北醫學報 第十三卷 1983年十二月
p.71-82

病原性大腸桿菌之研究第X報
健兒大腸桿菌莢膜多醣類菌株對抗生素之感受性

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摘 要

根據大腸桿菌在EMB瓊脂培養基菌落之特性可分爲3群，其中菌株在EMB具產生黑色及金屬光澤之菌落者是謂EN群，菌落顏色變化不定者爲EV群及產生灰白色菌落者爲EL群等。分離株對8種抗生素中之Gentamicin, Tobramycin及Amikacin 感受性較佳，其次是Cefazolin及Nalidixic acid,而Kanamycin, Ampicillin 及Oxytetracycline 等較差。分離株大部份集中於2－8 μg/ml 或＞128 μg / ml 之MIC。對8種抗生素之幾何平均最低生長抑制濃度EN群是6.52μg/ml，EV群8.19μg/ml及EL群是6.32μg/ml，仍具相當的感受性。但對Oxytetracycline, Ampicillin, Kanamycin, Cefazolin及Nalidixic acid 等抗生素之應用仍須經抗藥性試驗爲宜。

但以多劑耐性組合觀之，發現莢膜多醣類菌株（CPS 株），除EV群外（CPS：52.2%及NON－CPS：55.4% ）都較NON－CPS株爲高，如EN群分別佔38.1%及37.5%及EL群之52.2%及44.5%。全部414株CPS 株中190株（ 45.9% ）具多劑耐性，而78 株NON－CPS株中僅35株（ 44.9% ）。此種多劑耐性組合之偏高仍由於大部份菌株集中於2－16 μg／ml MIC的關係。

若以全部414 株CPS 株對8種抗生素的幾何平均最低生長抑制濃度7.6 μg／ml加以分析仍較78 株NON－CPS株之6.4 μg/ml 爲高。其中EN群之CPS 株及NON－CPS 株之MIC 是7.9μg/ml 及6.8μg／ml，EV群分別具8.5 μg／ml 及 7.7 μg／ml及EL群分別具6.6 μg/ml及 5.5 μg/ml 的生長最低抑制濃度。故CPS株雖然較NON－CPS 株具較高的耐性限閥但並不明顯，它們對抗生素仍具相當的感受性。

緒 論

病原性大腸桿菌之腸外感染，尤其是菌血症等，是革蘭氏陰性腸內桿菌中最常見的病原菌之一，感染後所導致嚴重的休克它與細胞壁之釋放具密切的關係。腸病原性大腸桿菌亦是引起痢疾之主要病原菌，它引起痢疾包括Epidemic infantile diarrhea, Summer diarrhea, Travelers diarrhea 及 Sporadic diarrhea等。腸病原性大腸桿菌之主要病原性，包括細菌的Enterotoxigenicity（heat-stable及heat-labile enterotoxins的產生）及Enteroinvassive 的能力等。（ 5－11 ）

目前對大腸桿菌之腸內及腸外感染是否來自相同的病原性株，尚無明顯的劃份（12-16）。本人曾報告應用PGS培養基，把大腸桿菌分成二大群：莢膜多醣類產生株即CPS 株及NON－CPS株，而CPS 株大腸桿菌之各種特性，如產毒性（小白鼠致死毒性及腸毒素等），定植能力及對抗生

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民國七十二年六月二十日受理

素之耐性等都較NON－CPS株爲高，亦即CPS株較NON－CPS具較強的病原性。並由以往研究得知來自不同檢體所分離之CPS株大腸菌間之種種特性亦無明顯的差異。所以推測CPS株不但是Enteropathogens，也是一般腸外感染的主要Pathogens。

由於目前對健兒及國小低年級學生腸道大腸桿菌，尤其是對乳糖醱酵及非醱酵之CPS株對抗生素感受性，尚未被報告過。故本文擬就健兒門診及國小學生肛門拭子，分離之大腸桿菌對抗生素之感受性提出報告，以期了解腸道正常大腸桿菌對抗生素產生耐性之程度與由患者分離之CPS株，對抗生素之感受性等之差異加以分析，供對由大腸桿菌引起疾患時之用藥及預防菌株對藥物耐性產生等之參考。

材料及方法

菌株分離之對象：1978年台北市大安區衞生所之健兒門診（嬰兒及小孩），大安國小及金華國小一二年級學生等計429件。

大腸桿菌之分離方法(17-19)：以肛門拭子直接塗抹於EMB瓊脂培養基（Difco）經37°C 24小時培養後，依其菌落之顏色加以檢出，包括正常大腸桿菌之黑色金屬光澤菌落群（EN），黑色而不具金屬光澤或易消失之菌落群（EV）及無顏色且呈灰白色之菌落群（EL）等。檢出之菌落再經EMB瓊脂培養基純化後，以TSI瓊脂培養基（Difco）做篩選試驗（Screening test）及進行IMVIC試驗（Difco）等加以鑑定之（如表1）。經純化及鑑定之菌株再分別種於PGS瓊脂培養基及Heart infusion瓊脂培養基（HI：Difco），經37°C 24小時培養後，依其菌落型態加以區分之。在PGS瓊脂培養基產生粘稠菌落而在HI瓊脂培養基僅產生光滑菌落者是謂CPS株，若PGS瓊脂培養基及HI瓊脂培養基都呈現光滑型菌落者是謂NON－CPS株。本試驗使用之菌株數包括EN群210株（CPS株及NON－CPS株各佔186株及24株）；EV群127株（109株及18株）及EL群155株（119株及36株）等共492株。

