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病原性大腸桿菌之研究
第VI報雞隻服用抗生素後其直腸拭子之莢膜多醣類菌株之各種抗生素之感受性

曾金章　　李玲玫　　郭萬福

摘　要

大腸桿菌 CPS 株在未經抗生素投與之雞肛門拭子中佔很高的比率，大腸桿菌分離株對藥物已具很高的耐性，其中NON-CPS 株之藥物耐性高於CPS株。

高劑量短期藥物投與會影響大腸桿菌 CPS 株之分佈，但藥物投與前後大腸桿菌（包括 CPS 株及 NON-CPS 株）對藥物之Geometric Mean MIC 增加或減少之變化不明顯且不定，它們受投與藥物種類之影響。投藥期間在雞肛門拭子檢體中，仍具多數對藥物感受性之 CPS 株及 NON-CPC 株。但以Minocycline低劑量長期投與，則耐性限閥或耐性率有顯著的變化，其中 CPS 株雖然對各種抗生素之Geometric Mean MIC較NON-CPS 株無顯著的提高，但投藥期間 CPS 株之耐性限閥的提高較NON-CPS 株快速，故 CPS 株之交叉耐性率亦相對的高於NON-CPS 株。

緒　論

大腸桿菌非莢膜產生株（NON-CPS株）在抗生素如Chloramphenicol及Oxytetracycline 等之處理下可獲得 CPS 變異株[1]。而 E-2 株經N-methyl-N′-nitro-N-nitrosoguanidine誘導之Spectinomycin 耐性株中14.8％是 CPS 變異株[2]，此等由NON-CPS 株徑誘導產生之 CPS 變異株與臨床分離株具類似的特性，如對藥物之感受性，生化特性，抗原性及病原性等[3,4,5]。故菌株之 CPS 產生能力不但和菌株之高頻率抗生素交叉耐性有關，而且由其 CPS 株之高變異率及它在培養基保存之安定性等來看，此種由獲得莢膜後所產生之藥物耐性在細菌之抗生素機轉中，是不可忽視的問題之一。

本文擬以抗生素在高劑量急速投與及低劑量長期投與後，抗生素對宿主腸內大腸桿菌之 CPS 株及NON-CPS 株之影響，及菌株對抗生素反應之關係等提出報告。

材料及方法

藥物之投與及檢體之採取：(1)長期投與[6]：以Minocycline（100mg／Kg）摻與之飼料，每天無限制給與連續飼養 8 週。及(2)高劑量短期投與：每隻中雞（約 1.5 Kg）每天經口投與 1 膠囊之抗生素，連續投與一星期。使用之口服抗生素(1) Tetracyclines類抗生素，包括立達出品的Minocycline（MIN; 100 mg／cap），Demethylchlortetracycline（DCT;

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150 mg／cap)及Tetracycline (TC; 250 mg／cap), 輝瑞公司的Oxytetracycline (OTC; 250 mg／cap), Methacycline (MC; 150 mg／cap)及Doxycycline (DOX;100 mg／cap), 氰胺公司的Chlortetracycline (CT; 250 mg／cap)等7種抗生素，其他抗生素包括中國化學的Chloramphenicol (CM; 250 mg／cap), 必治妥的Ampicillin (AP; 250 mg／cap), 禮來的Erythromycin (EM; 250 mg／cap), NBC的Nalidixic Acid (NA; 500 mg／cap)及萬有的Colistin-M (COL; 1000,000U／cap)。檢體之採取，雛雞經台糖飼料飼養4週後，在投藥前及投藥後1週或2週及8週，以肛門拭子採取肛門檢體，全部塗佈於EMB Agar (Difco)加以分離[7,8]。

莢膜多醣類菌株(CPS)之鑑定[1,2]; 選出在EMB Agar 產生黑色金屬光澤之菌落並分別接種於Proteose-Peptone-Glycerine-Salt Agar (PGS)及Heart-Infusion Agar (HI; Difco), 如在PGS培養基產生粘稠菌落而在HI培養基僅產生光滑型菌落菌株是謂CPS株。

