Knowledge, attitude, and behaviour toward antibiotics among Hong Kong people: local-born versus immigrants

TP Lam *, KF Lam, PL Ho, RWH Yung

KEY MESSAGES

- 1. The general public's knowledge about antibiotics is inadequate.
- 2. 30% of the public would expect or request antibiotics for a common cold, but 40% would not complete the full course.
- 3. <40% of the public thought that they could help prevent antibiotic resistance.
- 4. Age and education were the main determinants of knowledge, attitude, and behaviour toward antibiotics.
- 5. New immigrants did not differ from the localborn except that they were more likely to buy

antibiotics over the counter and to keep the leftover.

Hong Kong Med J 2015;21(Suppl 7):S41-7 RFCID project number: 09080852

¹ TP Lam, ² KF Lam, ³ PL Ho, ⁴ RWH Yung

The University of Hong Kong:

- ¹ Department of Family Medicine and Primary Care
- ² Department of Statistics & Actuarial Science
- ³ Department of Microbiology
- ⁴ Hong Kong Sanatorium and Hospital

* Principal applicant and corresponding author: tplam@hku.hk

Introduction

The World Health Organization marked "Antimicrobial resistance: no action today, no cure tomorrow" as the theme of World Health Day 2011. Antimicrobial resistance (AMR) is an urgent global threat.1 The misuse of antibiotics for upper respiratory tract infections (URTI) is a main cause of AMR. Local studies showed that 237 (23.7%) of 1002 interviewed citizens were prescribed antibiotics for their last URTI2; 27.5% of consultations for URTI ended with antibiotics³; and 33.9% of primary care doctors prescribed antibiotics for >40% of URTI consultations.⁴ Some doctors reported that their patients expected antibiotics,4 and at least 26% of patients required antibiotics when they consulted doctors for URTI.²

Patient knowledge, attitude, and behaviour toward the use of antibiotics might not only affect whether an antibiotic is prescribed appropriately but also how it is consumed. Cultural and economic factors also affect antibiotic use.⁵ There was one such study in Hong Kong, but it was limited by the small number (n=12) of questions, a restrictive scoring system, and a 14% response rate.²

We aimed to investigate the public's knowledge, attitude, and behaviour toward antibiotics in both local-born and immigrant populations.

Methods

This combined qualitative and quantitative study was conducted from August 2009 to January 2011.

The former comprised focus groups and in-depth interviews with purposively sampled participants. The latter comprised a territory-wide telephone survey.

Members of 236 social centres in Hong Kong were invited to participate. Eight focus groups with six to eight participants each were conducted. One of the groups consisted of eight new immigrants who had stayed in Hong Kong for about 5 years. An experienced facilitator and an investigator experienced in qualitative research conducted the discussions. Discussions were conducted in Cantonese, audio-taped, and transcribed verbatim. Thematic analysis was used to interpret the transcripts. Two independent investigators read and coded all the transcripts separately, and the two investigators jointly abstracted themes from the coded texts. The quotations below were translated into English for this report.

A questionnaire was developed based on the data collected from focus groups. It was then pilot tested on 50 successfully completed telephone interviews; these data were excluded from analysis.

The Social Sciences Research Centre, the University of Hong Kong, conducted the survey between 6 pm and 10 pm on weekdays from November to December 2010. All interviewers were trained to conduct the questionnaire and completed a practice interview before making phone calls. The target population was randomly selected Cantonesespeaking residents aged 18 years or over in Hong Kong. When contact was successfully established with a target household, an adult with the nearest next birthday was selected, excluding persons with communication difficulties. A maximum of five attempts were made for unanswered lines.

Of all immigrants, a 'new immigrants' subset was specified for those who had stayed in Hong Kong for ≤ 10 years. Those born in Hong Kong were compared with all immigrants, and with the new immigrants.

A 'half-half' proportion from the respondents was assumed. To ensure that the error would be at most 0.02 with 95% confidence, a sample size of 2401 was required. For binary or ordinal responses, multiple logistic or ordinal regression analysis was used to identify the risk factors associated with the respondent's choice. Pearson chi-squared test was used to determine whether nominal responses were dependent. The Student's *t*-test was used to compare interval responses between groups.