抗生素之感受性試驗：以HI瓊脂培養基平板連續稀釋法（plate serial dilution method）測定之。使用之抗生素稀釋濃度是128，64，32，16，8，4，2，及1 μg/ml。使用之抗生素包括：Oxytctracycline（OTC；Pfizer），Cefazolin（CEF;藤澤），Ampicillin（AP；Bristol），Kanamycin（KA；萬有），Nalidixic acid (NA; N.B. Co.)，Gentamicin（GM；Schering），Tobramycin（TO，Lilly Taiwan）及Amikacin（AM; Bristol）

結果

來自健兒門診及國小一二年級學生肛門拭子分離之大腸桿菌對8種抗生素之感受性如表2所示，全部分離株對GM，TO及AM三種Aminoglycoside抗生素具較佳感受性，而對OTC，AP及KA等抗生素之耐性則呈現較高的耐性濃度，尤其MIC在128 μg/ml以上者較其他抗生素明顯，由圖1所示，CPS株及NON－CPS株對8種抗生素的感受性並不具明顯的差異。由其對抗生素的感受性分佈來看，不論是EN群、EV群及EL群之CPS株及NON－CPS株對抗生素之感受性大部份集中在MIC 2 μg/ml及16 μg/ml之間及MIC大於128 μg/ml，故在32 μg/ml及128 μg/ml間之耐性株數分佈較少。此種現象如以往由人類臨床來源株及雞來源株對抗生素之感受性類似(14,18-19)，但由MIC在128μg/ml以上之菌株百分比來看，CPS株較NON－CPS株多，CPS株之總幾何平均生長抑濃度（Geometric mean MIC）是7.6 μg/ml較NON－CPS 6.4 μg/ml爲高。其中EN群之CPS株及NON－CPS株之總幾何平均生長抑制濃度是7.9 μg/ml及6.8μg/ml，EV群分別具8.5 μg/ml及7.7μg/ml及EL群具6.6 μg/ml及5.5μg/ml等之差異。EV群之總幾何平均生長抑制濃度是8.19

Table 1. Biochemical Characteristic of Escherichia coli

Biochemical Characteristics		Strains ** EN CPS(186)#	EN NON-CPS(24)	EN Total(210)	EV CPS(109)	EV NON-CPS(18)	EV Total(127)	EL CPS(117)	EL NON-CPS(35)	EL Total(152)	Standard *
TSI	—／A	5(2.7)	0	5(2.4)	0		0	4(3.4)	4(11.4)	8(5.3)	A／AG
	—／AG	8(4.3)	2(8.3)	10(4.8)	50(45.9)	11(61.1)	61(48.0)	112(95.7)	31(88.6)	143(94.1)	
	A／AG	166(89.2)	22(91.7)	188(89.5)	59(54.1)	7(58.9)	66(52.0)	1(0.8)	0	1(0.7)	
	A／A	7(3.8)	0	7(3.3)	0	0	0	0	0	0	
Motility		159(85.4)	16(66.7)	175(83.3)	93(85.3)	15(83.3)	108(85.0)	84(71.8)	27(77.1)	111(73.0)	V
Indole		179(96.2)	24(100.0)	205(96.7)	109(100.0)	18(100.0)	127(100.0)	107(91.5)	31(88.6)	138(90.8)	V
M.R.		186(100.0)	24(100.0)	210(100.0)	109(100.0)	18(100.0)	127(100.0)	117(100.0)	35(100.0)	152(100.0)	+
V.P.		0	0	0	0	0	0	0	0	0	—
Simmons citrate		0	0	0	0	0	0	0	0	0	—
H_2S		0	0	0	0	0	0	0	0	0	—
Adonitol		5(2.7)	1(4.2)	6(2.9)	1(0.9)	5(27.8)	6(4.8)	2(1.7)	2(5.7)	4(2.6)	—
Dulcitol		81(43.5)	8(33.3)	89(42.4)	37(33.9)	3(16.7)	40(31.5)	29(24.8)	1(2.9)	30(19.7)	V
Inositol		17(9.1)	0	17(8.1)	13(11.9)	0	13(10.2)	1(0.9)	1(2.9)	2(1.3)	—
Lactose		180(96.8)	23(95.8)	203(96.7)	83(76.1)	15(83.3)	98(77.2)	0	0	0	+
Mannitol		186(100.0)	23(95.8)	209(99.5)	109(100.0)	209(99.5)	127(100.0)	116(99.1)	33(94.5)	149(98.0)	+
Salcin		29(15.6)	4(16.7)	33(15.7)	33(30.3)	33(15.7)	0	2(1.7)	0	2(1.3)	V
Sucrose		107(57.5)	11(45.8)	118(56.2)	63(57.8)	118(56.2)	72(56.7)	23(19.7)	7(20.0)	30(19.7)	V
Sorbitol		178(95.7)	21(87.5)	199(94.8)	108(99.1)	18(100.0)	126(99.2)	111(94.9)	30(85.7)	141(92.8)	V
Arabinose		184(98.8)	24(100.0)	208(99.0)	107(98.2)	18(100.0)	125(98.4)	116(99.1)	34(97.1)	150(98.7)	+
Raffinose		82(44.1)	7(29.2)	89(42.4)	65(59.6)	9(50.0)	74(58.3)	32(27.4)	10(28.6)	42(27.6)	V
Rhamnose		166(89.2)	17(70.8)	185(87.1)	95(87.2)	11(61.1)	106(83.5)	117(100.0)	27(77.1)	144(94.7)	V
Xylose		185(99.5)	23(95.8)	208(99.0)	109(100.0)	18(100.0)	127(100.0)	114(97.4)	33(94.5)	147(96.7)	?

