

THE CLINICAL TOXICITY OF ANTIBIOTICS AND SULFONAMIDES
A COMPARATIVE REVIEW OF THE LITERATURE BASED ON 104,672
CASES TREATED SYSTEMICALLY*

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A PREVIOUS article¹ reviewed statistically the literature from 1936 to Nov. 1, 1950, concerning the manifestations of toxicity observed during and after the systemic administration of the following antibacterial agents: Aureomycin, Chloromycetin, dihydrostreptomycin, penicillin, streptomycin, sulfadiazine, sulfaguanidine, sulfamerazine, sulfanilamide, sulfapyridine, Sulfasuxidine, sulfathiazole, and Terramycin. At the same time the literature on Chloromycetin and Terramycin from Nov. 1, 1950, to April 15, 1951, was also reviewed. In accompanying studies the literature of the same period on the oral manifestations of toxicity following antibacterial therapy² and the unusual toxic reactions reported in individual case reports³ were similarly reviewed in detail.

The present cumulative article (which includes all of the data summarized and tabulated in the initial report¹) reviews, in addition, the literature on the clinical manifestations of toxicity following the systemic administration of Aureomycin, Chloromycetin, and Terramycin as reported in the literature from April 15, 1951, to Jan. 1, 1953; also included is a review of the literature on Elkosin, gantrisin, Magnamycin, Ilotycin, neomycin, bacitracin, and polymixin B from the time of the appearance of published reports on these drugs until Jan. 1, 1953. The literature up to October, 1953, on Magnamycin and Ilotycin, and on gantrisin up to May, 1953, has been included also. Only articles written in the English language were reviewed except in the literature on Elkosin.

Tables I and II summarize nearly all of the large clinical studies involving Aureomycin, Chloromycetin, penicillin, streptomycin, sulfadiazine, sulfaguanidine, sulfamerazine, sulfanilamide, sulfapyridine, sulfasuxidine, sulfathiazole, and Terramycin, as well as nearly every published clinical report which included more than five cases on the systemic administration of bacitracin, Elkosin,

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TABLE

TOTAL NUMBER CASES SYMPTOMS •	AUREOMYCIN 3,121			BACITRACIN (188)			CHLOROMYCETIN 2,968			ELKOSIN 994		
	A	B	C	A	B	C	A	B	C	A	B	C
1. <i>General</i>												
2. Acidosis	85	1.18	0.03									
3. Cephalgia	8	12.50	0.03	21	14.29	1.60	105	4.76	0.17			
4. Aggravation of symptoms							69	34.78	0.81			
5. Cyanosis	39	12.82	0.16									
6. Fever and chills										848	0.24	0.20
7. Flushing and heat (hyperemia)												
8. Burning							30	6.67	0.07			
9. Jaundice (*hepatic and hemo- lytic)							15	0	0			
10. Edema	200	1.00	0.09				30	3.33	0.03			
11. Malaise (*faintness, fullness, lassitude, weakness)							100	3.00	0.10			
12. Pruritus	92	5.43	0.16									
13. Sweating							13	53.85	0.24			
14. Testicular complaints (tingling pain, epididymitis)												
15. Backache												
16. <i>Allergic Manifestations</i>												
17. Sensitivity reactions												
18. Asthma												
19. Herxheimer reaction	271	2.95	0.26				17	29.41	0.17			
20. Id reaction												
21. Serum sickness-like (anaphy- lactoid reaction)							59	1.68	0.03			
22. Skin sensitivity				24	16.27	2.13	22	0	0			
23. Urticaria	223	2.24	0.16				66	9.09	0.20	350	0.29	0.10
24. Arthralgia and arthritis												
25. <i>Cardiac Complications</i>												
26. Bradycardia												
27. Circulatory disorder (*collapse, drop blood pressure)	24	8.33	0.06				33	12.12	0.13			
28. Precordial pain												
29. Tachycardia, palpitation												
30. Hypertension												
31. <i>Eye Signs</i>												
32. Conjunctivitis							33	12.12	0.13			
33. Miscellaneous (*episcleritis, iri- tis, injected sclera)												
34. Visual disturbances (*vision loss, filmy vision, yellow vision)							87	4.60	0.13			
35. <i>Gastrointestinal Disturbances</i>				24	8.33	1.06	59	1.68	0.03	496	4.44	2.21
36. Abdominal distention	393	2.80	0.35	100	1.00	0.53	116	27.59	1.08			
37. Abdominal pain	94	5.32	0.16	24	16.67	2.13	457	6.78	1.04			
38. Anorexia and indigestion	150	8.67	0.42	24	4.17	0.53	420	8.33	1.18			
39. Vomiting and/or nausea	2,344	23.34	17.53	24	4.17	0.53	1,495	5.62	2.83	498	0.80	0.40
40. Diarrhea	1,571	9.61	4.84	100	2.00	1.06	962	5.09	1.63			
41. Gastritis							41	2.44	0.03			
42. Gastroenteritis							25	8.00	0.07			
43. Miscellaneous												
44. Intestinal hemorrhage (*bloody diarrhea)												
45. Hemorrhoids	135	4.44	0.19									
46. Proctitis (*pruritus ani anal fissure, perianal fissure, anal irritation)	635	3.62	0.74	24	8.33	1.06	284	3.17	0.03			
47. <i>Hematologic Changes</i>										350	0	0
48. Anemia							231	1.29	0.10			
49. Acute hemolytic anemia												
50. Blood dyscrasias (other)	393	0	0				449	0.45	0.06			
51. Eosinophils	135	0.74	0.03				70	2.86	0.13			