Results

A total of 21 males and 35 females aged 20 to 73 years took part in eight focus groups (6-8 per group). Of these, 28.8% had completed tertiary education, 46.2% secondary, and 25.0% primary or below. Two males and two females aged 33 to 61 years participated in the in-depth interviews.

Of 3996 successful calls to households, 157 calls had language problems and 219 were not qualified. Of the remaining 3620 calls, 813 refused to be interviewed, 336 did not complete the interview, and 2471 (864 males and 1607 females) completed the interview (response rate, 68.3%). The age distribution was comparable with the Hong Kong population in the 2010 By-census. Of them, 1634 (66.1%) were born in Hong Kong, 729 (29.5%) in Mainland China,

88 (3.6%) elsewhere, and 20 (0.8%) refused to answer. The local-born and immigrants were comparable in terms of gender distribution (male:female ratio was 584:1050 and 275:542 respectively, χ^2 =1.92, P=0.38).

The immigrants had stayed in Hong Kong for 31.8 ± 17.99 (median, 30) years. The mean years of stay was 14.4 ± 8.18 for young adults (age <40 years), 30.76 ± 14.40 for older adults (age 40-64 years), and 49.1 ± 14.35 for the elderly (age ≥ 65 years). There were more elderly and fewer with tertiary education among the immigrants (P<0.001, Pearson Chi-squared test, Table 1). Young adults were more likely to have a higher education (χ^2 =520.31, P<0.001).

Of all the immigrants from mainland China, 134 were new immigrants. Their mean years in Hong Kong was 7.4 ± 2.74 years. Relative to the localborn, the new immigrants were younger (Wilcoxon V=325, P<0.001) and of a higher proportion of female (χ^2 =26.460, P<0.001) and secondary education (χ^2 =27.223, P<0.001).

Knowledge

Focus-group participants were uncertain about terms such as drug resistance, anti-inflammatory drugs, effectiveness against viral infections like URTI, and the side-effects. Those with a higher education or new immigrants did not differ to others. Some exemplary quotes were:

"Killing bacteria and anti-inflammation." (FG4.P1_p1)

- "...I perceive antibiotics are like those medicine with strong potency." (FG2.P1_p1)
- "I really have no idea." (FG3.P1_p28)

In the telephone survey, immigrants were more likely to give the response 'don't know' (Table 2). The local-born and immigrants did not significantly differ

TABLE I.	Distribution o	f age and o	education	groud	s among	telepho	ne survey	participants

Age and education	No. (%) of participants					
	Local-born (n=1602)	All immigrants (n=803)	New immigrants (subgroup of all immigrants) [n=131]			
Age <40 years						
Primary education or below	6 (0.4)	6 (0.7)	2 (1.5)			
Secondary education	218 (13.6)	109 (13.6)	57 (43.5)			
Tertiary education	306 (19.1)	72 (9.0)	18 (13.7)			
Age 40-64 years						
Primary education or below	151 (9.4)	106 (13.2)	5 (3.8)			
Secondary education	567 (35.4)	239 (29.8)	39 (29.8)			
Tertiary education	251 (15.7)	58 (7.2)	8 (6.1)			
Age ≥65 years						
Primary education or below	54 (3.4)	110 (13.7)	0			
Secondary education	37 (2.3)	75 (9.3)	1 (0.8)			
Tertiary education	12 (0.7)	28 (3.5)	1 (0.8)			