*Enteric Bacteriology, DHEW-PHS-CDC Atlante Ga, 30333 July, 1975.

Number of positive strains; figure in parentheses indicate percentage.

** Strains which developed normal (EN), variable (EV) and colorless colonies on EMB agar.
Capsular polysaccharide-synthesizing Escherichia coli (CPS strains) was induced by proteose-peptone No. 3 glycerine salt agar.

Table 2. Susceptibility to 8 Antibiotics of Escherichia coli

Drug**	Strains * (No. of strains)		MIC (μg/ml) 1≥	2	4	8	16	32	64	128	≥ 128	Geometric # mean MIC
OTC	EN	CPS(186)		52¢	21			1	4	2	106	39.3
		NON-CPS(24)		7	2				1	1	13	40.3
	EV	CPS(109)	7	35	6	1		3	5	2	50	24.3
		NON-CPS(18)		8	2				1		7	17.3
	EL	CPS(119)	9	44	4	5	2	5	4	3	43	18.3
		NON-CPS(36)	2	14		1	1	1	2	1	14	19.8
CEF	EN	CPS(186)		71	81	18	9	1	3		3	4.0
		NON-CPS(24)		11	12	1						3.0
	EV	CPS(109)		30	35	24	11	7	1		1	5.4
		NON-CPS(18)		6	4	2	5	1				5.7
	EL	CPS(119)	30	40	21	20	3	1		2	2	2.5
		NON-CPS(36)	14	14	4	2	1				1	1.7
AP	EN	CPS(186)			44	100	7				35	13.4
		NON-CPS(24)			7	14	1				2	9.0
	EV	CPS(109)			2	28	21	2			56	54.9
		NON-CPS(18)			1	5	5				7	35.9
	EL	CPS(119)			8	20	27	2			62	55.6
		NON-CPS(36)			2	12	8	2			12	30.8
KA	EN	CPS(186)		2	58	88	10				28	11.1
		NON-CPS(24)		1	8	11	3				1	7.6
	EV	CPS(109)			31	53	2				23	13.8
		NON-CPS(18)			5	7	1				5	18.0
	EL	CPS(119)		7	68	11	1		1		31	12.5
		NON-CPS(36)		1	22	4					9	12.0
NA	EN	CPS(186)		34	119	29		2			2	4.2
		NON-CPS(24)		5	18	1						3.6
	EV	CPS(109)		11	83	7		2		2	4	5.0
		NON-CPS(18)		1	17							3.9
	EL	CPS(119)		17	83	9	1	1	1	1	6	5.1
		NON-CPS(36)		7	24	4					1	4.2
GM	EN	CPS(186)	1	7	100	60	18					5.5
		NON-CPS(24)		2	10	10	2					5.7
	EV	CPS(109)		40	27	41	1					4.1
		NON-CPS(18)		6	2	10						4.7
	EL	CPS(119)	2	42	55	17	2	1				3.5
		NON-CPS(36)	2	16	14	4						2.8
TO	EN	CPS(186)	1	41	109	32	3					3.9
		NON-CPS(24)		5	14	4	1					4.1
	EV	CPS(109)	4	46	49	9	1					3.0
		NON-CPS(18)		10	7	1						2.8
	EL	CPS(119)	3	49	60	5	2					3.0
		NON-CPS(36)	1	15	20							2.8
AM	EN	CPS(186)		1	64	85	34	2				7.2
		NON-CPS(24)			13	5	6					6.5
	EV	CPS(109)	39	15	4	37	14					2.6
		NON-CPS(18)	6	1		9	2					3.2
	EL	CPS(119)	41	61	15	1	1					1.4
		NON-CPS(36)	20	11	5							1.0

*See table 1 for strains description.

**OTC: Oxytetracycline; CEF: Cefazolin; AP: Ampicillin; KA: Kanamycin; NA: Nalidixic acid; GM: Gentamycin; TO: Tobramycin and AM: Amikacin.

For calculation of the geometric mean MIC, a value of 256 μg/ml was used in all cases where the MIC was ≥128 μg/ml.

¢ Number of strains.

