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## APPENDIX

- I - Admission summary note
  
- II - Naranjo 's algorithm used to evaluate gentamicin adverse reaction.
  
- III - The data and method for calculation Clcr in ml/min/1.73 m<sup>2</sup> to Clcr in l/hr.
  
- IV - Temperature and white blood cell of the patients in the TDD group.
  - Temperature and white blood cell of the patients in the ODD group.
  
- V - Diagnosis, evidence, and assessment of the patients in the TDD group.
  - Diagnosis, evidence, and assessment of the patients in the ODD group.









## APPENDIX II

### Naranjo 's algorithm used to evaluate gentamicin adverse reaction

(Using patient number 8 in TDD group as example.)

	Yes	No	Do not know	Score
1. Are there previous conclusive report on the reaction?	+1	0	0	+1
2. Did the adverse event appear after the suspected drug was administration?	+2	-1	0	+2
3. Did the adverse reaction improve when the drug was discontinued or a specific antagonist was administered?	+1	0	0	+1
4. Did the adverse reaction reappear when the drug was readministered?	+2	-1	0	0
5. Are there alternative cause (other than the drug) that could on their own have caused the reaction?	-1	+1	0	-1
6. Did the reaction appear when the placebo was given?	-1	+1	0	0
7. Was the drug detected in the blood(or other fluids) in concentrations know to be toxic?	+1	0	0	0
8. Was the reaction more severe when the dose was increased, or less severe when the dose was decrease?	+1	0	0	0
9. Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	+1	0	0	0
10. Was the adverse event confirmed by any objective evidence?	+1	0	0	+1 (Scr=1 .47mg/ dl)
TOTAL				4

Total score	≥ 9	Definite ADR
Total score	5 – 8	Possible ADR
Total score	1 – 4	Probable ADR
Total score	0	Unlikely

## APPENDIX III

The data and method for calculation Clcr in ml/min/1.73m<sup>2</sup> to Clcr in l/hr.

Pt. no	TDD group					ODD group				
	Wt. (gm)	Ht. (cm)	SA (m <sup>2</sup> )	Clcr (ml/min/1.73 m <sup>2</sup> )	Clcr (l/hr)	Wt. (gm)	Ht. (cm)	SA (m <sup>2</sup> )	Clcr (ml/min/1.73 m <sup>2</sup> )	Clcr (l/hr)
1.	3.8	52	0.238238	111.43	0.920702	2.8	50	0.199037	173.08	1.194774
2.	4	53	0.246758	27.41	0.234577	3.2	45	0.205108	31.64	0.225074
3.	4	53	0.246758	95.4	0.816441	2.6	48	0.18819	108	0.704897
4.	2.9	57	0.213642	85.5	0.633517	2.05	45	0.161427	24.75	0.138566
5.	2	45	0.159297	35.36	0.195355	2.15	45	0.165615	20.63	0.118496
6.	2.15	45	0.165615	46.41	0.266573	3.4	52	0.224405	47.76	0.371709
7.	2.9	49	0.201211	78.75	0.54955	2.75	50	0.197117	32.14	0.219723
8.	2.05	44	0.159995	20.74	0.115085	2.45	47	0.180756	62.04	0.388929
9.	3.2	50	0.213856	56.25	0.417205	2.4	47	0.178763	34.02	0.19232
10.	2.25	45	0.169714	64.57	0.380061	3.95	52	0.243251	43.33	0.365551
11.	2.65	48	0.190128	30	0.197821	2.25	47	0.172665	33.07	0.216001
12.	2.75	48	0.193953	50.23	0.337883	2.75	49	0.195545	53.03	0.393554
13.	2.5	49	0.185775	30.63	0.197351	3.8	51	0.236412	57.38	0.470473
14.	2.85	48	0.197715	72	0.493716	3	50	0.206561	43.91	0.350389
15.	3.05	47	0.203356	105.75	0.745833	3.5	52	0.227931	43.33	0.342529
16.	2.55	48	0.186235	26.34	0.170131	4.3	57	0.264051	116.59	1.067714
17.	3	48	0.203245	90	0.634407	2.4	47	0.178763	43.08	0.26709
18.	4.75	57	0.27857	80.16	0.774458	3.7	51	0.233045	35	0.687012
19.	2.55	48	0.186235	108	0.697574	2.6	50	0.19126	44.12	0.292661
20.	2.5	47	0.182731	49.19	0.311741	2.5	49	0.185775	33.92	0.218548
21.	3.4	50	0.220944	37.5	0.287354	3.5	53	0.229659	61.15	0.487062
22.	3.35	50	0.21919	187.5	1.42537	2.5	48	0.184262	33.75	0.215683
23.	3.3	50	0.217425	62.5	0.471296	3.25	50	0.215647	37.5	0.280465
24.	2.9	48	0.199573	93.91	0.650008	2.4	49	0.18174	16.17	0.101922
25.	3.8	52	0.238238	43.33	0.358019	2.55	48	0.186235	30.86	0.199325
26.	2.8	49	0.197449	61.25	0.419437	3.4	50	0.220944	102.27	0.783673
27.	2.7	48	0.192049	54	0.359675	2.8	48	0.195842	32.73	0.222309

