 24)

Table 6 Incidences of ADR from CAP in 306 hospitalized patients in Ramathibodi Hospital, 1980

Type of ADR	number of Incidences	% of Incidences to total pt.	probable		possible		doubtfully		no. of pt. with conc. AB
			no.	% to total	no.	% to total	no.	% to total	
nausea, vomiting	9	2.9	2	0.7	3	1.0	4	1.3	9
hematological side effect	8	2.6	4	1.3	2	0.7	2	0.7	8
-leukopenia	2	0.7	2	0.7	-	-	-	-	2
-anemia	5	1.6	1	0.3	2	0.7	2	0.7	5
-pancytopenia	1	0.3	1	0.3	-	-	-	-	1
diarrhea	8	2.6	-	-	3	1.0	5	1.6	8
thrombophlebitis	5	1.6	-	-	5	1.6	-	-	5
superinfection (oral moniliasis and fungal UTI)	5	1.6	1	0.3	3	1.0	1	0.3	5
elevated BUN	3	1.0	-	-	-	-	3	1.0	3
rash	2	0.7	-	-	-	-	2	0.7	2
drug fever	1	0.3	-	-	1	0.3	-	-	1
TOTAL	41	22.1	7	2.3	17	5.6	17	5.6	41

conc. AB = concomitant antibiotics

Table 7 Age, Duration and Dosage of CAP in 9 patients with nausea, vomiting and 8 patients with hematological side effect, with suspected ADR from CAP.

Groups of Patients	total no.of pt.	nausea, vomiting		hematalogical side effect	
		no.	% total	no.	% total
age (years)					
≤15	66	2*+1°+1▲	6.1	2*+1°+1▲	6.1
16-30	82	1°+2▲	3.7	-	-
31-45	64	-	-	1*	1.6
46-60	61	-	-	2°+1▲	4.9
≥60	33	1°+1▲	6.1	-	-
duration (days)					
1- 7	130	1▲	0.8	1°	0.8
8-14	140	1*+3°+2▲	4.3	1*+1▲	1.4
15-21	24	-	-	1*+1°+1▲	12.5
22-35	10	1°+1▲	20.0	1*+1°	20.0
≥35	2	-	-	-	-
dose (g/d)					
1 (≤25mg/kg/day)	2	-	-	-	-
2 (25-50mg/kg/day)	166	2▲	1.2	1*+2°+1▲	2.4
3 (50-75mg/kg/day)	19	-	-	-	-
4 (75-100mg/kg/day)	45	1*+4°+2▲	15.6	2*+1°+1▲	8.9

* = probably related to CAP

° = possibly related to CAP

▲ = doubtfully related to CAP

Prospective Results

There were 33 children in this study as shown in table 8. Eleven of them were female and 22 were male. Age of patients ranged from 5 months to 13 years of age. About one third (12 out of 33) of the patients were 9-13 years of age. Site of infection included central nervous systems (brain abscess 9, Meningitis 6), gastrointestinal-hepato-biliary system (appendectomy 8, others 3), soft tissue (2), respiratory system (1), and others (5); eg. meningitis prophylaxis, septic arthritis. Other diagnosis of each patients before CAP treatment showed that they were 3 cases of liver impairment (patient no.11, 15, 17), 2 cases of iron deficiency anemia (patient no.16, 31), 3 cases of other hematologic diseases (patient no.2, 6, 17), and 1 case of renal impairment from gentamicin (patient no.30).

Doses of CAP varied from 40 mg/kg/day to more than 100 mg/kg/day, 19 out of 33 (57.6%) received 100 mg/kg/day. Duration of CAP therapy varied from 2 days to 78 days, about one-third (12 out of 33) were 1-7 days. Only 3 out of 33 children (patient no.11, 15, 26) were treated with CAP alone, the other patients received concomitant antibiotics PGS or ampicillin or amoxicillin were given in 23 cases, gentamicin in 10 cases and kanamycin in 2 cases. Other concomitant antibiotics were methicillin (1 case) and amikacin (1 case). Other concomitant drugs were vitamin K (3 cases:- patient no.17, 30, 31), phenobarbital (5 cases:- patient no.6, 19, 20, 24, 30) and paracetamol (2 cases:- patient no.12, 29)