TABLE 2. Responses to questions on knowledge

Question		No. (%) of participant	S	χ²	P value
	Local-born All immigrants		Total sample	-	
Know why antibiotics prescribed				44.138*	< 0.001
Yes	997 (61.1)	404 (49.5)	1401 (57.3)		
No	551 (33.8)	323 (39.6)	874 (35.7)		
Don't know	83 (5.1)	89 (10.9)	172 (7.0)		
Different antibiotics for different infections				2.519	0.284
Yes	1380 (84.5)	677 (82.9)	2057 (83.9)		
No	80 (4.9)	36 (4.4)	116 (4.7)		
Don't know	174 (10.6)	104 (12.7)	278 (11.3)		
Effective for bacteria				37.029*	<0.001
Yes	1208 (73.9)	550 (67.3)	1758 (71.7)		
No	126 (7.7)	36 (4.4)	162 (6.6)		
Don't know	300 (18.4)	231 (28.3)	531 (21.7)		
Effective for virus				39.491*	<0.001
Yes	926 (56.7)	413 (50.6)	1339 (54.6)		
No	269 (16.5)	89 (10.9)	358 (14.6)		
Don't know	439 (26.9)	315 (38.6)	754 (30.8)		
Effective for common cold	. ,			36.242	<0.001
Yes	774 (47.4)	331 (40.5)	1105 (45.1)		
No	560 (34.3)	249 (30.5)	809 (33.0)		
Don't know	300 (18.4)	237 (29.0)	537 (21.9)		
Effective for inflamed throat			,	42.365	<0.001
Yes	888 (54.3)	409 (50.1)	1297 (52.9)		
No	456 (27.9)	173 (21.2)	629 (25.7)		
Don't know	290 (17.7)	235 (28.8)	525 (21.4)		
Effective for urinary tract infection	200 (1111)	200 (20.0)	020 (2111)	35.323	<0.001
Yes	949 (58.1)	377 (46.1)	1326 (54.1)	00.020	<0.001
No	146 (8.9)	73 (8.9)	219 (8.9)		
Don't know	539 (33.0)	367 (44.9)	906 (37.0)		
Undesirable to stop early when symptom-free	555 (55.5)	007 (44.0)	300 (07.0)	81.874*	<0.001
Yes	1136 (69.5)	453 (55.4)	1589 (64.8)	01.074	<0.001
No	343 (21.0)	182 (22.3)	525 (21.4)		
Don't know		. ,			
Undesirable to purchase over the counter	155 (9.5)	182 (22.3)	337 (13.8)	34.779	<0.001
•	1141 (60.6)	406 (60 7)	1607 (66.9)	34.779	<0.001
Yes	1141 (69.6)	496 (60.7)	1637 (66.8)		
No	314 (19.2)	163 (20.0)	477 (19.5)		
Don't know	179 (11.0)	158 (19.3)	337 (13.7)		0.001
Antibiotics have possible side-effects		500 (7 0 0)		35.540*	<0.001
Yes	1197 (73.3)	590 (72.2)	1787 (72.9)		
No	238 (14.6)	69 (8.4)	307 (12.5)		
Don't know	199 (12.2)	158 (19.3)	357 (14.6)		
Drowsiness as a side-effect				18.601*†	<0.001
Yes	494 (41.3)	255 (43.2)	749 (41.9)		
No	591 (49.4)	244 (41.4)	835 (46.7)		
Don't know	112 (9.4)	91 (15.4)	203 (11.4)		

Remains significant after exclusion of 'don't know'
Only interviewees who agreed with possible side-effects from antibiotics were analysed

‡ Only interviewees who always finished the full course of antibiotics were analysed

TABLE 2. Cont'd

Question	I	χ²	P value		
	Local-born	All immigrants	Total sample	-	
Loss of appetite as a side-effect				28.476*†	<0.001
Yes	507 (42.4)	280 (47.5)	787 (44.0)		
No	557 (46.5)	205 (34.7)	762 (42.6)		
Don't know	133 (11.1)	105 (17.8)	238 (13.3)		
Sweating as a side-effect				21.129*†	<0.001
Yes	382 (31.9)	240 (40.7)	622 (34.8)		
No	592 (49.5)	225 (38.1)	817 (45.7)		
Don't know	223 (18.6)	125 (21.2)	348 (19.5)		
Only full course to be effective				1.868‡	0.393
Yes	913 (85.2)	383 (82.9)	1296 (84.5)		
No	111 (10.4)	52 (11.3)	163 (10.6)		
Don't know	47 (4.4)	27 (5.8)	74 (4.8)		
May be ineffective next time if not full course				3.473‡	0.176
Yes	652 (60.9)	274 (59.3)	926 (60.4)		
No	272 (25.4)	108 (23.4)	380 (24.8)		
Don't know	147 (13.7)	80 (17.3)	227 (14.8)		
Duration of common cold				14.870*	0.005
1-3 days	381 (23.3)	162 (19.8)	543 (22.2)		
4-6 days	419 (25.6)	189 (23.1)	608 (24.8)		
1-2 weeks	756 (46.3)	401 (49.1)	1157 (47.2)		
>2 weeks	37 (2.3)	29 (3.5)	66 (2.7)		
Don't know	41 (2.5)	36 (4.4)	77 (3.1)		

for questions: (1) different antibiotics for different infections, (2) only full course to be effective, and (3) incomplete course leading to ineffectiveness next time. The local-born were more likely to give the correct response except for questions: (1) antibiotics having possible side-effects and (2) expected duration of a common cold. Of all interviewees, 223 (9.0%) were not familiar with the term 'drug-resistance'.