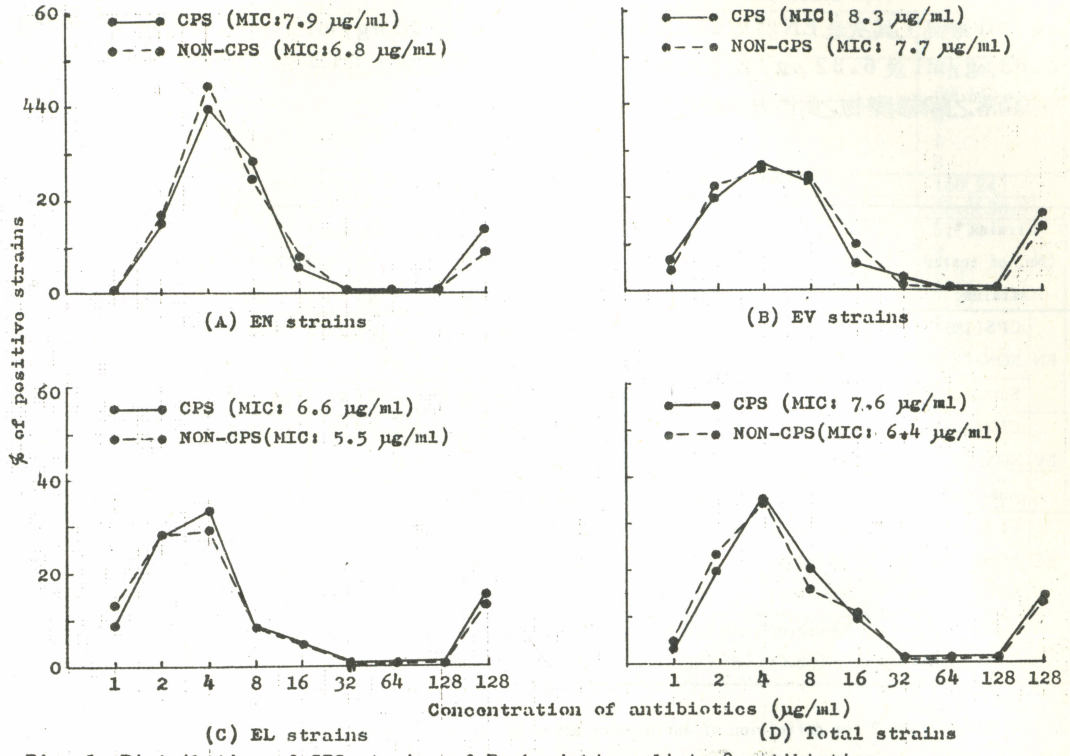

Fig. 1. Distribution of CPS strains of Escherichia coli to 8 antibiotics.

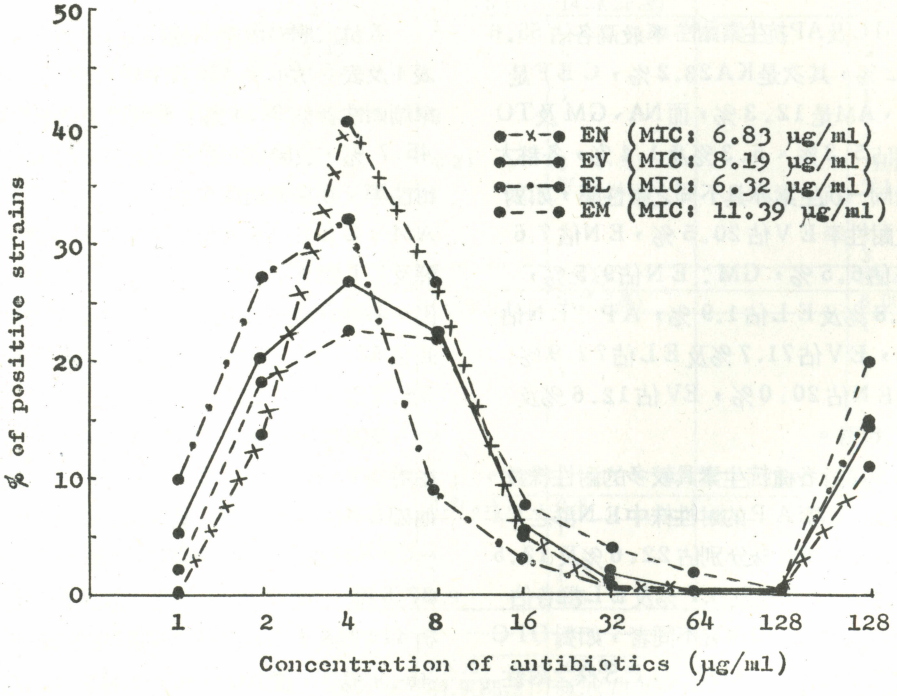

Fig. 2. Susceptibility to 8 antibiotics (average MICs) of Escherichia coli.