藥物感受性測定[3]: 以HI 瓊脂平板稀釋法測定各種藥物對菌株之最低生長抑制濃度(MIC)。18小時HI Broth (Difco)培養稀釋液(MacFarland and Nephelometer Standards No. 1), 以帶狀接種法分別接種於含100, 50, 25, 12.5, 6.3, 3.2, 1.6及0.8μg／ml各種不同藥物濃度之HI瓊脂平板培養基，經37°C 24小時培養後，觀察其生長情形，並以12.5 μg／ml的MIC做爲菌株耐性及感受性之指標濃度。測定之抗生素乃購自各大公司之注射劑，種類如雞隻投與之抗生素外，尚包括Streptomycin (SM; 明治), Kanamycin (KA; 万有), Gentamicin (GM; Schering), Cefazolin (CEF;藤澤)及Nalidixic Acid (NA; NBC)等。

簡稱一覽表 (Abbreviations used):

CPS: Capsular polysaccharide synthesis, EMB agar: Eosin methylene blue agar, PGS agar: Proteose-peptone glycerine salt agar, HI agar: Heart-infusion agar, MIC: Minimum Inhibitory Concentration, MIN: Minocycline, DCT: Demethylchlortetracycline, TC: Tetracycline, OTC: Oxytetracycline, MC: Methacycline, DOX: Doxycycline, CT: Chlortetracycline, CM: Chloramphenicol, AP: Ampicillin, EM: Erythromycin, NA: Nalidixic acid, COL: Colistin-M, SM: Streptomycin, KA: Kanamycin, GM: Gentamicin and CEF: Cefazolin.

結　果

高劑量每日經口投與抗生素之雞隻(100 mg-250 mg of cap／1.5 Kg of chicken)，其肛門拭子分離之大腸桿菌CPS株百分比如圖1所示，其中大腸桿菌CPS株50%以上陽性分離率者，由藥物未投藥前24隻中16隻(66.7%)增加到藥物投與後24小時之19隻(79.2%)，7天後降到13隻(54.2%)(其中NA及COL投與群未能獲得細菌之分離)，但停藥7天後，CPS株分離率又恢復到將近原來的狀態。由此結果知道，

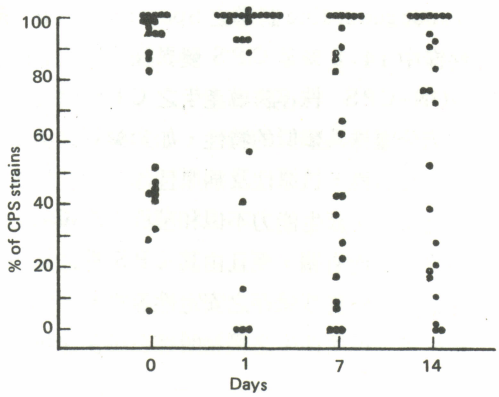

Fig. 1. Distribution of CPS Strains of Escherichia coli during Antibiotics Administration.

Table 1. Geometric Mean MIC to Antibiotics of Escherichia coli was Isolated From Chicken's Rectal Swabs after Tetracyclines Administration