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ERYTHROMYCIN 74			GANTRISIN 2,010			MAGNAMYCIN 148			NEOMYCIN 405			PENICILLIN 18,519			POLYMYCIN B 75		
A	B	C	A	B	C	A	B	C	A	B	C	A	B	C	A	B	C
			489	2.04	0.50				30	23.33	1.73	12,600	0.63	0.43			
												1,724	10.38	0.97			
			1,239	0.73	0.45				30	33.33	2.47	15,775	6.25	5.32	48	62.50	40.00
			25	4.00	0.05							10,420	0.62	0.35			
												182	0.55	0.01			
			31	6.45	0.10							124	3.23	0.02			
			237	2.11	0.25	15	6.67	0.67				10,420	0.62	0.35	6	33.33	2.67
												10,420	0.13	0.07	6	100.00	8.00
												182	0.55	0.01			
												10,920	0.05	0.03			
			112	1.79	0.10							182	0.55	0.01	32	78.13	33.33
												10,420	0.02	0.01			
												7,906	55.45	-			
												900	0.89	0.04			
												11,044	0.10	0.06			
			1,143	0.17	0.10	57	5.26	2.02				13,338	1.40	1.00	6	100.00	8.00
												10,420	0.16	0.09			
			25	4.00	0.05										6	16.67	1.33
			106	0.94	0.05												
									30	10.00	0.74				6	16.67	1.33
33	3.03	1.35															
						58	5.17	2.02									
			1,122	0.80	0.45	30	16.67	3.38	30	10.00	0.74						
41	2.44	1.35	1,786	2.02	1.79	124	13.71	11.49	66	7.58	1.23	12,100	0.58	0.38	6	16.67	1.33
						124	13.71	11.49									
												1,724	0.58	0.05			
												10,420	0.17	0.10			
			25	12.00	0.15	15	20.00	2.02									
56	0	0							26	0	0						
			175	1.14	0.10												
7	0	0	93	3.23	0.15				26	0	0						