Equation 1(form Haycock, G.B. et al.)<sup>90</sup>

$$SA = Wt^{0.5378} \times Ht^{0.3964} \times 0.024265$$

SA = Surface area (m<sup>2</sup>)

Wt = Weight (kg)

Ht = Height (cm)

Equation 2

$$Clcr (l/hr) = \frac{Clcr (ml/min/1.73m^2) \times 60 (mins) \times SA (m^2)}{1,000 (ml) \times 1.73 (m^2)}$$

## APPENDIX IV

Table 1 Temperature and white blood cell of the patients in the TDD group.

Pt.No.	Temperature (°c)			White blood cell( $\times 10^3$ cell/cm <sup>3</sup> )**	
	day1	day3	day-off	day1	day-off
1.	36.7	36.4	36.8	14.7	14.5
2.	36.6	37.2	36.6	22.1*	5.0
3.	38.0*	36.3	37.2	23.9*	10.0
4.	36.5	36.9	37.2	9.1	12.2
5.	36.4	36.0	36.6	10.8	10.1
6.	37.7	36.8	37.2	15.8	9.4
7.	36.2	36.6	36.6	15.7	13.8
8.	36.6	37.2	36.6	18.1	9.6
9.	36.3	37.2	37.2	22.6*	16.7
10.	36.9	36.7	37.0	15.9	13.5
11.	36.6	37.2	37.4	23.2*	9.2
12.	36.2	37.2	37.3	17.6	15.2
13.	36.5	36.6	36.6	13.7	13.5
14.	38.1*	36.6	37.0	9.3	13.9
15.	36.6	37.5	36.6	15.0	12.0
16.	36.6	37.0	37.2	16.8	14.9
17.	37.4	37.1	36.6	35.7*	14.2
18.	37.2	36.8	36.6	30.7*	14.7
19.	36.1	37.0	36.6	3.30*	9.9
20.	37.2	36.0	36.8	10.1	16.1
21.	36.8	36.7	37.0	27.6*	13.1
22.	37.0	37.2	37.2	15.9	12.5
23.	36.6	37.5	36.4	14.1	11.1
24.	37.2	36.1	36.6	41.2	11.5
25.	37.4	36.9	36.6	26.6	16.7
26.	37.1	37.2	36.5	12.0	11.0
27.	37.3	36.5	37.2	13.9	7.7
Mean (range)				18.4 $\pm$ 8.5 (3.3-41.2)	12.3 $\pm$ 2.8(5.0- 16.7)

\*\* The mean of WBC were significant different (P&lt;0.05)

Table 2 Temperature and white blood cell of the patients in the ODD group

Pt.No.	Temperature (°c)			White blood cell ( $\times 10^3$ cell/cm <sup>3</sup> )**	
	day1	day3	day-off	day1	day-off
1.	36.0	37.7	36.9	26.1*	12.5
2.	36.2	36.8	36.9	20.0	15.7
3.	36.6	37.2	37.2	16.4	11.7
4.	36.5	37.2	36.8	15.5	12.0
5.	36.8	36.5	36.4	14.1	15.0
6.	36.5	36.1	37.0	21.3*	14.4
7.	37.0	37.0	37.1	18.4	9.5
8.	38.2*	36.1	36.6	13.5	17.7
9.	36.5	36.6	36.1	13.0	9.5
10.	36.8	37.2	36.8	23.7*	15.0
11.	34.6*	37.0	36.2	11.0	8.7
12.	37.0	37.2	37.0	7.9	11.0
13.	36.5	37.1	36.7	5.4	8.3
14.	37.0	36.6	36.7	5.0*	11.5
15.	36.6	37.7	37.6	12.3	15.1
16.	36.9	37.1	36.0	17.3	11.5
17.	37.2	36.6	37.3	16.9	8.1
18.	37.7	36.6	36.8	27.0*	7.9
19.	37.4	36.7	37.0	14.7	9.7
20.	37.0	36.1	36.8	19.7	11.2
21.	36.6	36.6	37.1	18.3	12.5
22.	37.5	37.2	37.2	6.5	10.1
23.	37.0	36.8	37.0	17.7	14.6
24.	38.3*	37.3	37.0	17.6	9.2
25.	36.7	36.7	37.2	20.5*	9.4
26.	37.0	36.6	36.6	24.6*	12.7
27.	36.0	36.4	37.1	15.3	17.7
Mean (range)				16.3 $\pm$ 5.9(5.0- 27.0)	11.9 $\pm$ 2.9(7.9- 17.7)

\*\* The mean of WBC were significant different (P<0.05)

## APPENDIX V

Table1 Diagnosis, evidence, and assessment of the patients in the TDD group.