Administration with*	Response to ** (No. of strains)		Ratio (After/Before)
TC	TCs	CPS (10/7)# NON-CPS (4/0)	-1.23 (46.7/57.6)+ - (110.4/-)
	NON—TCs	CPS (10/7) NON-CPS (4/0)	1.18 (8.2/7.0) - (8.2/ -)
OTC	TCs	CPS (9/9) NON-CPS (10/0)	1.28 (66.0/51.6) - (118.3/ -)
	NON-TCs	CPS (9/9) NON-CPS (10/0)	1.16 (9.1/7.9) - (10.5/-)
DCT	TCs	CPS (9/10) NON-CPS (10/10)	1.14 (46.0/32.6) -3.89 (13.4/52.2)
	NON-TCs	CPS (9/10) NON-CPS (10/10)	-1.18 (7.4/8.7) -1.04 (8.2/8.5)
CT	TCs	CPS (10/7) NON-CPS (5/5)	-2.59 (23.3/60.3) -21.26 (7.9/167.3)
	NON-TCs	CPS (10/7) NON-CPS (5/5)	-1.15 (6.8/7.8) -1.68 (6.7/11.2)
MC	TCs	CPS (5/9) NON-CPS (4/7)	1.07 (66.1/61.6) 4.90 (110.5/22.5)
	NON-TCs	CPS (5/9) NON-CPS (4/7)	1.54 (11.0/7.1) 1.25 (8.5/6.8)
DOX	TCs	CPS (9/10) NON-CPS (5/10)	2.93 (46.5/15.9) 1.45 (31.9/22.0)
	NON-TCs	CPS (9/10) NON-CPS (5/10)	1.13 (8.6/7.6) 1.68 (12.8/7.6)
MIN	TCs	CPS (8/9) NON-CPS (5/6)	1.30 (61.9/47.5) 6.40 (181.1/28.3)
	NON-TCs	CPS (8/9) NON-CPS (5/6)	1.02 (9.0/8.8) -1.06 (8.9/9.5)
Total	TCs	CPS (60/61) NON-CPS (43/38)	1.14 (46.7/40.9) 1.23 (46.4/37.7)
	NON-TCs	CPS (60/61) NON-CPS (43/38)	1.05 (8.3/7.9) 1.08 (9.0/8.4)
	Sum	CPS (60/61) NON-CPS (43/38)	1.09 (18.6/17.0) 1.15 (19.4/16.9)

* TC=Tetracycline, OTC=Oxytetracycline, DOX=Doxycycline, MIN=Minocycline, MC=Methacycline, CT=Chlortetracycline, DCT=Demethychloratetracycline,

** TCs: As (*).
NON-TCs: Colistin-M, ampicillin, Streptomycin, Kanamycin, Gentamicin, Cefazolin, Nalidixic acid, Erythromycin and Chloramphenicol.

\# Strains which developed mucoid colonies (CPS) on PGS medium (1-3). Tested strains was isolated from chicken's rectal swabs before and after antibiotics administration.

\+ For calculation of the geometric mean MIC, a value of 200 μg/ml was used in all cases where the MIC was higher than 100 μg/ml.

Table 2. Geometric Mean MIC to Antibiotics of Escherichia coli from Chicken's Rectal Swabs After Antibiotics Administration

Administration with*	Response to ** (No. of strains)		Ratio (After/Before)
COL	TCs	CPS (5/9)**	1.30 (61.9/47.5)**
		NON-CPS (5/5)	6.40 (181.1/28.3)
	NON-TCs	CPS (5/9)	1.02 (9.0/8.8)
		NON-CPS (5/5)	-1.06 (8.9/9.5)
CM	TCs	CPS (8/9)	-1.97 (42.2/83.0)
		NON-CPS (8/10)	3.13 (67.4/21.5)
	NON-TCs	CPS (8/9)	1.05 (8.4/8.0)
		NON-CPS (8/10)	1.30 (8.9/6.8)
AP	TCs	CPS (15/15)	1.04 (74.4/71.7)
		NON-CPS (15/1)	-4.04 (18.4/74.4)
	NON-TCs	CPS (15/15)	1.35 (10.5/7.8)
		NON-CPS (15/1)	-1.31 (8.8/11.6)
EM	TCs	CPS (8/14)	-4.17 (22.0/92.0)
		NON-CPS (15/14)	-2.34 (15.4/36.0)
	NON-TCs	CPS (8/14)	-1.08 (7.7/8.4)
		NON-CPS (15/14)	1.38 (9.5/6.9)
Total	TCs	CPS (36/47)	-1.48 (49.7/73.4)
		NON-CPS (33/30)	1.16 (34.7/29.8)
	NON-TCs	CPS (36/47)	1.12 (9.1/8.2)
		NON-CPS (33/30)	1.20 (9.0/7.5)
	Sum	CPS (36/47)	-1.13 (20.1/22.8)
		NON-CPS (33/30)	1.18 (16.8/14.2)

* COL=Colistin-M, CM=Chloramphenicol, AP=Ampicillin, EM=Erythromycin.
** See table 1 foot note.