μg/ml 最高，其次是EN群及EL 群分別是6.83 μg/ml 及6.32 μg/ml（如圖2）。故粘稠菌落之菌株對藥物之耐性都具較高之耐性限閥。

以16 μg/ml 的MIC 做爲菌株之耐性濃度加以判定則如表3所示，492株對8種抗生素中產生

Table 3. Resistance of Escherichia coli to 8 Antibiotics

Strains * (No. of tested strains)		Antibiotics *							
		OTC	CEF	AP	KA	NA	GM	TO	AM
EN	CPS(186)	113(60.8) #	16 (8.6)	42 (22.6)	38 (20.4)	4 (2.2)	18 (9.7)	3 (1.6)	36 (19.4)
	NON-CPS(24)	15 (62.5)	0	3 (12.5)	4 (16.7)	0	2 (8.3)	1 (4.2)	6 (25.0)
	Subtotal(210)	128(61.0)	16 (7.6)	45 (21.4)	42 (20.0)	4 (1.9)	20 (9.5)	4 (1.9)	42 (20.0)
EV	CPS(109)	60 (55.1)	20 (18.4)	79 (72.5)	25 (22.9)	8 (7.3)	1 (0.9)	1 (0.9)	14 (12.8)
	NON-CPS(18)	8 (44.4)	6 (33.3)	12 (6.7)	6 (33.3)	0	0	0	2 (11.1)
	Subtotal(127)	68 (53.5)	26 (20.5)	91 (71.7)	31 (24.4)	8 (6.3)	1 (0.8)	1 (0.8)	16 (12.6)
EL	CPS(119)	57 (47.9)	9 (6.7)	91 (76.5)	33 (27.7)	10 (8.4)	3 (2.5)	2 (1.7)	1 (0.8)
	NON-CPS(36)	18 (50.0)	2 (5.6)	22 (61.1)	9 (25.0)	1 (2.8)	0	0	0
	Subtotal(155)	75 (48.4)	10 (6.5)	113(72.9)	42 (27.1)	11 (7.1)	3 (1.9)	2 (1.3)	1 (0.6)
Total	CPS(414)	230(55.6)	45 (10.9)	212(51.2)	96 (23.2)	22 (5.3)	22 (5.3)	6 (1.4)	51 (12.3)
	NON-CPS(78)	41 (52.6)	8 (10.3)	37 (47.3)	19 (24.4)	1 (1.3)	2 (2.6)	1 (1.3)	8 (10.3)

*See tables 1 and 2 for definition of antibiotics abbreviation and strains description.

Number of strains; figures in parentheses indicate percentage.

耐性者以OTC及AP抗生素耐性率最高各佔55.6%及51.2%，其次是KA23.2%，CEF是10.9%、AM是12.3%，而NA、GM及TO較小分別佔5.3%、5.3%及1.4%，各群大腸桿菌對同一抗生素亦具不同之耐性率，如對CEF之耐性率EV佔20.5%，EN佔7.6%及EL佔6.5%，GM：EN佔9.5%，EV佔0.8%及EL佔1.9%，AP：EN佔21.4%，EV佔71.7%及EL佔72.9%，AM：EN佔20.0%，EV佔12.6%及EL佔0.6%。

CPS株對各種抗生素具較多的耐性株數，但並不明顯，如對AP的耐性株中EN群之CPS株及NON—CPS株分別佔22.6%及12.5%，EV群佔72.5%及6.7%及EL群各佔76.5%及61.1%，但亦有不同者，如對OTC、EN群之CPS及NON—CPS株之耐性率分別佔60.8%及62.5%，EV群佔55.1%及44.4%及EL群佔47.8%及50.0%。

各群大腸桿菌對8種抗生素的耐性組合如表4及表5所示。492株中對8種抗生素產生單劑耐性者佔37.4%，雙劑以上之耐性率是45.7%，故腸道大腸桿菌已具相當高的多劑耐性率，在單劑耐性包括：AP、OTC、AM、CEF及KA等抗生素中EN群，EV群及EL群各佔38.1%、36.2%及31.0%，多劑耐性組合中以EV群之多劑耐性率最高佔52.7%，其他EN群及EL群分別佔38.2%、50.3%。

在多劑耐性組合中除EV群之CPS株52.2%耐性率較NON—CPS株55.4%低外，其他如EN群及EL群CPS株之耐性率則較NON—CPS株爲高，其耐性率分別是38.1%及37.5%、52.0及44.5%。以多劑耐性加以分析414株CPS株中，多劑耐性者佔190株（45.9%），而NON—CPS株之78株中佔35株（44.9%），二者之多劑耐性率亦無明顯差異。