One mark was given for a correct response to each of 16 questions; the mean total score was 7.8 ± 3.14 . The local-born scored better than all immigrants (8.1 ± 3.02 vs 7.2 ± 3.28 , t=7.241, P<0.001), but the subset of new-immigrants scored similarly to the local-born (7.7 ± 2.78 vs 8.1 ± 3.02 , t=1.64, P=0.10).

Attitude

Many focus-group participants trusted the doctor's decision on whether to prescribe antibiotics. However, some participants in the new-immigrant group had different ideas:

"When you get sick and have to consult a doctor, you have to trust the doctor. When the doctor's prescription requires you to finish all the medicine, you have to finish it all...." (FG1.

P2_p22)

"He had a casual look [at my son] and then decided to prescribe an antibiotic. Hence I refused." (FG7.P8_p25)

"Prescribing [antibiotics] for colds and flu is not necessary. For doctors, you should prescribe antibiotics only with inflammation, with bacteria; otherwise, you should not." (FG7.P2_p19)

The focus-group participants generally opined that the doctors and the government were the main groups responsible for the prevention of antibiotic resistance.

"I think, the doctor has the greatest responsibility [for antibiotic abuse]." (FG5. P1_p19)

"I gather that there should be two aspects that can be worked on. First is the doctors' integrity.... Second, the government's education department...should be very important." (FG8.P4_p20)

In the telephone survey, both the localborn and immigrants agreed that fewer courses of antibiotics would diminish drug resistance (Table

TABLE 3. Responses to questions on attitude

Question	No. (%) of participants			χ^2	P value
	Local-born	All immigrants	Total sample	-	
Taking more courses of antibiotics would weaken immunity				7.567	0.006
Agree	1267 (85.4)	617 (89.7)	1884 (86.7)		
Disagree	217 (14.6)	71 (10.3)	288 (13.33)		
Types of doctor's antibiotics-prescribing behaviour preferred				10.996	0.012
Rarely	631 (41.7)	264 (37.1)	895 (40.2)		
Readily	25 (1.7)	21 (2.9)	46 (2.1)		
On request	69 (4.6)	48 (6.7)	117 (5.3)		
Indifferent	790 (52.1)	379 (53.2)	1169 (52.5)		
Fewer courses of antibiotics taken would lead to less drug resistance				0.096*	0.818
Agree	1214 (88.6)	547 (89.1)	1761 (88.8)		
Disagree	156 (11.4)	67 (10.9)	223 (11.2)		
Fewer prescriptions by doctors would lead to less drug resistance				0.13*	0.72
Agree	1139 (85.4)	503 (84.8)	1642 (85.3)		
Disagree	194 (14.6)	90 (15.2)	284 (14.7)		
Antibiotic resistance was a serious problem in Hong Kong				8.17*	0.004
Agree	887 (72.9)	402 (79.4)	1289 (74.8)		
Disagree	330 (27.1)	104 (20.6)	434 (25.2)		
Interviewee could help in reducing antibiotics resistance				15.65*	<0.001
Agree	543 (41.7)	182 (32.0)	725 (38.8)		
Disagree	758 (58.3)	386 (68.0)	1144 (61.2)		

* 223 interviewees did not know what drug resistance was and were excluded from analysis

3). Although 50% of each group were indifferent to doctors' antibiotic-prescribing behaviour, the local-born were more likely to prefer more cautious doctors. Likewise, although <40% of all respondents thought that they could help prevent drug resistance, the local-born were more likely to agree.

The immigrants were more likely to agree that (1) more antibiotics might weaken the body's immunity, and (2) antibiotic resistance was a serious problem in Hong Kong.