CPS 株是普遍存於雞腸道中之大腸桿菌，其頻率甚高，如 24 隻雞隻肛門拭子檢體中，50%以上 CPS 株分離率之雞隻佔 66.7%，而且其中不乏高達 100%者。

抗生素投與方法會影響腸道中大腸桿菌之分佈，無論是經口投與或肌肉注射都會影響 CPS 株之百分比，如 AP 投與後不論是經口投與或肌肉注射對雞隻肛門拭子之 CPS 株分離率全部都有下降之趨勢，而 EM則顯著提高。

高劑量 Tetracyclines 類抗生素每日投與後大腸桿菌之抗生素反應如表 1 所示。各種抗生素對投藥前後之分離株之 Geometric mean MIC 並不一定，與投藥種類及菌株種類有關

。在7種Tetracyclines抗生素投與之效果來看，DCT及CT最爲優越，投與後不論CPS株或NON-CPS株之藥物耐性限閥都低於投藥前。以整個Tetracyclines抗生素投與群分離之CPS株及NON-CPS株對Tetracyclines類或非Tetracyclines抗生素之Geometric mean MIC來看，都較投藥前略爲提高，但不明顯。

高劑量Non-Tetracyclines類抗生素投與者之分離株對抗生素之反應由表2顯出，Non-Tetracyclines類抗生素投與前後菌株對各種抗生素MIC之差異，與投與藥物種類及菌株之種類等而呈現輕微差異之結果，如EM投與群不論是CPS或NON-CPS株對Tetracyclines類抗生素之MIC都較投藥前爲低，相差4.2及2.3倍，對Non-Tetracyclines類抗生素則分別下降1.1倍及提高1.4倍。由Non-Tetracyclines類抗生素投與群全部CPS分離株對Tetracyclines類抗生素之Geometric mean MIC由投藥前之73.4 μg/ml下降到投藥後之49.7 μg/ml相差1.5倍，而對Non-Tetracyclines類抗生素之反應則由投藥前之8.2 μg/ml提高到9.1μg/ml相差1.1倍。NON-CPS株則對兩類抗生素都略爲提高1.2倍（由29.8μg/ml提高到34.7μg/ml）及1.2倍（由7.5μg/ml提高到9.0μg/ml）。

抗生素投與雖影響大腸桿菌CPS株及NON-CPS株在腸道之分佈，但對分離株之藥物感受性分佈則藥物投與前後並無顯著差異。以Tetracyclines類及Non-Tetracycline類抗生素投與前後分離株之藥物感受性分佈如圖2及3所示，雖然各種抗生素投與群間仍有些微的差異，但以全部分離株對抗生素感受性分佈來看，並不受Tetracyclines類或Non-Tetracyclines類抗生素投與之顯著影響，亦即抗生素之短期投與對菌株之藥物感受性並不顯著變化。在高劑量連續投與過程中，腸道內

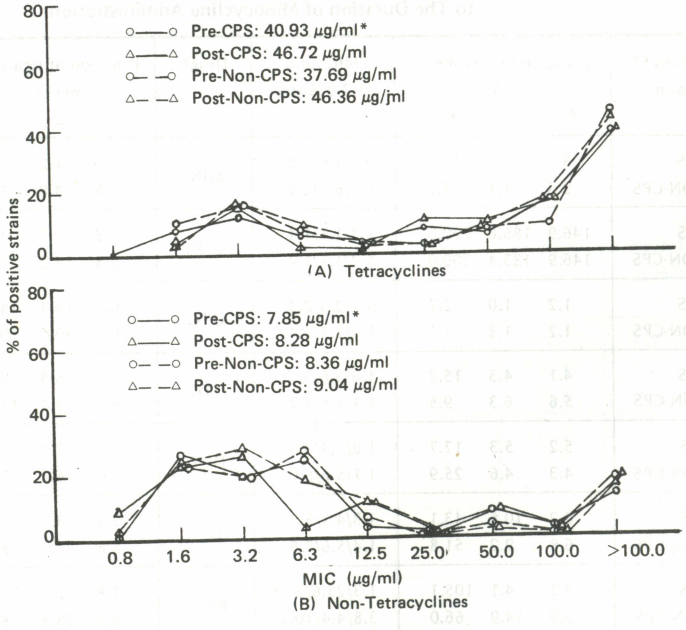

Fig. 2. Susceptibility of CPS Strains of Escherichia coli to Tetracyclines and Non-Tetracyclines Before and After Tetracyclines Administration. * Geometric Mean MICs.

