CONTENTS

	F	Page
Ab	stract (Thai)	(3)
Αb	stract (English)	(4)
Ac	knowledgement	(5)
Со	ntents	(6)
Lis	t of Tables	(8)
Lis	t of Figures	(10)
Ab	breviations	(11)
Ch	apter	
1	Introduction	1
	1.1 Introduction	1
	1.2 Objectives	3
2	Review of Literature	4
	2.1 Streptococcus pneumoniae	4
	2.2 Definition of Drug-Resistant Streptococcus pneumoniae	6
	2.3 Mechanisms of Antimicrobial Resistance	7
	2.4 History of Drug-Resistant Streptococcus pneumoniae	12
	2.5 Prevalence of Drug-Resistant Streptococcus pneumoniae	13
	2.6 Risk Factors for Infected Drug-Resistant Streptococcus pneumoniae	16
	2.7 Clinical Outcome of Infection Caused by Drug-Resistant	17
	Streptococcus pneumoniae	
	2.8 Management of Pneumococcal Infectious Diseases	20
	2.9 Susceptibility Testing	27
3	Materials and Methods	29
	3.1 Setting	29
	3.2 Sample Size Calculation	29
	3.3 Ethics	30

			Page
	3.4 Inclusion	and Exclusion Criteria	30
	3.5 Methods	of Study	31
4	Results		40
5	Discussion		74
6	Conclusion		_ 84
Bibliography			86
Appendix A		McFarland	95
Appendix B		Streptococcus pneumoniae Collection Form	96
Appendix C		Templates for Application of E test Strips	97
Appendix D		E test Reading Guide	98
Appendix E		Clinical Data Collection Form	99
Appendix F		Simplified Acute Physiology Score (SAPS) II	103
Appendix G		Pediatric risk of mortality (PRISM) score	104
Vit	ae		105

LIST OF TABLES

Table		Page
1	NCCLS breakpoints for interpretation of MICs for	7
	Streptococcus pneumoniae	
2	Mechanisms for pneumococcal resistance to macrolides	11
3	β -lactam antibiotics for treatment of drug-resistant pneumococcal	22
	pneumonia for adults	
4	Non $\beta\mbox{-lactam}$ antibiotics for treatment of drug-resistant pneumococcal	23
	pneumonia for adults	
5	Doses of intravenous antimicrobials for children with pneumococcal	26
	infections	
6	Pneumococcal vaccination for adults	28
7	Pneumococcal vaccination for children ≤ 2 year	28
8	MICs interpretation for Streptococcus pneumoniae	35
9	Quality control ranges of MICs for Streptococcus pneumoniae	35
	ATCC 49619	
10	Susceptibility of Streptococcus pneumoniae to penicillin in Southern	41
	Thailand stratified by province	
11	Prevalence of drug resistant Streptococcus pneumoniae in Southern	42
	Thailand stratified by selected antibiotic agents	
12	Multidrug-resistant pneumococci in Southern Thailand	42
13	Pneumococci with intermediate and high level of resistance stratified	44
	by specimen source	
14	Drug-resistant Streptococcus pneumoniae stratified by site of	45
	infection (pneumonia, bacteremia and meningitis)	
15	The MICs for Streptococcus pneumoniae to selected antibiotic	46
	agents	

Table		Page
16	The MICs for Streptococcus pneumoniae stratified by specimen	47
	source	
17	Susceptibility of penicillin-susceptible and penicillin-nonsusceptible	53
	Streptococcus pneumoniae to selected antibiotic agents	
18	Antimicrobial MIC distributions according to penicillin-susceptibility	54
	for S. pneumoniae in Southern Thailand	
19	Antimicrobial MIC distributions according to erythromycin-	55
	susceptibility for S. pneumoniae in Southern Thailand	
20	General characteristics of patients with pneumococcal infection	57
	stratified by penicillin susceptibility	
21	Results of multiple logistic analysis of the potential variable for	59
	penicillin-and erythromycin-nonsusceptible Streptococcus	
	pneumoniae infection in adult	
22	Susceptibility of Streptococcus pneumoniae to penicillin	60
	stratified by co-morbidity	
23	Comparison of difference between penicillin-susceptible and	62
	-nonsusceptible among patient who received $\beta\text{-lactam}$ therapy	
24	Characteristics and outcomes of patients with pneumococcal	64
	pneumonia stratified by penicillin susceptibility	
25	Antibiotic administered and clinical outcome of patient with	69
	pneumococcal bacteremia	
26	Antibiotic pattern and clinical outcome of patient with pneumococcal	71
	meningitis	
27	Clinical outcome and pattern antibiotic use of patients whose	73
	microbiological outcome was eradicated	

LIST OF FIGURES

Figure		Page
1	Streptococcus pneumoniae replicates in pair and lancet-shaped	4
2	Targets, mode of action and mechanisms of resistance of the major	8
	classes of antibacterial drugs	
3	Schematic representation of mechanism of penicillin-resistance in	9
	Streptococcus pneumoniae	
4	Efflux pump, bacteria manufacture protein pumps that pump the	10
	antibiotic out so that it does not accumulate to a high enough internal	
	concentration to block protein synthesis	
5	The penicillin MIC for Streptococcus pneumoniae	48
6	The cefotaxime MIC for Streptococcus pneumoniae	49
7	The imipenem MIC for Streptococcus pneumoniae	50
8	The levofloxacin MIC for Streptococcus pneumoniae	51
9	The erythromycin MIC for Streptococcus pneumoniae	52

ABBREVIATIONS

AIDS = acquired immunodeficiency syndrome

 $BaCl_2.2H_2O$ = barium chloride

BaSO₄ = barium sulfate

°C = Celsius

CAD = coronary artery disease

cfu = colony-forming unit

CI = confidence interval

CNS = central nervous system

 CO_2 = carbon dioxide

COPD = chronic obstructive pulmonary disease

CSF = cerebrospinal fluid

DRSP = drug-resistant Streptococcus pneumoniae

E test = epsilometric test

ESRD = end state renal disease

g = gram

μg = microgram

h = hour

 H_2SO_4 = sulfuric acid

HIV = Human immunodeficiency virus

I = intermediately susceptible

ICU = intensive care unit

IV = intravenous

kg = kilogram

M = mole

mg/kg/d = milligram per kilogram per day

ml = milliliter

mm = millimeter

mm³ = cubic millimeter

MIC = minimum inhibitory concentrations

NCCLS = the National Committee for Clinical Laboratory Standard

No = number

OR = odds ratio

PBP = penicillin binding protein

PO = by mouth (per os)

q = every

R = resistant

S = susceptible

SD = standard deviation

SLE = systemic lupus erythematosus

% V/V = % volume by volume

WBC = white blood cell (count)

wks = weeks

yrs = years