CAP levels results

Twenty-nine children were monitored trough and peak serum levels. The lack of correlation between dose and serum concentration has been observed in the study. Table 9 showed that CAP-S were given intravenously in 25 cases, 18 trough and 32 peak serum levels were assayed, and provided trough levels ranged from <5-19.25 mcg/ml with the average of 8.99 ± 4.37 mcg/ml, peak serum levels ranged from < 5-39 mcg/ml with the average of 15.07 ± 6.57 mcg/ml.CAP-G were given intravenously in 8 cases, 2 trough and 10 peak serum levels were assayed, and provided trough levels with the average of 9.88 ± 7.13 mcg/ml, peak serum levels ranged from 11.5-24 mcg/ml with the average of 18.2 ± 4.71 mcg/ml. CAP-G were given intramuscularly in 10 cases, 3 trough and 12 peak serum levels, provided trough levels ranged from 7.9-10.75 mcg/ml with the average of 9.38 ± 1.43 mcg/ml, peak serum levels ranged from 9-23 mcg/ml with the average of 16.08 ± 4.29 mcg/ml. CAP bases were given orally in 4 cases, 5 trough and 6 peak serum levels, provided trough and peak serum levels ranged from <5-18.75 mcg/ml and 25-19.5 mcg/ml with the average of 10.17 ± 5.22 and 13.55 ± 5.52 mcg/ml, respectively. From these data showed that the CAP concentrations were within the desirable range (peak concentration between 10-25 mcg/ml) in most children.

There was no significant difference between peak serum concentration after CAP-S(IV) and CAP-G(IM) as analyzed by t-test ($P > 0.05$). But there was significant difference between peak serum concentration after CAP-S(IV) and CAP-G(IV) as analyzed by t-test ($P < 0.05$)

Table 10. summerized the trough and peak serum levels of children in different age groups as well as in different period of treatment. There was no significant difference among peak serum levels in different age groups as well as in different period of treatment, as analyzed by ANOVA ($P > 0.05$). From this study it could be said that there was no correlation between serum levels and age of children as well as to periods of treatment. But trough levels could not be eveluated by statistic method because of unadequate data.

Table 11. demonstrated that CAP levels in urine were determined in 3 cases; case 1 (patient no. 15) 1.5 hours after oral route, case 2 (patient no. 18) 2 hours after CAP-S (IV), case 3 (patient no. 21) 3 hours after CAP-G (IM). The results of active CAP levels in urine were approximately 126, 82 and 908 mcg/ml respectively.

CSF levels were determined in 3 cases, all were given CAP-S, 100 mg/kg/day, intravenously. Active CAP levels in CSF were <4, <4, 4 and 6 mcg/ml after 2, 5, 0.5, and 4 hours after administration respectively. (Table 11)

ADR results

Table 12. showed the incidences of ADR that were found in 33 children. Nine out of 33 children (33.3%) developed 11 incidences of ADR. Patient no. 19 (table 8) had two types of ADR, patient no. 29 had 3 types of ADR. There was no significant difference in sex as analyzed by chi-square test.

Hematologic side effects were found in 6 children or 18.18% (leukopenia 5 cases, neutropenia 1 case). Other ADR were thrombophlebitis (3cases or 9.09%), superinfection; included oral moniliasis and

candidiasis (2 cases or 3.03%). Thrombophlebitis and superinfection occurred when CAP was combined with other antibiotics.

Table 13. demonstrated the white blood cell count and peak serum levels of 6 patients who developed leukopenia and neutropenia during the periods of CAP treatment. Patient no. 1 showed no sign of leukopenia (WBC = 8,000 cell/mm^3) on the 71st day of CAP therapy, but on the 78th day WBC dropped to 3,700 cell/mm^3, which was lower than normal, while peak serum levels on the 72nd and 75th day of therapy were within the desirable range (13, 19 mcg/ml respectively)

Patient no. 7 showed leukopenia (WBC = 4,300 cell/mm^3) on the 4th day after CAP therapy was discontinued. White blood cell count rised up to 7,300 cell/mm^3 11 day later. Serum levels during CAP therapy could not be measured.

Patient no. 19 showed leukopenia on the 25th day of treatment (WBC = 3,800 cell/mm^3), while the peak serum level on the 2, 9 and 15th day of therapy were 11.5, 14.5 and 21.5 mcg/ml respectively.