TABLE

TOTAL NUMBER CASES SYMPTOMS*	AUREOMYCIN 3,121			BACITRACIN (188)			CHLOROMYCETIN 2,968			ELKOSIN 994		
	A	B	C	A	B	C	A	B	C	A	B	C
52. Leukocytosis	13	7.69	0.03							350	0	0
53. Leukemoid												
54. Leukopenia	135	0.74	0.03									
55. Granulocytopenia (*neutro- penia, agranulocytosis)							214	0	0			
56. Thrombocytopenia (*thrombo- cytopenic purpura)												
57. Thrombosis of vein												
58. <i>Hepatic Damage-Hepatitis</i> (*hepatitis, ascites)	304	0.33	0.03									
59. <i>Local Reactions</i> (*thrombophlebi- tis, soreness, necrosis, slough, transient pain)							28	21.43	0.20			
60. Myalgia												
61. <i>Neurological Disturbances</i>												
62. Mental disorders and psycho- ses (*confusion, disorientation, drunkenness, C.N.S. dist.)							96	4.17	0.13			
63. Cerebral stimulation (*mental irritation, tenseness, nervous- ness, insomnia)	36	11.11	0.13									
64. Depression (*drowsiness)	308	3.57	0.35							350	0	0
65. Neurological disorders	209	0	0									
66. <i>Auditory Disturbances</i> (tinnitus, deafness—temporary and per- manent, partial and total)												
67. Encephalopathy (*toxic neu- ropathy)												
68. Peripheral neuritis (*nerve palsy, nerve root pain)												
69. Paresthesia (*numbness—fin- gers, legs, toes, hyperesthesia)	108	0.93	0.03									
70. Vertigo	401	2.74	0.35				399	4.76	0.64			
71. Vestibular disturbances (*eighth nerve damage ataxia)							**					
72. <i>Oral Disturbances</i>	99	7.07	0.22				129	29.46	1.28			
73. Stomatitis	134	22.90	0.90				987	4.15	1.38			
74. Glossitis	298	1.34	0.13				413	11.86	1.65			
75. Cheilosis	262	2.29	0.19				293	3.41	0.34			
76. Tongue discoloration	319	2.19	0.22				200	2.00	0.13			
77. Metallic taste	16	12.50	0.06									
78. Bitter taste							428	15.89	2.29			
79. <i>Respiratory Disturbances</i> (*dyspnea, breathlessness, re- spiratory failure)												
80. Pharyngitis	99	7.07	0.22				121	7.44	0.30			
81. <i>Skin Reactions</i>												
82. Dermatitis	222	1.80	0.13				149	6.04	0.30			
83. Desquamative and exfoliative dermatitis	245	1.63	0.13									
84. Dermatitis venenata												
85. Photosensitivity	150	2.67	0.13				46	8.70	0.13			
86. Vulvovaginitis and vaginitis	123	12.20	0.48				201	5.97	0.40			
87. Rash (*scarlatino, fleeting ery- thema)	670	2.99	0.64				525	3.62	0.64	848	2.00	1.71
88. <i>Urinary System Disturbances</i>												
89. Bladder irritation (*burning urination)	245	6.63	0.51				71	8.45	0.20			
90. Kidney disturbances (*renal impairment, nephritis, urinary disturbances, nephrotoxicity)	250	0	0	50	2.00	0.53	121	0	0	848	0.83	0.70

I—CONT'D

ERYTHROMYCIN 74			GANTRISIN 2,010			MAGNAMYCIN 148			NEOMYCIN 405			PENICILLIN 18,519			POLYMYCIN B 75		
A	B	C	A	B	C	A	B	C	A	B	C	A	B	C	A	B	C
			159	8.81	0.70												
			102	2.94	0.15												
												10,420	0	0			
												12,100	2.77	1.81			
												500	0.40	0.01			
			270	3.33	0.45	57	3.51	1.35				182	0.55	0.01	27	0	0
															6	16.67	1.33
1	0	0							241	13.69	8.15				6	16.67	1.33
												10,420	0.11	0.06			
			25	16.00	0.19				30	33.33	2.47				6	16.67	1.33
			25	4.00	0.05	15	6.67	0.68	24	4.17	0.25	1,686	0.18	0.02			
															12	25.00	4.00
															4	25.00	1.33
												51	5.88	0.02			
												297	2.02	0.03			
						57	1.76	0.68				59	6.78	0.02			
			1,484	0.67	0.50							10,420	0.21	0.12			
												10,520	0.06	0.03			
31	0	0	71	1.41	0.05				8	12.50	0.25	2,711	1.92	0.28			
33	0	0	153	0.65	0.05				97	46.39	11.11	36	0	0	69	5.80	5.33