Table 4 Pattern of Resistance to 8 Antibiotics of Escherichia coli

Pattern	Combination *	Strains				Total
		EN	EV	EL		
1	AP	4	27(3) #	30(7)		61(10)
	OTC	51(8)	12(2)	6(4)		69(14)
	AM	6				6
	CEF	1				1
	KA		2	1		3
	Subtotal	62(8)	41(5)	37(11)		140(24)
	Percentage	33.3(33.3)	37.6(27.8)	31.1(30.6)		33.8(30.8)
2	AP,OTC	11(2)	16(2)	24(3)		51(7)
	AP,AM		2			2
	AP,CEF		(1)	1(1)		1(2)
	AP,KA		1(2)	6		7(2)
	AP,NA			1		1
	OTC,AM	4(2)	3			7(2)
	OTC,KA	10	3			13
	OTC,NA	1		1		2
	GM,AM	5				5
	AM,KA	2(1)				2(1)
	CEF,KA		(1)			(1)
	Subtotal	33(5)	25(6)	33(4)		91(15)
	Percentage	17.7(20.8)	22.9(33.3)	27.7(11.1)		22.0(19.2)
3	AP,OTC,GM			1(1)		1(1)
	AP,OTC,AM		3			3
	AP,OTC,CEF	4	4	1(1)		9(1)
	AP,OTC,KA	6	5	12(8)		23(8)
	AP,OTC,NA	1	1			2
	AP,CEF,KA		3	2		5
	AP,KA,NA		3	1		4
	OTC,TO,KA	1				1
	OTC,GM,AM	5(1)				5(1)
	OTC,AM,CEF		(1)			(1)
	OTC,AM,KA	1(1)				1(1)
	GM,AM,KA	1(1)				1(1)
	Subtotal	19(3)	19(1)	17(10)		55(14)
	Percentage	10.2(12.5)	17.4(5.6)	14.3(27.8)		13.3(17.9)
4	AP,OTC,TO,CEF		1			1
	AP,OTC,TO,KA	1(1)		2		3(1)
	AP,OTC,GM,KA			1		1
	AP,OTC,GM,NA			1		1
	AP,OTC,AM,CEF	1	3			4
	AP,OTC,AM,KA	2				2
	AP,OTC,CEF,KA	5	4(2)	1		11(2)
	AP,OTC,KA,NA			5(1)		5(1)
	AP,GM,AM,CEF	1				1
	AP,CEF,KA,NA			1		1
	OTC,GM,AM,KA	3				3
	Subtotal	13(1)	8(2)	11(1)		33(4)
	Percentage	7.0(4.2)	7.3(11.1)	9.2(2.8)		8.0(5.1)
5	AP,OTC,GM,AM,CEF		1			1
	AP,OTC,GM,AM,KA	1				1
	AP,OTC,GM,CEF,KA			1		1
	AP,OTC,AM,CEF,KA	1				1
	AP,OTC,AM,KA,NA	1				1
	AP,OTC,CEF,KA,NA	1	2			3
	AP,GM,AM,CEF,KA	1	1(1)			2(1)
	Subtotal	5	4(1)	1		10(1)
	Percentage	2.7	3.7(5.6)	0.8		2.4(1.5)
6	AP,OTC,GM,AM,CEF,NA			1		1
	AP,OTC,AM,CEF,KA,NA		1			1
	Subtotal		1	1		2
	Percentage		0.9	0.8		0.5
7	AP,OTC,TO,GM,AM,CEF,KA	1				1
	Percentage	0.5				0.2
	Total	133(17)	98(15)	100(26)		332(58)
	Percentage	71.5(70.8)	89.9(83.3)	84.0(72.2)		80.2(74.4)

*See tables 1 and 2 for definition of antibiotics abbreviation and strains description.
Number of CPS strains; figures in parentheses indicate NON-CPS strains.

Table 5. patterns of Resistance to 8 Antibiotics of Escherichia coli

Strains * (No. of tested strains)	Combination **						
	1	2	3	4	5	6	7
EN CPS(186)	62 (33.3)#	33 (17.7)	19 (10.2)	13 (7.0)	5 (2.7)	0	1 (0.5)
EN NON-CPS(24)	8 (33.3)	5 (20.8)	3 (12.5)	1 (4.2)	0	0	0
EN Subtotal(210)	80 (38.1)	38 (18.1)	22 (10.5)	14 (6.7)	5 (2.4)	0	1 (0.5)
EV CPS(109)	41 (37.6)	25 (22.9)	19 (17.4)	8 (7.3)	4 (3.7)	1 (0.9)	0
EV NON-CPS(18)	5 (27.8)	6 (33.3)	1 (5.5)	2 (11.1)	1 (5.5)	0	0
EV Subtotal(127)	46 (36.2)	31 (24.4)	20 (15.7)	10 (7.9)	5 (3.9)	1 (0.8)	0
EL CPS(119)	37 (31.1)	33 (27.7)	17 (14.3)	11 (9.2)	1 (0.8)	0	0
EL NON-CPS(36)	11 (30.6)	4 (11.1)	10 (27.8)	1 (2.8)	1 (2.8)	0	0
EL Subtotal(155)	48 (31.0)	37 (23.9)	27 (17.4)	12 (7.7)	2 (1.3)	0	0
Total CPS(414)	160(38.6)	91 (22.0)	55 (13.3)	32 (7.7)	10 (2.4)	1 (0.2)	1 (0.2)
Total NON-CPS(78)	24 (30.8)	15 (19.2)	14 (17.9)	4 (5.1)	2 (2.6)	0	0

*See table 1 for strains description.

**See table 4 for drug combinations.

Number of strains; figures in parentheses indicate percentage.

Table 6 Gemetric mean MIC of CPS and NON-CPS strains of Escherichia coli

Drug*	Geometric mean MIC (μg / ml)								
	EN			EV			EL		
	CPS	NON-CPS	Total	CPS	NON-CPS	Total	CPS	NON-CPS	Total
AP	13.4#	9.0	9.9	54.9	35.9	51.7	55.6	30.8	48.5
OTC	39.3	40.3	39.4	24.3	17.3	23.2	18.3	19.8	17.1
KA	11.1	7.6	10.6	13.8	18.0	14.3	12.5	12.0	12.4
NA	4.2	3.6	4.1	5.0	3.9	4.8	5.1	4.2	4.9
CEF	4.0	3.0	3.8	5.4	5.7	5.4	2.5	1.7	2.3
GA	5.5	5.7	5.5	4.1	4.7	4.2	3.5	2.8	3.3
TO	3.9	4.1	3.9	3.0	2.8	3.0	3.0	2.8	3.0
AM	7.2	6.5	7.1	2.6	3.2	2.7	1.4	1.0	1.3
Mean	7.9	6.8	6.8	8.3	7.7	8.2	6.6	5.5	6.3

* See table 1 for definition of antibiotics abbreviation and strains description.