Patient no. 24 developed neutropenia on the 8th, 15th day of therapy (PMN = 36% and 10%), while peak serum levels were 17, 13 mcg/ml on the 3, 13th day of therapy respectively. PMN rised up to normal range (42%), 25 days after CAP was discontinued.

Patient no. 29 showed the sign of leukopenia on the 3rd day after CAP was discontinued (WBC = 4,900 cell/mm^3), while the peak serum levels were monitored only on the 6th and 7th day of CAP therapy (11.5 and 13 mcg/ml respectively).

Patient no. 31 showed the sign of leukopenia (WBC = 3,200 cell/mm^3) on the 38th day of therapy. But when she was treated with iron supplement ($FeSO_4$), WBC rised up to normal range (WBC = 8,000 cell/mm^3) on the 49th day.

Table 8 Data analysis of 33 patients who received CAP in 3 different route of administration (Oct., 1981 to March, 1982)

pt. no.	sex	age (years)	dose (mg/kg/day)	day of CAP treatment	indication for CAP treatment	concomitant antibiotic	route of admin.	CAP level trough	CAP level peak	total duration of CAP therapy (days)	remarks
1.	M	12	100	38	brain abscess	PGS,G	IV(CAP-S)	6.2	19.7		
			100	50		PGS,G	IV(CAP-S)	7.8	11.5		
			100	58		Pen V.	oral	10.8	19.5	78	WBC ↓↓ during CAP treatment
			100	65		Pen V.	oral	8.1	13.0		
			100	72		Pen V.	oral	8.2	13.0		
			100	74		Pen V.	IM(CAP-G)	9.5	19.5		
			100	75		Pen V.	IM(CAP-G)	N.D.	11.0		
2.	M	8	100	4	brain abscess	PGS	IV(CAP-S)	4.1	14.5		
			100	15		PGS	IV(CAP-S)	11.2	17.2		
			100	22		PGS	IV(CAP-S)	8	21.5		
			80	29		PGS	IV(CAP-S)	10	14.5	43	congenital tetralogy of follot
			90	36		PGS	IV(CAP-S)	16	20.75		
			100	43		PGS	IV(CAP-S)	19.25	39		
3.	F	13	100	10	AVM	PGS,G	IV(CAP-S)	N.D.	∠5	10	-
4.	M	7	100	3	Meningitis	PGS	IV(CAP-S)	N.D.	18	14	-
5.	M	13	40	7	Appendicitis	G	oral	N.D.	4.8	12	-
				9		G	IV(CAP-G)	2.75	11.5		
+6.	F	4½	100	7	ALL	PGS	IV(CAP-S)	∠5	8.5	7	-
7.	M	5	100	-	brain abscess	Kf,Ak	IV(CAP-S)	N.D.	N.D.	16	WBC ↓↓

Table 8 (Continued)

pt. no.	sex	age (years)	dose (mg/kg/day)	day of CAP treatment	indication for CAP treatment	concomitant antibiotic	route of admin.	CAP level		total duration of CAP therapy (days)	remarks
								trough	peak		
8.	M	8	100	6	appendicitis	PGS,G	IV(CAP-S)	5.85	15	12	-
9.	F	5	70	4	toxic -	G	IV(CAP-S)	N.D.	7.2	9	-
				8	enterocolitis	G	IV(CAP-S)	5	7	7	-
10.	M	13	50	4	appendicitis	G	IV(CAP-S)	6	12	5	-
11.	M	5	100	1	enteric fever	-	IV(CAP-S)	17.5	27.5	13	G-6-PD deficiency, Jaundice
		7				-	IM(CAP-G)	7.9	14		
12.	M	4	70	1	orbital cellulitis	Meth	IV(CAP-S)	5	14	13	WBC ↓ (∵ Meth)
13.	M	3½	100	4	appendicitis	PGS,K	IV(CAP-S)	N.D.	24		
				4		PGS,K	IM(CAP-G)	N.D.	23	9	-
				7		A	IM(CAP-G)	10.75	18		
14.	F	8/12	100	2	meningitis	PGS	IV(CAP-S)	10	18.25	2	-
15.	M	11	80	3	enteric fever	-	oral	18.75	19.5	4	hepatosplenomegaly