TABLE

TOTAL NUMBER CASES SYMPTOMS*	AUREOMYCIN 3,121			BACITRACIN (188)			CHLOROMYCETIN 2,968			ELKOSIN 994		
	A	B	C	A	B	C	A	B	C	A	B	C
91. Decreased urinary function (*elevated N.P.N., nitrogen retention, azotemia, oliguria, decreased P.S.P.)	36	0	0				85	15.29	0.44			
92. Albuminuria (*cylindruria, urinary casts)	10	10.00	0.03	50	30.00	7.98	15	0	0			
93. Nephrosis												
94. Renal calculi (*kidney stones, renal colic, renal obstruction, crystalluria)							15	0	0			
95. Anuria												
96. Hematuria												
97. Hematuria—microscopic												
98. Hematuria—gross												
99. Renal pain (*loin pain, backache, costovertebral pain)												
Reference Numbers	1-45 368-386			387-390			46-116 358-362 391-412			413-415		

Key:

- A, Number of patients studied for the specific reaction.
 B, Percentage of patients studied for the specific reaction, who manifested these reactions.
 C, Percentage of the total number of patients receiving the antibacterial agent, who manifested the specific reactions.

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*Titles and authors are omitted to save space. Numbers are indexed by specific drugs at the bottom of Tables I and II.

I—CONT'D

ERYTHROMYCIN 74			GANTRISIN 2,010			MAGNAMYCIN 148			NEOMYCIN 405			PENICILLIN 18,519			POLYMYCIN B 75		
A	B	C	A	B	C	A	B	C	A	B	C	A	B	C	A	B	C
			165	0.61	0.05												
									73	6.85	1.23				10	90.00	12.00
			1,640	1.59	1.29				18	16.67	0.74	10,420	0	0			
			31	3.23	0.05												
			1,619	0.68	0.55				49	4.08	0.49						
			1,000	0	0												
416-417			418-433			434-439			440-450			117-138			451-455		

*Including.

†Following treatment of spirochetal diseases only.

•When one investigator reported two or more reactions which were grouped together in this article under one symptom, only the largest figure was included.

**For streptomycin all reports of vertigo were included under vestibular disturbances.

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(Bibliography continued on p. 146.)