Behaviour

A frequent comment in the focus groups was that doctors seldom mentioned information about antibiotics (eg nature of the drug, reason for taking) apart from reminders to complete the full course. Trust in their doctor was the main reason for a participant's passive acceptance. A few expected to receive antibiotics on cultural or economic grounds:

"This could be seen as a value-for-money.... And during most of the time, my family members would only take the drugs for 2 days, then illness and pain gone...." (FG6.P5_p2) "During the time when my children and I were still in China, my daughter got sick and she was given intravenous infusion to tackle her fever. It was really effective to control her fever. To almost every child and adult in the mainland, when they got sick, they always received this kind of treatment. However, in Hong Kong, doctors tend to prescribe ordinary drugs, not to mention antibiotics. It took longer to recover from the ailments." (indepth interview, immigrant from Mainland China aged 36 years)

In addition to failure to complete the full course of treatment, other examples of inappropriate use of antibiotics included buying over-the-counter drugs without a prescription, and keeping left-over drugs.

"I didn't have doubt about [the doctor and/or medicine], but I felt getting better, up to 70% and 80%, then took no more." (FG5.P3_p12) "Those drugs are bought [from a drug store] for prevention.... My home always has some kinds of drugs." (FG1.P4_p5)

Of all the telephone interviewees, <10% had ever requested antibiotics from their doctors, kept left-over antibiotics for future use, or bought antibiotics over the counter (Table 4). The immigrants were more likely to buy antibiotics over

TABLE 4. Responses to questions on behaviour

Question	I	No. (%) of participant	s	χ^{2}	P value
	Local-born	All immigrants	Total sample		
Ever asked doctor for antibiotics				0.590	0.442
Yes	136 (8.3)	76 (9.4)	212 (8.7)		
No	1493 (91.7)	735 (90.6)	2228 (91.3)		
Accepted doctor's offer of antibiotics				0.855	0.355
Yes	464 (62.5)	194 (59.3)	658 (61.6)		
No	278 (37.5)	133 (40.7)	411 (38.4)		
Kept left-over for future use				1.642	0.200
Yes	93 (6.1)	54 (7.6)	147 (6.5)		
No	1443 (93.9)	657 (92.4)	2100 (93.5)		
Treated with antibiotics during last common cold				2.805	0.094
Yes	204 (13.6)	123 (16.3)	327 (14.5)		
No	1298 (86.4)	631 (83.7)	1929 (85.5)		
Finished the full course				190.159	<0.001
Always	1071 (69.1)	462 (42.1)	1533 (57.9)		
Not always	480 (30.9)	635 (57.9)	1115 (42.1)		
Expected but did not ask				0.079	0.410
Yes	311 (21.4)	153 (22.0)	464 (21.6)		
No	1141 (78.6)	544 (78.0)	1685 (78.4)		
Bought antibiotics over the counter				5.356	0.021
Yes	112 (6.9)	78 (9.6)	190 (7.8)		
No	1518 (93.1)	732 (90.4)	2250 (92.2)		

TABLE 5. Regression models with birthplace, sex, age, and education as independent variables

Knowledge, attitude, and behaviour	Coefficient (95% CI) relative to local-born*				
	All immigrants	New immigrants			
Total knowledge score	-0.467 (-0.721, -0.213)	-0.578 (-1.094, -0.061)			
Can help preventing antibiotic resistance	1.307 (1.048, 1.630)	0.916 (0.590, 1.420)			
Always finish the full course of antibiotics	1.207 (0.978, 1.490)	0.696 (0.465, 1.044)			
Keep the left-over antibiotics	0.697 (0.481, 1.010)	2.490 (1.385, 4.477)			
Buy over-the-counter antibiotics	0.601 (0.436, 0.829)	2.205 (1.230, 3.953)			

Slope coefficient for total knowledge score and odds ratios for all other dependent variables

the counter and the local-born were more likely to finish the full course. Apart from these two, there was no significant difference in the general behaviour toward antibiotics between the two groups. For young adults, there was no difference between the local-born and the immigrants in their responses to these behaviour questions.

Regression models

immigrants were put into regression models. The independent variables included age-group, gender, education level, and immigration status. After adjusting for these variables in a linear regression, the total knowledge score was associated with birthplace (all immigrants, P<0.001) or new-immigrant status (P=0.028) [Table 5]. For attitude items, only the ability to help prevent antibiotic resistance was associated with birthplace (but not for new-immigrants) in The knowledge, attitude, and behaviour items that the logistic regression. There was no association differed significantly between the local-born and the between the local-born and immigrants (all or new) for completing a full course of antibiotics. All the immigrants were more likely to buy antibiotics overthe-counter, and new immigrants were more likely to keep the left-over drugs.