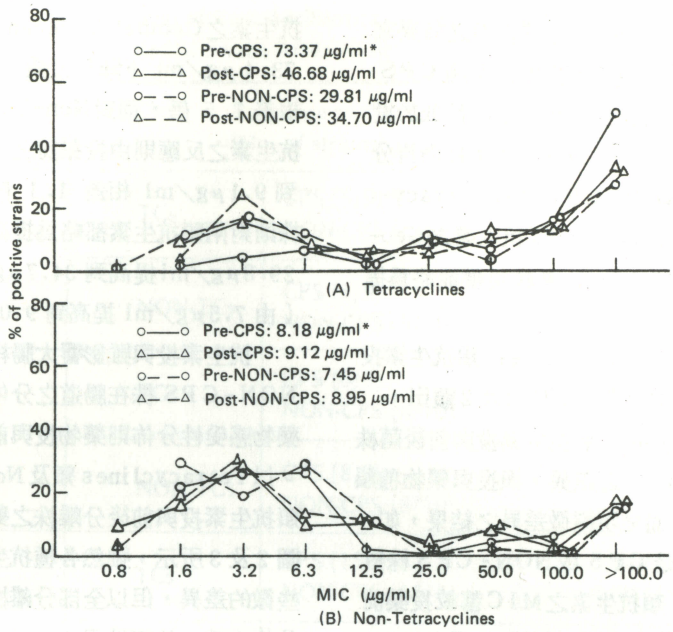

Fig. 3. Susceptibility of CPS Strains of Escherichia coli to Tetracyclines and Non-Tetracyclines Before and After Non-Tetracyclines Antibiotics Administration. * Geometric Mean MICs.

Table 3. Relation of Antibiotics Resistance (Geometric Mean MIC) to The Duration of Minocycline Administration

Drug*	Colony** form	Duration of treatment (week) 0	2	8	MIC ratio 0:2/2:8/0:8	Drug*	Duration of treatment (week) 0	2	8	MIC ratio 0:2/2:8/0:8
NA	CPS	3.4	3.0	10.8	0 /3.6/3.2	MIN	1.0	1.2	11.3	1.2/9.4/11.3
	NON-CPS	2.5	1.1	7.2	0 /6.5/2.9		1.8	4.8	11.7	2.7/2.4/6.5
CM	CPS	146.9	186.6	200.0	1.3/1.1/1.4	DOX	1.3	1.7	35.4	1.3/20.8/27.2
	NON-CPS	146.9	183.4	200.0	1.2/1.1/1.4		2.8	14.2	39.2	5.1/2.8/14.0
CEF	CPS	1.2	1.0	2.7	0 /2.6/2.3	OTC	6.0	10.4	148.6	1.7/14.3/24.7
	NON-CPS	1.2	1.3	1.7	1.0/1.3/1.4		10.3	40.3	107.2	3.9/2.7/10.4
AP	CPS	4.1	4.3	15.2	1.0/3.6/3.7	CTC	4.1	6.3	105.1	1.5/16.7/25.6
	NON-CPS	5.6	6.3	9.5	1.1/1.5/1.7		6.8	32.4	114.9	4.8/3.5/16.9
NEO	CPS	5.2	5.3	17.7	1.0/3.4/3.4	DCT	1.3	2.1	78.1	1.6/37.2/60.0
	NON-CPS	4.3	4.6	25.9	1.1/5.6/6.0		3.0	16.2	61.6	5.4/3.8/20.5
KA	CPS	8.2	10.5	43.1	1.3/4.1/5.3	TC	2.1	3.1	110.4	1.5/35.6/52.8
	NON-CPS	6.8	9.2	51.8	1.4/5.6/7.6		5.6	29.7	87.1	5.3/2.9/15.6
SM	CPS	3.3	4.1	105.1	1.3/25.6/31.8	MC	1.8	2.7	116.0	1.5/43.0/64.4
	NON-CPS	3.9	14.9	66.0	3.8/4.4/16.7		3.7	28.5	84.1	7.8/3.0/22.7

* NA=nalidixic acid, CM=chloramphenicol, CEF=cefazolin, AP=ampicillin, NEO=neomycin, KA=kanamycin, SM=streptomycin, MIN=minocycline, DOX=doxycycline, OTC=oxytetracycline, CTC=chlortetracycline, DCT=demethylchlortetracycline, TC=tetracycline, MC=methacycline.