TABLE

TOTAL NUMBER CASES SYMPTOMS •	DIHYDRO- STREPTO- MYCIN 462			STREPTOMYCIN 11,305			TERRAMYCIN 3,033			SULFAMER- AZINE 2,875		
	A	B	C	A	B	C	A	B	C	A	B	C
1. <i>General</i>												
2. Acidosis												
3. Cephalgia				7,797	2.81	1.94	230	2.61	0.20	381	1.05	0.14
4. Aggravation of symptoms							12	25.00	0.10			
5. Cyanosis												
6. Fever and chills				2,396	15.07	3.19	190	5.79	11.36	2,988	3.15	3.27
7. Flushing and heat (hyperemia)				3,097	3.91	1.07						
8. Burning							7	14.29	0.03	428	3.74	0.56
9. Jaundice (*hepatic and hemolytic)				930	0.22	0.02						
10. Edema							208	0.48	0.03	151	0.66	0.04
11. Malaise (*faintness, fullness, lassitude, weakness)				3,097	0.19	0.05						
12. Pruritus				3,203	0.38	0.11						
13. Sweating				3,097	0.07	0.02						
14. Testicular complaints (tingling pain, epididymitis)				3,097	0.07	0.02						
15. Backache												
16. <i>Allergic Manifestations</i>												
17. Sensitivity reactions				72	61.11	0.39						
18. Asthma												
19. Herxheimer reaction												
20. Id reaction												
21. Serum sickness-like (anaphylactoid reaction)												
22. Skin sensitivity												
23. Urticaria				3,169	0.88	0.25						
24. Arthralgia and arthritis				3,803	1.13	0.38				278	0.36	0.04
25. <i>Cardiac Complications</i>												
26. Bradycardia												
27. Circulatory disorder (*collapse, drop blood pressure)				3,803	0.47	0.16						
28. Precordial pain												
29. Tachycardia, palpitation				3,134	0.06	0.02						
30. Hypertension												
31. <i>Eye Signs</i>												
32. Conjunctivitis										365	1.64	0.21
33. Miscellaneous (*episcleritis, iritis, injected sclera)												
34. Visual disturbances (*vision loss, filmy vision, yellow vision)				7,190	0.28	0.18						
35. <i>Gastrointestinal Disturbances</i>												
36. Abdominal distention												
37. Abdominal pain				3,097	0.03	0.01	124	3.23	0.13			
38. Anorexia and indigestion							937	6.94	2.14	135	0.74	0.04
39. Vomiting and/or nausea	195	0.03	0.01	8,152	3.77	2.72	2,231	14.48	10.65	2,425	2.43	2.05
40. Diarrhea				32	2.70	0.01	2,440	14.51	11.67			
41. Gastritis												
42. Gastroenteritis												
43. Miscellaneous										292	0.34	0.04
44. Intestinal hemorrhage (*bloody diarrhea)												
45. Hemorrhoids												
46. Proctitis (*pruritus ani, anal fissure, perianal fissure, anal irritation)							1,098	3.01	1.09			
47. <i>Hematologic Changes</i>												
48. Anemia							36	0	0			
49. Acute hemolytic anemia										1,436	0.28	0.14
50. Blood dyscrasias (other)				5,695	0.58	0.29	177	0	0	103	0	0
51. Eosinophils	20	0.30	0.01	10,264	1.89	1.71						

II

SULFADIAZINE 15,852			SULFAGUANIDINE 3,955			SULFANILAMIDE 14,573			SULFAPYRIDINE 10,484			SULFASUXIDINE 1,230			SULFATHIAZOLE 12,863		
A	B	C	A	B	C	A	B	C	A	B	C	A	B	C	A	B	C
3,071	0.59	0.11	206	5.83	0.30	7,895	2.32	1.26	588	36.05	2.02	61	1.64	0.08	271	0	0
216	0.46	0.01				3,220	20.90	4.62	1,772	6.55	1.11	28	7.14	0.16	5,777	0.45	0.20
13,738	1.57	1.36	2,131	1.78	0.96	13,811	7.70	7.29	6,748	3.38	2.18	1,002	0.80	0.65	261	0.38	0.01
100	11.00	0.07	44	6.82	0.08										7,388	5.59	3.21
1,360	0.07	0.01				2,079	1.15	0.17	100	10.00	0.01				490	0.82	0.03
55	5.64	1.02															
100	30.00	0.19	191	23.56	1.14	7,695	2.08	1.10	450	12.00	0.52				375	0.80	0.02
902	0.44	0.03							380	0.79	0.03	102	1.96	0.16			
									70	1.43	0.01				5,037	0.02	0.01
5,500	0.22	0.08	191	1.57	0.08	1,725	0.12	0.01	236	0.85	0.02				100	10.00	0.01
1,063	0.38	0.03				6,176	0.50	0.21	108	0.93	0.01	511	0.78	0.33	1,522	0.59	0.07
100	63.00	0.40				6,170	0.97	0.41							71	2.82	0.02
									377	0.80	0.03						
									380	1.05	0.04				360	0.28	0.01
						1,083	0	0									
2,803	0.46	0.08	50	2.00	0.03				797	0.38	0.03				4,970	1.85	0.72
901	0.22	0.01							102	0.98	0.01						
660	0.15	0.01				6,070	0.10	0.04	508	0	0				642	0.31	0.02
500	2.40	0.08	191	2.62	0.13	6,070	1.12	0.47	502	2.99	0.14						
1,235	1.50	1.17	1,129	1.33	0.38	7,695	1.34	0.71	480	14.79	0.68	50	2.00	0.08			
						8,854	2.01	1.22	7,827	39.50	29.49	683	0.88	0.49	11,383	7.12	6.30
						7,795	0.73	0.39	960	0.73	0.07	210	7.14	1.22	1,408	0.64	0.07
						1,625	3.69	0.41	864	0.69	0.49						
									297	0	0				271	0	0
						6,070	0.02	0.01									
												11	3.64	0.33			
4,207	0.31	0.08	590	0.34	0.05	4,500	1.56	0.48	1,636	2.57	0.04	28	7.14	0.16	993	2.82	0.22
221	0	0	22	0	0	9,202	0.67	0.43	5,376	1.75	0.90				3,265	0.34	0.09
						100	0	0				290	0	0	400	0	0
												50	2.00	0.08			