μg/ml

雖然由16 μg /ml以上的最低生長抑制濃度來判斷各群大腸桿菌對各種抗生素已達相當高的耐性率及多劑耐性組合，但由表6之各群大腸桿菌對各種抗生素之幾何平均最低生長抑制濃度顯出，除ＥＮ群對ＯＴＣ、ＥＶ群對ＡＰ及ＯＴＣ、ＥＬ群對ＡＰ外，大都仍具相當良好的感受性如ＮＡ、ＣＥＦ、ＧＭ、ＴＯ及ＡＭ等之幾何平均最低生長抑制濃度仍在1.0 μg /ml 及8.0μg /ml 之間，其他部份仍在相當感受性範圍內。

討　論

來自健兒門診及國小低年級學生肛門拭子之微生物主要是大腸桿菌（17），根據其在ＥＭＢ瓊脂培養基之菌落特性等區分爲3群，即產生黑色及具金屬光澤之ＥＮ群，產生黑色不具光澤之ＥＶ群及無色而呈灰白色的ＥＬ群，各群再根據其在ＰＧＳ瓊脂培養基之菌落型態，可再分爲粘稠菌落及非粘稠光滑型菌落等。全部大腸桿菌分離株中ＥＮ群之分離率佔全部分離菌株之74.0％，ＥＶ群佔12.8％及ＥＬ群佔13.2％，故在ＥＭＢ瓊脂培養基非典型大腸桿菌分離率高達26.0％之多，各群ＣＰＳ株所佔比率亦相當高，如ＥＮ群32.2％，ＥＶ群45.4％及ＥＬ群35.3％，ＣＰＳ株佔全部分離菌株之37.6％，由以往對CPS株之研究得知（12-16），得自臨床檢體之ＣＰＳ株，其對小白鼠的致死毒力等外毒素之產生能力較ＮＯＮ－ＣＰＳ株強。ＣＰＳ株對Adrenal cell的圓變作用及定植能力，比NON－ＣＰＳ株亦具較高的比率。

故在健兒及國小低年級學生肛門拭子中佔37.6％ＣＰＳ株之分離，它在公共衛生上或預防醫學上是一件不可忽視的問題，尤其目前大腸桿菌在非腸道感染疾患中首屈一指的情況下及Opportunistic或Nosocomial Infection愈來愈重要情形下。

我們曉得細菌的病原性除本身的侵犯能力及毒素之產生外，對抗生物質的耐性限閥（Threshold）及耐性獲得能力等，亦是一不可或缺的重要因子，而大腸桿菌對抗生素之耐性獲得不但容易得自其他細菌的耐性基因（Plasmid）的傳遞，本身亦受所處環境的影響，如來自食物所含防腐劑及抗生素之誘導。由臨床檢體來源之大腸桿菌ＣＰＳ株對多種藥物之耐性限閥或多劑耐性率都高於NON—CPS株。或由ＮＯＮ－ＣＰＳ株在藥物如Chloramphenicol及Oxytetracyline或變異劑的Ｎ－methyl－N′－Nitro－N－Nitrosoguanidin誘導下都會使其突變成CPS變異株（15, 20）。由CPS變異株之特性來看，不但具很高的藥物耐性限閥且同時對多種抗生素產生耐性，而且其病原性及多種特性亦相繼發生變化，如生化特性、抗原性及對天竺鼠紅血球的凝集反應（Hemagglutination）等。故此種變異不但影響大腸桿菌之致病性等且及於臨床上的分離及鑑別。

但由健兒門診及國小低年級學生肛門拭子，大腸桿菌對8種抗生素的反應來看ＣＰＳ株較ＮＯＮ－ＣＰＳ株對抗生素的感受性稍低但並無明顯差異。如ＥＮ群ＣＰＳ株之幾何平均最低生長抑制濃度是7.9μg /ml 較NON—CPS株的6.8μg /ml 稍微提高，其他各群亦具類似的型態，如ＥＶ群是8.5μg /ml 及7.7μg /ml 及ＥＬ群是6.6μg /ml 及5.5μg /ml 。在其各種抗生素濃度的菌珠分佈中亦可發現ＣＰＳ株在128μg /ml 以上濃度的菌株數高。以全部ＣＰＳ株之抗生素耐性限閥來看（ＭＩＣ；7.6μg /ml）較ＮＯＮ－ＣＰＳ株（ＭＩＣ；6.4μg /ml）爲高。

由健兒及國小低年級學生肛門拭子的大腸桿菌ＣＰＳ株對抗生素的感受性等和來自雞肛門拭子的大腸桿菌CPS株相同（20）。雞來源ＣＰＳ株對抗生素的感受性較ＮＯＮ－ＣＰＳ株略低，如ＣＰＳ株對7種Tctracycline 類抗生素的幾何平均最低生長抑制濃度是17.0μg /ml ，其他非Tctracycline 類抗生素是22.8μg /ml ，較雞來源大腸桿菌ＮＯＮ－ＣＰＳ株對Tesracycline 類抗生素及非Tetracycline類抗生素的16.9μg /ml 及14.2μg /ml 的幾何平均最低生長抑制濃度爲高，而且菌株之感受性大部亦集中於低濃度或高濃度。大腸桿菌ＣＰＳ株來自臨床檢體者和健兒門診或國小學生者對多種抗