仍存在相當感受性之菌株，此種感受性株之分佈在大腸桿菌 CPS 株與NON-CPS 株間亦無太大的差異。

雖然以Minocycline 長期投與後CPS株與NON-CPS 株間之藥物感受性都略爲提高，但並無明顯差異。⑴菌株之藥物感受性與藥物投與時間有關，接觸愈久則對抗生素之耐性限閥則愈爲提高（表 3 ），雖然未投藥前 CPS 株對 Tetracyclines類抗生素之Geometric mean MIC都低於NON-CPS株，但其耐性限閥都隨藥物投與時間之延長而增加，其速度較NON-CPS 株爲快。如 MIN 投與前及投與 8 週後之Geometric mean MIC， CPS 株由 1.0μg/ml 提高到 11.3μg/ml 相差 11.3 倍，而NON-CPS 株則由 1.8μg/ml 提高到 11.7μg/ml 僅相差 6.5倍，但此種現象對Non-Tetracyclines 類抗生素之反應並不明顯，如CPS株對NA之Geometric mean MIC由 3.4μg/ml 提高到 10.8μg/ml 相差 3.2倍及 NON-CPS 株由 2.5μg/ml 到 7.2μg/ml僅相差2.9倍。⑵與菌株之交叉耐性株之出現亦有關係（表 4 ），CPS株及 NON-CPS 株對藥物之交叉耐性劑數隨投與時間之延長而增加，如對 7 種Tetracyclines 類抗生素產生交叉耐性者由藥物投與前之 4 株（11.1％）增加到 8週之 16 株（47.1％）及

Table 4. Multiple Drug Resistance of Escherichia coli Isolated from Minocycline Administrated-Chickens

Patterns	Drug combinations*	Duration of treatment (week)**					
		0		2		8	
		CPS	NON-CPS	CPS	NON-CPS	CPS	NONE-CPS
1	OTC	–	–	1 (5.0)#	1 (6.3)	–	–
2	OTC & MC	1 (5.6)	1 (5.6)	1 (5.0)	–	1 (7.1)	–
4	OTC,MC,CTC & DCT	–	–	–	–	–	1 (5.0)
	OTC,MC,CTC & DOX	–	–	–	–	1 (7.1)	–
6	OTC,MC,TC,CTC,DCT & DOX	1 (5.6)	2 (11.1)	3 (15.0)	1 (6.3)	6 (42.9)	5 (25.0)
7	OTC,MC,TC,CTC,DCT,DOX & MIN	1 (5.6)	3 (16.7)	1 (5.0)	9 (56.3)	5 (35.7)	11 (55.0)
Positive strains		3 (18.6)	6 (33.3)	6 (30.0)	11 (68.8)	13 (92.9)	17 (85.0)
1	SM	–	1 (5.6)	1 (5.0)	4 (25.0)	3 (21.4)	2 (10.0)
	KA	7 (38.9)	3 (16.7)	14 (70.0)	3 (18.8)	2 (14.3)	3 (15.0)
	AP	2 (11.1)	–	–	–	–	–
2	SM & KA	–	–	–	2 (12.5)	3 (21.4)	2 (10.0)
	SM & AP	–	–	1 (5.0)	1 (6.3)	–	–
	KA & AP	–	–	1 (5.0)	1 (6.3)	–	–
3	SM,KA & NEO	–	–	–	1 (6.3)	1 (7.1)	7 (35.0)
	SM,KA & CEF	–	–	–	–	2 (14.3)	1 (5.0)
	SM,AP & CEF	–	–	–	–	–	1 (5.0)
4	SM,KA,AP & NEO	–	–	–	–	3 (21.4)	–
	SM,KA,AP & CEF	–	–	–	–	–	1 (5.0)
Positive strains		9 (50.0)	4 (22.2)	17 (85.0)	12 (75.0)	14 (100.0)	17 (85.0)
Tested strains		18	18	20	16	14	20

* See table 1 and 2 for definition of antibiotics abbreviaion.
** CPS: Strains which developed mucoid and non-mucoid colonies on proteose-peptone No. 3 glycerine salt agar (PGS) (1).
\# Number of positive strains: figures in parenthese show the percentage.