Discussion

In focus-group discussions, some participants who were recent immigrants (mostly about 5 years) had different views to others. However, the telephone survey showed that birthplace was not associated with attitude or behaviour (except for knowledge) toward antibiotics after adjusting for age and education. The only difference between the localborn and the new immigrants was in the behaviour of buying antibiotics over the counter and keeping left-over drugs, although <10% of them did so. Age and education were the main determinants of the public's knowledge, attitude, and behaviour toward antibiotics.

Hong Kong has been, and still is, an immigrant society. Its population was four million in 1970 and reached seven million in 2010. Its birth rate is among the lowest in the world: declining from 16.8 live births per 1000 population in 1981 to 7.0 in 2003. A very large proportion of the Hong Kong population comprises immigrants who are Hong Kong locals but not locally born. Among the young adults aged \leq 40 years, there was no difference between the local-born and the immigrants in their knowledge, attitude, and behaviour toward antibiotics. It is probable that younger people were more receptive to new knowledge and concepts, and more ready to change their behaviour, whereas the elderly 'Hong Kong locals' retained their old ideas and habits.

In this study, 14.5% of people were prescribed antibiotics for their last URTI, very different from the 27.5% reported in 2002 from a group of selected doctors³ and the 23.7% reported in 2008.² This might suggest a decreasing antibiotic prescription rate. In the 2008 report, 78% of the interviewees completed the full course of antibiotics, but in this study only 57% *always* did so. About 70% of the interviewees in 2008 were deemed to have adequate knowledge (3 out of 5), but in this study the mean total score on knowledge was 7.8 out of 16 indicating inadequate knowledge about antibiotics. Nonetheless, 9% of the interviewees in 2008 and 7.8% in this study bought antibiotics without a prescription.

Although >80% of the interviewees agreed that cautious use of antibiotics could help prevent drug resistance, <40% agreed that they could help. This was probably because in most consultations, antibiotics were simply prescribed without further explanation rather than being actively requested.

Less than 10% of all the interviewees had ever asked their doctors for antibiotics, kept left-over antibiotics for future use, or bought antibiotics over the counter. Nonetheless, <60% always finished the full course, which is unacceptable.

In the telephone survey, the characteristics of the non-respondents could not be obtained. It was uncertain whether or how the non-response rate would affect the results although the response rate of 68.3% was satisfactory. It is possible that the most recent new-immigrants who did not speak Cantonese were excluded from this study.

Conclusion

The main determinants of the general public's knowledge, attitude, and behaviour toward antibiotics were age and education. New immigrants performed comparably with the local-born. The Hong Kong public's knowledge about antibiotics was inadequate. The awareness of their role in preventing AMR should be raised.

Acknowledgements

This study was supported by the Research Fund for the Control of Infectious Diseases, Food and Health Bureau, Hong Kong SAR (#09080852). We thank all those who participated in the focus groups, interviews, and telephone surveys.

Results of this study have been published in: Wun YT, Lam TP, Lam KF, Ho PL, Yung WH. Are there differences in antibiotic use between the recent-immigrants from mainland China and the local-born in Hong Kong? J Immigr Minor Health 2015;17:1177–84.

Wun YT, Lam TP, Lam KF, Ho PL, Yung WH. The public's perspectives on antibiotic resistance and abuse among Chinese in Hong Kong. Pharmacoepidemiol Drug Saf 2013;22:241-9.

References

- Wernli D, Haustein T, Conly J, Carmeli Y, Kickbusch I, Harbarth S. A call for action: the application of The International Health Regulations to the global threat of antimicrobial resistance. PLoS Med 2011;8:e1001022.
- 2. You JH, Yau B, Choi KC, Chau CT, Huang QR, Lee SS. Public knowledge, attitudes and behavior on antibiotic use: a telephone survey in Hong Kong. Infection 2008;36:153-7.
- Dickinson JA, Chan CS. Antibiotic use by practitioners in Hong Kong. Hong Kong Pract 2002;24:282-91.
- Lam TP, Lam KF. Management of upper respiratory tract infection by family doctors. Int J Clin Pract 2001;55:358-60.
- Avorn J, Solomon DH. Cultural and economic factors that (mis)shape antibiotic use: the nonpharmacologic basis of therapeutics. Ann Intern Med 2000;133:128-35.