生素的幾何平均最低生長抑制濃度具明顯差異（　　如表７），除ＧＭ外，其他如ＯＴＣ，ＡＰ，ＫＡ

Table 7. Geometric Mean MIC of Clinical and Healty Human Isolates of Escherichin coli

Durg*	Strains**	Clinical isolates	Healty human (Rectal swab)		
			EN	EV	EL
OTC	CPS	165.2	39.3	24.3	18.3
	NON-CPS	18.7	40.3	17.3	19.8
AP	CPS	502.5	13.4	54.9	55.6
	NON-CPS	88.6	9.0	35.9	50.8
KA	CPS	161.9	11.1	13.8	12.5
	NON-CPS	23.2	7.6	18.0	12.0
NA	CPS	17.5	4.2	5.0	5.1
	NON-CPS	7.5	3.6	3.9	4.2
CEF	CPS	12.6	4.0	5.4	2.5
	NON-CPS	14.3	3.0	5.7	1.7
GM	CPS	3.4	7.2	2.6	1.4
	NON-CPS	3.6	6.5	3.2	1.0

* See table 1 for definition of antibiotics and species abbrivations.

** Strains which developed mucoid and non-mucoid colonies on proteosepeptone No.3 glyeerine salt agar.

，ＮＡ及ＣＥＦ等都具明顯的差異，尤其是ＣＰＳ株相差３倍到９倍等，雖然此種獲得可能是來自選擇性壓力的結果，但對ＮＯＮ－ＣＰＳ株變異成ＣＰＳ株也應是可能的機轉，若高劑量短期連續投與時，在雞肛門拭子的大腸桿菌ＣＰＳ株的數目或耐性限閥或耐性株數並無明顯的增加，但若低劑量長期連續投與，則發現ＣＰＳ株的耐性限閥及耐性株數則具明顯的增加（19）故在抗生素感受性的ＣＰＳ株來說它對抗生素之抵抗及耐性的獲得仍較同是抗生素感受性的ＮＯＮ－ＣＰＳ株快速（20）。故在健兒門診及國小低年級學生腸道大腸桿菌之 37.6%ＣＰＳ株分離率是值得注意及探討的問題。

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曾金章

STUDIES ON PATHOGENIC ESCHERICHIA COLI (X). THE ANTIBIOTICS SUSCEPTIBILITY OF CAPSULAR POLY-SACCHARIDE-SYNTHESIZING ESCHERICHIA COLI IN HEALTHY CHILDREN

Cheng-Chuang Tseng

SUMMARY

According to the character of colonies on the EMB agar medium, the Escherichia coli classified into three groups, i.e. strains which produced black, metalic sheen colonies on the EMB agar medium were classified as EN group, strains whose colonies showed variable color as EV group, and those which produced grey white colored colonies as EL group. The isolated strains were more susceptible to Gentamicin, Tobramycin and Amikacin, less susceptible to Cefazolin and Nalidixic acid, least susceptible to Kanamycin, Ampicillin and Oxytetracycline. The MICs of the 8 tested antibiotics for the isolated strains mostly lay in the range of 2-8 μg/ml or > 128 μg/ml. The geometric mean MIC of 8 antibiotics for EN group was 6.83 μg/ml, for EV group was 8.19 μg/ml and for EL group was 6.32 μg/ml, which showed some degree of drug susceptibility. However, drug sensitivity test is recommended before application of antibiotics such as Oxytetracycline, Ampicillin, Kanamycin, Cefazolin and Nalidixic acid.

With respect to their multi-drug-resistance combination, the capsular poly-saccharide-synthesizing (CPS) strains were found to have higher percentage of multi-drug-resistant strans than the NON-CPS strains. For example, in the EN group, 38.1% of CPS and 37.5% of NON-CPS were multi-drug-resistant, and in the EL group, 52.2% of CPS and 44.5% of NON-CPS were so. Only in the EV group, 52.2% of CPS and 55.4% of NON-CPS were multi-drug-resistant. Of the total 414 CPS strains 190 strains (45.9%) were multi-drug-resistant, whereas only 35 (44.9%) out of the 78 NON-CPS strains were so. The high percentage of the multi-drug-resistant strains was due to the fact that the MICs for the most of strains lay within the range of 2-16 μg/ml.

The geometric mean MIC of the total 414 CPS strains was 7.6 μg/ml, higher than that of total 78 NON-CPS strains (6.4 μg/ml). The geometric mean MICs of the CPS and NON-CPS strains in the EN group were 7.9 μg/ml and 6.8 μg/ml respectively, those in EV group were 8.3 μg/ml and 7.7 μg/ml, in EL group were 6.6 μg/ml and 5.5 μg/ml respectively. There-fore, the CPS strains had higher resistance threshold than NON-CPS strains, but not so distinctly, they still had some degree of susceptilility to the tested antibiotics.

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Received for Publication: June 20, 1983.