* II—CONT'D

SULFADIAZINE 15,852			SULFAGUANIDINE 3,955			SULFANILAMIDE 14,573			SULFAPYRIDINE 10,484			SULFASUXIDINE 1,230			SULFATHIAZOLE 12,863		
A	B	C	A	B	C	A	B	C	A	B	C	A	B	C	A	B	C
1,037	0.29	0.02	44	0	0	300	0.33	0.01	862	0.35	0.03				1,387	0.22	0.02
741	0.41	0.02															
11,107	1.64	1.15	605	0.17	0.03	10,553	0.52	0.38	6,601	2.12	1.34	28	0	0	12,935	0.70	0.71
6,628	0.02	0.01	15	0	0	11,116	0.23	0.17	3,543	0.79	0.27				2,387	0.36	0.06
						1,114	0.10	0.01							271	0	0
2,506	0	0				3,303	0.52	0.12	2,302	0.26	0.06				3,258	0.09	0.02
									80	1.25	0.01						
100	15.00	0.10				245	1.62	0.03	450	17.33	0.74				399	0.51	0.02
100	3.00	0.20				1,729	1.74	0.21	806	4.72	0.36				52	1.92	0.01
380	0.53	0.01				2,825	0.60	0.12	100	5.00	0.05				271	0	0
141	2.84	0.03															
1,513	0.33	0.03				1,658	0	0	1,164	0.86	0.10				984	0.10	0.01
						6,170	2.80	0.50	108	0	0				5,237	0.04	0.02
1,858	0.38	0.04				7,895	3.80	2.06	778	16.71	1.24	50	2.00	0.08	5,617	2.51	1.10
						6,070	0.08	0.03									
6,070	0.03	0.01							5,037	0.04	0.02						
						6,070	0.89	0.37									
10,145	1.57	1.00				4,691	1.66	0.54	5,510	2.09	1.10				5,807	4.31	1.94
						106	0	0							110	0.91	0.01
10,607	1.18	0.79	1,163	2.67	0.78	11,908	2.26	1.85	3,222	3.85	1.18				2,484	4.79	0.93