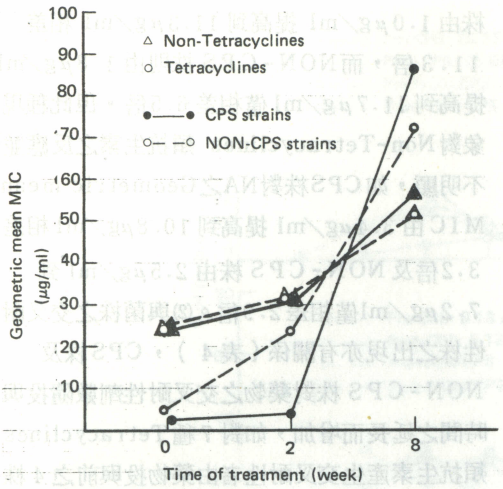

Fig. 4. Geometric Mean MICs of Tetracycline (○) and Non-Tetracycline Antibiotics (△) in CPS Strains of Escherichia coli with Long-term Minocycline Administration.

對4劑Non-Tetracyclines 類抗生素發生交叉耐性者由無耐性株增加到8週之4株（11.8%）。但以整個耐性株之發生率來看，CPS株較NON-CPS株高，如CPS株及NON-CPS株對Tetracyclines類抗生素之耐性率由投藥前之18.6%及33.3%到投藥8週之92.9%及85.0%，及對Non-Tetracyclines類抗生素由投藥前之50.0%及22.2%到投藥8週後之100.0%及85.0%。

在低劑量Mincoycline投與2週時CPS株對Tetracyclines類抗生素之Geometric mean MIC（3.2μg/ml）仍較NON-CPS株23.0μg/ml爲低，但8週後則CPS株（86.4μg/ml）較NON-CPS株（72.5μg/ml）增加（圖4）。對Non-Tetracyclines類抗生素之平均Geometric mean MIC和Tetracyclines類抗生素具類似之耐性型態，但較不明顯（圖4）。

討　論

高劑量藥物連續投與會影響CPS株的分佈，以Tetracycline類或Non-Tetracyclines類抗生素高劑量投與1週後，其分離株對Tetracyclines類抗生素或Non-Tetracyclines類抗生素之感受性，雖然與投與藥物種類有關，即處理前後分離株之Geometric Mean MIC增加或減少不定，但以全部分離株之MIC來看，Tetracyclines類抗生素投與群投藥後之分離株（包括CPS株及NON-CPS株）較投藥前要高但不明顯，而Non-Tetracyclines類抗生素投與群分離株之抗生素感受性雖具類似的現象，但CPS株對Tetracyclines類抗生素之MIC反而較投藥前爲低相差1.5倍，故高劑量藥物連續投與雖然影響大腸桿菌CPS株之分離，但對菌株藥物耐性之影響並不明顯。而且投藥後腸道仍分佈多數藥物感受性株（包括CPS株及NON-CPS株），故無Selective Pressure的作用。

但以Minocycline長期投與8週後，雖然CPS株對各種抗生素之Geometric mean MIC較之NON-CPS株並無顯著提高，但投藥期間CPS株對抗生素耐性限閥的提高則較NON-CPS株快速，尤其是2週以後，此現象亦見於CPS株之交叉耐性率的相對提高。

作者前曾報告[2]雖然同是抗生素感受性之CPS株（SP-CPS-S株）與NON-CPS株，但對各種抗生素之抵抗性則兩者之間卻具非常明顯差異，由本實驗之結果來看，不論是CPS株或NON-CPS株在生體內對藥物耐性限閥的提高必須長期間的適應。尤其是CPS株經長期投與藥物後對各種抗生素耐性之獲得能力較NON-CPS株更爲明顯。雖然在雞腸道中之CPS株對藥物耐性限閥低於NON-CPS株，但由抗生素添與飼料做爲促進劑時對動物本身或附近人類居住環境來說，對細菌尤其是CPS株之耐性獲得率是不可忽視的問題。Acar氏[9,10,11]探討Aminoglycoside抗生素使用前後菌株之耐性型態時發現它們具統計學上有意義的差別，尤其Citrobacter,