Pt. No.	Diagnosis	Evidence	Assessment
1.	PROM,Sepsis	PROM > 24 hr., Respiratory distress, Chest x-ray infiltration, Poor feeding, RR $\uparrow$ 110, Deminished activity	Clinical improvement, Normal Respiratory rate, feeding, and activity
2.	Sepsis	Tachypnea,Hypotonia	Clinical improvement, no Tachypnia,hypotonia
3.	Pneumonia	T= 38°C , WBC $\uparrow$ 23900, Chest x-ray infiltration, Tachypnea	Clinical improvement, T=37.2°C, WBC=10000, no tachypnea
4.	PROM,Sepsis	PROM > 24 hr., Poor feeding	Clinical improvement
5.	NEC	Abdominal distention, Poor feeding	Clinical improvement after 1 day of NPC
6.	Sepsis	Cyanosis at birth, on respirator 1 day, apnea	Clinical improvement
7.	NEC	Abdominal distention, Poor feeding, maternal fever x-ray – bowel ilus	Clinical improvement after 3 day of NPC
8.	Pneumonia, Sepsis	Chest x-ray bilateral pulmonary infiltration On ET tube 3 day, dypnea, tachypnea	Clinical improvement, no dypnea, Tachypnea
9.	PROM,Sepsis	PROM 19 hrs. , WBC $\uparrow$ 22600, tachypnea	Clinical improvement, no tachypnea ,WBC 16700
10.	PROM	PROM > 24 hr, foul smell aminotic fluid, irregular breath	Clinical improvement after 5 day of NPC
11.	Pneumonia	Chest x-ray infiltration of both lung WBC $\uparrow$ 23200, Moderate birth asphyxia, tachypnea	Clinical improvement, no tachypnea WBC 9200
12.	PROM	PROM > 24 hr, cyanosis	Clinical improvement, no cyanosis
13.	Clinical sepsis	Poor feeding, drowsiness	Clinical improvement, Normal feeding and activity after 2 days of therapy
14.	Pneumonia	T= 38.1-38.5°C, Chest x-ray infiltration, CBC band 3%, plt $\downarrow$ 143000 (<150000)	Clinical improvement after 2 days of therapy , T= 36.6 ,plt > 150000
15.	MAS	Chest x-ray infiltration, tachypnea	Clinical improvement, no tachypnea
16.	MAS Pneumonia	Chest x-ray infiltration plt $\downarrow$ 80000(<150000)	Clinical improvement ,plt $\uparrow$ 296000
17.	RD	tachypnea WBC $\uparrow$ 35700	No tachypnea, WBC 14200



Continue

**Table 2 Diagnosis, evidence, and assessment of the patients in the TDD group.**

Pt. No.	Diagnosis	Evidence	Assessment
18.	MAS	Chest x-ray infiltration ,WBC ↑30700 NE 80%, tachypnea	Clinical improvement, no Tachypnea, WBC 14700
19.	NEC	PROM 13 hrs., bloody stools, plt ↓5000, ↓WBC 3300	Normal feeding after NPO 3 days WBC ↑9900, plt ↑149000
20.	NEC	Coffee ground	Normal feeding after NPO 3 days
21.	PROM	PROM >24 hrs , WBC ↑27600 Chest x-ray infiltration, Pneumothorax, tachypnea, neonata, asphyxia	Clinical improvement, no tachypnea
22	Pneumonia, Sepsis	Chest x-ray infiltration, tachypnea, maternal T= 38°C	Clinical improvement, no tachypnea
23	Pneumonia	PROM, asphyxia, on respirator 4 days, CBC band=8 %, H/C gr+ve cocci	Clinical improvement, no Tachypnea, H/C no growth
24.	RD	WBC ↑41700, tachypnea	Clinical improvement, no tachypnea
25.	Pneumonia	WBC ↑26600, Chest x-ray infiltration	Clinical improvement, WBC 16700
26.	Pneumonia	Chest x-ray infiltration, black content in NG tube	Clinical improvement
27.	Sepsis	x-ray mild cardiomegaly, ileus of abdomen, Abdominal distention	Clinical improvement after 4 days

Table2 Diagnosis, evidence, and assessment of the patients in the ODD group.