Table 8 (Continued)

pt. no.	sex	age years	dose (mg/kg/day)	day of CAP treatment	indication for CAP treatment	concomitant antibiotic	route of admin.	CAP level trough	CAP level peak	total duration of CAP therapy (days)	remarks
16.	F	3	100	2	brain abscess	PGS	IV(CAP-S)	5.8	13		
				14		PGS	IV(CAP-G)	N.D.	24	32	iron deficiency
				15		PGS	IM(CAP-G)	N.D.	15		
				28		PGS	IV(CAP-G)	N.D.	23.5		
*17.	M	13	50	8	brain abscess	PGS	IV(CAP-S)	4	9	19	cyanosis, abnormal agulogram
18.	M	13	80	2	appendicitis	PGS,G	IV(CAP-S)	6.3	13.5	5	thrombophlebitis
				5		PGS,G	IV(CAP-G)	N.D.	17.5		
+19.	M	2	100	2	brain abscess	PGS	IV(CAP-S)	8	11.5	25	thrombophlebitis
				9		A	IV(CAP-G)	N.D.	14.5		leukopenia
+20.	M	5	100	2	pneumonia	PGS	IV(CAP-G)	17	23	4	-
21.	M	13	50	1	appendicitis	K	IV(CAP-S)	7.2	10.5	7	-
				3		K	IV(CAP-G)	N.D.	19		
22.	F	12	100	6	cerebral	PGS	IV(CAP-S)	5.5	20	10	
				6	concussion	PGS	IV(CAP-G)	N.D.	23		
23.	M	12	50	1	appendicitis	G	IV(CAP-S)	N.D.	6	4	
				3		G	IV(CAP-G)	N.D.	15		
				3		G	IM(CAP-G)	N.D.	9		

Table 8 (Continued)

pt. no.	sex	age years	dose (mg/kg/day)	day of CAP treatment	indication for CAP treatment	concomitant antibiotic	route of admin.	CAP level trough	CAP level peak	total duration of CAP therapy (days)	remarks
+24.	M	1½	100	3	meningitis	PGS	IV(CAP-S)	N.D.	17	15	PMN ↓↓
				13		PGS	IM(CAP-G)	N.D.	13		
25.	M	13	60	3	prophylaxis of	PGS	IV(CAP-S)	N.D.	6	5	
				4	meningitis	PGS	IV(CAP-G)	N.D.	16		
26.	M	2	100	14	meningitis	-	IV(CAP-S)	N.D.	13.5	27	oral moniliasis, condidiasis
				15		-	IV(CAP-S)	N.D.	13		
				15		-	IV(CAP-S)	N.D.	15		
				27		-	IV(CAP-G)	N.D.	17		
27.	F	8	50	4	appendicitis	PGS,G	IV(CAP-S)	N.D.	8.5	4	
28.	F	13	50	5	facial cellulitis	PGS	oral	N.D.	11.5	5	
▲29.	M	.9	100	6	brain abscess	PGS,G	IV(CAP-S)	N.D.	11.5	46	rash (⁺PGS)
				7		PGS,G	IM(CAP-G)	N.D.	13		WBC ↓
				7		PGS,G	IV(CAP-G)	N.D.	12.5		thrombophlebitis
+*30.	M	5/12	100	10	meningitis	A	IV(CAP-S)	N.D.	12	18	nephrotoxic (⁺gentamicin)

Table 8 (Continued)

pt. no.	sex	age years	dose (mg/kg/day)	day of CAP treatment	indication for CAP treatment	concomitant antibiotic	route of admin.	CAP level		total duration of CAP therapy (days)	remarks
								trough	peak		
*31.	F	8	100	-	brain abscess	PGS,St	IV(CAP-S) + oral	N.D.	N.D.	62	WBC ↓
32.	F	8	100	-	brain abscess	PGS,Am,Er	IV(CAP-S) + oral	N.D.	N.D.	43	allergy to penicillin
33.	F	1	100	-	septic arthritis	Meth,Bc	IV(CAP-S)	N.D.	N.D.	17	

* = treated with vitamin K, (patient no. 17, 30,31)

\+ = treated with phenobarbital (patient no. 6, 19, 20, 24, 30)

▲ = treated with paracetamol (patient no. 12, 29)