Table 5. Geometric Mean MIC to Minocyclin of Escherichia coli with Other Antibiotics Administration

Strains*		Administration with*									
		TC	OTC	DOX	MIN	MC	CT	DCT	COL	AP	EM	CM
CPS	B	4.6	4.2	2.5	5.8	3.6	3.5	2.9	5.0	5.7	9.8	9.2
	A	21.8	29.2	3.1	3.7	8.2	11.7	19.8	5.4	15.0	3.4	16.2
A/B		4.74	6.95	1.24	−1.57	2.28	3.34	6.83	1.08	2.63	-2.88	1.76
Non-CPS	B	–	–	15.4	5.0	8.4	75.8	12.5	3.6	6.3	6.6	7.7
	A	70.7	66.0	10.9	100.0	25.0	3.6	9.5	5.4	4.3	10.9	8.8
A/B		–	–	-1.41	20.00	2.98	-21.06	-1.32	1.50	-1.47	1.65	1.14

* See table 1 foot notes.

Neomycin, Paramycin, Lividomycin, Gentamicin及Tobramycin等之耐性組合更屬明顯，故藥物之使用頻率與菌株之耐性率具密切的關係。

Minocycline在Tetracyclines類抗生素中是最被推薦的藥物，其靜菌能力強於其他Tetracyclines類抗生素，尤其對耐性株更具明顯的效果，它和其他Tetracyclines衍生物無交叉耐性，不易使細菌對之產生藥物耐性，而且易得到較高且長時間的有效血中濃度及較少的副作用[6,12,19]。Minocycline之長期投與（ 8週 ）後對雞腸內大腸桿菌之抗生素感受性反應，它雖不易誘導大腸桿菌對Minocycline 本身MIC之提高，但仍易引起菌株對其他抗生素，尤其是同類衍生物及一些Aminoglycoside 抗生素之耐性限閥及耐性株數的提高。而其高劑量急速投與一星期後，其分離株中之CPS株對Tetracyclines 類抗生素之Geometric mean MIC都較投藥前爲高，尤其NON-CPS株則更爲明顯。其他抗生素投與後之分離株對Minocycline之Geometric mean MIC如表5所示，除Minocycline及Erythromycin 投與群之CPS分離株對Minocycline之Geometric mean MIC較未處理前下降外，其他抗生素投與群之分離株都有相當的提高。

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Studies on Pathogenic Escherichia coli: (VI) Antibiotics Susceptibility of Capsular Polysaccharide-Synthesizing Strains Isolated from Chicken Rectum After Antibiotics Administration

CHENG -CHUANG TSENG, LING-WEN LEE AND WEN-FU KAO

SUMMARY

The capsular polysaccharide-synthesizing (CPS) strains occupied very high percentage of the Escherichia coli isolated from the chicken rectal swabs. All the isolated E. coli strains had very high drug resistance. The NON-CPS strains had higher resistance to tetracyclines than CPS strains.

High-dose short period (6 days) drug administration affected the distribution of E. coli CPS strains. However the geometric mean MIC of the drug for E. coli (CPS as well as NON-CPS strains) after drug administration sometimes increased sometimes decreased, depending on the kinds of the drugs, but the difference was not significant before the administration. Many drug sensitive CPS and NON-CPS strains were still found in the chicken rectal swabs specimens even during the drug administration period. However after long period (8 weeks) administration of minocycline, the resistance threshold and the resistance rate were significantly raised. The geometric mean MICs of antibiotics for CPS strains were only a little higher than the NON-CPS strains, but the rise of the resistance threshold of the CPS strains was faster than the NON-CPS strains, and consequently the cross resistance rate of the CPS strains was higher than the NON-CPS strains.

Department of Microbiology, Taipei Medical College
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