Pl No.	Diagnosis	Evidence	Assessment
1.	Pneumonia, Sepsis	Chest x-ray infiltration, WBC $\uparrow$ 26100, anemia H/C MRSA (after 5 days of therapy)	On ampi + gentamicin 3 days, ampi + cefuroxime 2 days then changing to Vancomycin
2.	MAS	tachypnea	Clinical improvement, no Tachypnea
3.	NEC	x-ray bowel ileus, Abdominal distention, poor feeding	Clinical improvement, normal feeding
4.	Pneumonia, Sepsis	Hypotonia, Respiratory distress, birth asphyxia	Clinical improvement, no tachypnea
5.	Sepsis	foul smell amniotic fluid, tachypnea, C/S gastric content (P.aeruginosa), amniotic fluid find E.coli, K. pneumoniae	Clinical improvement, no tachypnea, normal activity
6.	PROM	PROM > 24 hrs., WBC $\uparrow$ 21300, drawsiness, Hypotonia	Clinical improvement, no tachypnea, normal activity WBC 14400
7.	PROM	PROM > 24 hrs., drawsiness, tachypnea	Clinical improvement, no Tachypnea, normal activity
8.	RD, TTNB	Maternal fever, infant fever T= 38.2°C ,tachypnea	Clinical improvement, no tachypnea
9.	PROM	PROM > 24 hrs., On respirator 5-6 days, shock (hypotension)	Clinical improvement
10.	RD	Tachypnea, RR 100, WBC 23700	Clinical improvement, no tachypnea
11.	RD	Tachypnea, PROM 6 hrs.,On respirator Chest x-ray R/O RDS	Clinical improvement, no tachypnea
12.	MAS	Tachypnea, dyspnea	Clinical improvement, no tachypnea, dyspnea
13.	NEC	Abdominal distension,WBC 5400	Clinical improvement within 2-3 days WBC 8300
14.	Omphalitis	WBC $\downarrow$ 5000 ,C/S Umbilical/ E.coli.,Diaperoids, Inflammation at skin around umbilicus	Clinical improvement no omphalitis after 3 days of therapy
15.	MAS	Asphyxia, tachypnea	Clinical improvement, decrease tachypnea, need O <sub>2</sub> $\downarrow$

Continue

**Table 2** Diagnosis, evidence, and assessment of the patients in the ODD group.

Pl. No	Diagnosis	Evidence	Assessment
16.	MAS	Chest x-ray , minimal infiltration IMP: MAS is possible, tachypnea	Clinical improvement, decrease tachypnea,
17.	PROM	PROM >24 hrs., NE ↑ 84, poor feeding	Clinical improvement, could Feeding after 2 days of NPO
18.	RD,TTNB	Tachypnea, WBC ↑ 27000, irregular breathing	Clinical improvement, on O2 1 day normal breathing WBC ↓ 900
19.	MAS	Tachypnea, pale, mild birth asphyxia form fetal distress	Clinical improvement, decrease tachypnea,
20.	MAS	Tachypnea, Hypoglycemia	Clinical improvement, no tachypnea after 2 days of therapy
21.	Pneumonia	Chest x-ray infiltration, Tachypnea	Clinical improvement, decrease tachypnea,
22.	Sepsis	CBC, WBC 6500 band/NE 0.18(>0.16), Hypoglycemia, mild ileus abdomen	Clinical improvement after 2 days of therapy WBC 10100
23.	NEC	PROM, Film bowel ileus	Clinical improvement, could Feeding after 5 days of NPO
24.	Sepsis	Fever T=38.3 Chest x-ray infiltration, Tachypnea	Clinical improvement, no tachypnea
25.	MAS	Chest x-ray infiltration of both lungs, medial pneumothorax, dyspnea, Tachypnea, plt 64000 (<15000)	Clinical improvement, no tachypnea, dyspnea
26.	RD,TTNB	Tachypnea, WBC 24600	Clinical improvement, no tachypnea
27.	Pneumonia	Chest x-ray infiltration, NE 79%, on ET and respirator 8 days	Clinical improvement, could off respirator, decrease tachypnea

## VITAE

Miss Amporn Narongsanti was born on December 11, 1968, in Bangkok, Thailand. She graduated with Bachelor Degree of Science in Pharm in 1992 form the Faculty of Pharmacy, Chulalongkorn University, Bangkok, Thailand. Her current position is a staff in Department of Pharmacy, Pichit Hospital, Pichit, Thailand.