F = female

M = male

ND = not done

AVM = Arterio-ventricular malformation

ALL = Acute lymphoblastic leukemia

A = ampicillin
Ak = amikacin
Am = amoxicillin
Bc = bactrim
Er = erythromycin
G = gentamicin
K = kanamycin
Kf = keflex
Meth = methicillin
MTZ = metronidazole
PGS = penicillin G sodium
Pen V = penicillin V
St = streptomycin

Table 9 Peak and trough serum levels of CAP in 4 different routes of administration

Route of Administration	IV (CAP- S)	IV (CAP- G)	IM (CAP- G)	Oral (base)
No of patients	25	8	10	4
trough (mean ± S.E) mcg / ml	8.99 ± 4.37 (n = 18)	9.88 ± 7.13 (n = 2)	9.38 ± 1.43 (n = 3)	10.17 ± 5.22 (n = 5)
peak (mean ± S.E) mcg / ml	15.07 ± 6.57 (n = 32)	18.2 ± 4.71 (n= 10)	16.08 ± 4.29 (n = 12)	13.55 ± 5.52 (n = 6)

n = number of Sample

Table 10 Peak and trough serum levels of CAP in different group of patients, classified by age and day of treatment

Day of treatment	Age (years)	no of patients	CAP level	
			trough (mean ±S.E)	peak (mean ± S.E)
1 - 7	≤ 2	2	10	17.63 ± 0.88
	> 2 - 6	9	8.84 ± 5.01	16.07 ± 6.83
	> 6 - 13	18	8.27 ± 5.17	12.91 ± 4.65
8 - 21	≤ 2	4	ND	15.63 ± 3.97
	> 2 - 6	5	ND	15.33 ± 8.50
	> 6 - 13	4	7.6 ± 3.6	14.0 ± 6.61
22 - >35	≤ 2	1	ND	17
	> 2 - 6	1	ND	23.5
	> 6 - 13	10	10.39 ± 4.09	18.45 ± 7.9

ND = not done

Table 11 Chloramphenicol levels in urine and CSF in 6 patients

Specimen	Route of Administration	Dose (mg/kg/day)	Time (hr.) after administration	CAP levels (mcg/ml)
urine				
patient no 15	Oral	80	1½	126
patient no 18	IV (CAP-S)	80	2	82
patient no 21	IM (CAP-G)	50	3	908
CSF				
patient no 3	IV (CAP-S)	100	2,5	<4
patient no 4	IV (CAP-S)	100	0.5	4
patient no *	IV (CAP-S)	100	4	6

Table 12 Incidence of ADR in 9 children out of 33 children studied

types of ADR	number of patients	percent of total
Leukopenia	5 (pt.no.1,7,19,29,31)	15.15
Neutropenia	1 (pt.no. 24)	3.03
Thrombophlebitis	3* (pt.no.18,19,29)	9.09
Superinfection (oral moniliasis and candidiasis)	2* (pt.no.26,29)	3.03
total	11	33.3

* = Combined with other antibiotics.

Table 13 Data analysis of hematological side effect (leukopenia and neutrepenia), from bone marrow suppression.

pt. no.	white blood cell count		Assay of peak level		total duration of CAP treat--ment
	Day of treatment	WCB (cell/mm^3)	level (mcg/ml)	Day of treatment	
1.	71	8,000	13.0	72	78
	78	3,700	19.5	75	
7.	15	44,000	N.D.	-	16
	4 days after discontinued	4,300	-	off	
	11 days after discontinued	7,300	-	off	
19.	7	9,000	11.5	2	
	11	5,300	14.5	9	25
	25	3,800	21.5	15	
24.	8	8,300 (PMN = 36)	17	3	15
	15	+ 7,500 (PMN = 10)	13	13	
	25 days after discontinued	15,800 (PMN = 42)	-	off	
29.	6	ND	11.5	6	
	7	ND	13	7	46
	34	6,300	N.D.		
	3 days after discontinued	4,900	-	off	
31.	23	19,200	N.D.	-	
	38	3,200	N.D.	-	62
	49*	8,000	N.D.	-	

$\bar{X}$ = 38.17 $\pm$ 24.36 days

\+ = neutropenia
* = received iron supplement ($FeSO_4$)
ND = not done