TABLE

TOTAL NUMBER CASES SYMPTOMS •	DIHYDRO- STREPTO- MYCIN 462			STREPTOMYCIN 11,305			TERRAMYCIN 3,033			SULFAMER- AZINE 2,875		
	A	B	C	A	B	C	A	B	C	A	B	C
90. Kidney disturbances (*renal im- pairment, nephritis, urinary dis- turbances, nephrotoxicity)	41	0.02	0.01				153	0	0	585	2.05	0.42
91. Decreased urinary function (*ele- vated N.P.N., nitrogen retention, azotemia, oliguria decreased P.S. P.)				10,891	4.20	4.04				238	0.42	0.04
92. Albuminuria (*cylindruria urinary casts)	42	0	0	5,754	22.70	11.55	7	14.25	0.03	135	0.74	0.04
93. Nephrosis												
94. Renal calculi (*kidney stones, renal colic, renal obstruction, crystalluria)				131	17.56	0.20				1,582	7.78	4.28
95. Anuria										497	0.40	0.07
96. Hematuria	21	0	0	3,944	4.13	1.44	7	14.25	0.03	88	0	0
97. Hematuria—microscopic										1,558	6.35	3.44
98. Hematuria—gross										1,550	1.23	0.66
99. Renal pain (*loin pain, backache, costovertebral pain)										1,025	0.78	0.28
Reference Numbers				139-154			347 363 456- 357 367 489			204-220		

Key:

A, Number of patients studied for the specific reaction.

B, Percentage of patients studied for the specific reaction, who manifested these reactions.

C, Percentage of the total number of patients receiving the antibacterial agent, who manifested the specific reactions.

(Bibliography for Tables I and II continued from p. 141.)

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* II—CONT'D

SULFADIAZINE 15,852			SULFAGUANIDINE 3,955			SULFANILAMIDE 14,573			SULFAPYRIDINE 10,484			SULFASXIDINE 1,230			SULFATHIAZOLE 12,863		
A	B	C	A	B	C	A	B	C	A	B	C	A	B	C	A	B	C
7,503	1.45	0.69	843	0.12	0.03	811	0.12	0.01	169	0	0				1,293	1.01	0.10
2,212	0.63	0.09	191	0.52	0.03	347	1.73	0.04	5,203	2.04	1.01	177	0	0	796	3.64	0.23
			520	0	0	106	1.89	0.01									
503	0.60	0.02													2,459	0.48	0.09
2,400	4.04	0.06	1,738	31.30	13.76	33	0	0	2,929	2.12	0.59	461	0.43	0.16	5,434	2.01	0.85
1,465	0	0				1,000	0	0	756	1.06	0.08				371	0.54	0.02
2,270	1.81	0.26	761	0.53	0.10	1,553	0.58	0.06	6,524	3.94	2.45	511	0.39	0.16	4,445	5.74	1.98
9,217	2.82	1.64							1,780	2.64	0.45				1,162	5.51	0.50
1,640	1.59	0.16							1,499	1.67	0.24				1,139	0.35	0.03
1,260	2.70	0.21	191	1.05	0.05				490	2.25	0.11						
155-184			185-203			221-241			242-284			285-304			305-346		

*Including.

†Following treatment of spirochetal diseases only.

●When one investigator reported 2 or more reactions which were grouped together in this article under one symptom, only the largest figure was included.

**For streptomycin all reports of vertigo were included under vestibular disturbances.

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Owing to the varied manner in which clinicians have recorded and interpreted toxicity and side reactions, the true incidence of a given toxic reaction

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probably lies somewhere between the two percentage figures in columns B and C in Tables I and II. The percentage in column B, usually a higher one, represents a compilation of reported percentage reactions. The percentage in column C has been obtained by dividing the total number of reactions by the total number of cases reported for that drug in this study. The figures at the

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bottom of the column for each drug in Tables I and II refer to the bibliographic reference numbers for that drug.

Some of the reactions listed (particularly those in which only a very small percentage of the total patients receiving a drug manifested such a reaction) could have occurred coincidentally. Thus, association of symptoms with a particular antibacterial agent does not necessarily denote causation.

It is unfortunate that this study could not be based exclusively on investigations directed specifically and exclusively at observations of the toxic reactions to drug therapy. Such worth-while researches have been performed⁴⁻⁶ in some areas of the investigation of drug action, but seemingly only rarely.

These figures are presented solely as an extensive comparative survey of the literature. It is not possible to draw conclusions or discuss the findings within the confines of this article.

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