CENTER FOR DISEASE CONTROL





# MORBIDITY AND MORTALITY WEEKLY REPORT

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# Current Trends

# **Guidelines For Short-Course Tuberculosis Chemotherapy**

# The following recommendations on short-course chemotherapy for tuberculosis form a joint statement of the American Thoracic Society and the Center for Disease Control.\*

# Introduction

The objective of tuberculosis therapy is to achieve lifetime control of the disease for the patient. There are now available many drug regimens which offer virtually certain "cure" of tuberculosis. The primary factor which thwarts this promise of cure in the United States and other developed nations is noncompliance or failure to complete the prescribed regimen. Shortening the total duration of chemotherapy is a potential means of combating this problem. However, in choosing a short-course chemotherapy (SCC) regimen, consideration must be given to (1) assuring overall therapeutic success comparable to therapy of conventional duration, (2) avoiding any significant increase in drug toxicity, and (3) keeping the cost within an acceptable range.

# **Duration of Chemotherapy: Current State**

Extensive experience with chemotherapy regimens of long duration has shown what results may be anticipated from them, even when accompanied by some irregularity or interruption in drug taking. Most patients apparently receive a quantity of medication sufficient to achieve an enduring cure.

A Public Health Service trial conducted in the United States has shown that daily isoniazid (INH) and rifampin (RIF) given for 20 weeks, followed by daily INH and ethambutol (EMB) until sputum has remained culture negative for 1 year, is an extremely effective and well-tolerated regimen (1). Therefore, depending on the patient's initial bacteriologic status and therapeutic response, a treatment duration of no longer than 12 to 18 months can now be considered acceptable in the United States, provided that INH and RIF are given for at least the first 20 weeks. In those patients with obvious difficulty in adhering to self-administered regimens, directly supervised treatment on a daily or intermittent basis has been shown to enhance substantially the prospect for a successful outcome (2). The reports of these regimens, which reflect results achieved under field conditions, should therefore serve as standards of successful outcome against which to measure SCC. An acceptable SCC regimen should allow reduction in the duration of therapy while resulting in a rate of relapse not greater than 5%.

<sup>\*</sup>This statement was prepared by an ad hoc committee of the Scientific Assembly on Tuberculosis, and the Tuberculosis Control Division of CDC. The committee members are Michael D. Iseman, MD, Chairman, Richard Albert, MD, Matthew Locks, MD, James Raleigh, MD, Frank Sutton, MD, and Laurence S. Farer, MD (CDC).

## Tuberculosis Chemotherapy – Continued

The incidence of adverse drug reactions with the conventional-duration and supervisedintermittent chemotherapy regimens is also quite low. Fewer than 5% serious drug reactions were reported with these drug regimens. Thus, to be generally acceptable, an SCC regimen should not entail toxic reactions above this level.

The fiscal comparisons are somewhat more difficult because of the "hidden" costs of tuberculosis care. In addition to the expense of the drugs, consideration must be given to the cost of hospitalization, cost of supervision of drug administration, and long-term medical, social, and economic consequences of inadequate or incomplete chemotherapy. However, unless there are vast differences in the cost, such considerations should be of secondary importance.

#### Short-Course Chemotherapy: Current State

Many of the published reports of SCC trials are difficult to evaluate because of (1) insufficient numbers of subjects in each treatment category to permit reliable conclusions with regard to relative effectiveness, (2) poor definition of the populations studied, or (3) unclear criteria for exclusion from the study. Furthermore, in many of the published clinical trials, every dose of medication was administered under inpatient and/or outpatient direct supervision; thus, these results denote the best possible outcome obtainable with these drug regimens. Results obtained with direct supervision of treatment should not be extrapolated to a similar but unsupervised regimen. The proportion of drug doses that can be missed before a decrease in regimen efficacy occurs is unknown, but under routine program conditions, equally good results are not likely to ensue.

A review of published reports of regimens of 6-month duration shows that most of them were followed by 5% or more relapses during 5 months' to 5 years' observation (3-9), and a few involved inpatient treatment for the entire 6 months (3,4). For these reasons, a 6-month short-course chemotherapy regimen cannot be recommended for general use in the treatment of tuberculosis in the United States at this time. Regimens of this length are currently under study in this country and abroad and should be considered experimental.

Chemotherapeutic regimens in the range of 8 to 12 months' duration show more promise than the shorter programs. However, several regimens of this duration have shown either relapse frequencies greater than 5% (8,9) or unacceptable levels of drug toxicity (9). Some of these regimens have given acceptable results but employed such drugs as streptomycin (SM) and pyrazinamide (which result in modestly increased toxicity, the inconvenience and administrative problems of long-term drug injections, and unpleasant subjective reactions to an extent which this committee would deem impractical for widespread and prolonged use) or thiacetazone (which is unavailable in this country).

It should be noted that the regimen of INH, RIF, SM, and pyrazinamide results in extremely rapid sterilization of tissues and that various combinations, durations, and rhythms of these agents (4,5,8,9,10) have proved highly effective. However, for the reasons stated above such drug regimens should not be employed universally; rather, they might be used in selected patients in whom there is a high probability of premature termination of treatment.

There are 3 reported SCC regimens that are most relevant to shortening the duration of chemotherapy in the United States. The British Thoracic and Tuberculosis Association (BTTA) treated patients with various regimens that included 2 months of INH, RIF, and SM or EMB, followed by 4 to 10 months of INH and RIF; all drugs were given daily and presumably self-administered except during the hospital period (duration not reported) and the SM injections (6). The regimen that is of greatest interest is the 9-

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# Tuberculosis Chemotherapy - Continued

month therapy applied to patients with more extensive disease. In this group, all 135 patients showed good initial response, and no relapses were detected in 2 years' post-treatment observation. It should be noted, however, that a bias toward compliant patients may have operated in the enrollment for this study.

A variant on SCC was reported from Singapore by the British Medical Research Council. In this study, patients were given 2 weeks of daily INH, RIF, and SM; this was followed by 50 weeks of intermittent INH and RIF (11). During the intermittent phase, the INH and RIF were given either once or twice a week, and the RIF was given either in 900 mg or 600 mg doses. The regimen that was composed of twice-weekly INH and RIF (600 mg per dose) was highly efficacious, well-tolerated, and relatively free of adverse effects.

The most extensive published domestic experience with SCC has been accumulated in the state of Arkansas, where a regimen of 1 month of daily INH and RIF followed by 8 months of twice-weekly INH and RIF was employed (12). There were 10 initial failures among 185 patients and 1 relapse in the remaining 175 patients. The intermittent therapy was generally self-administered although those patients deemed significantly noncompliant were put on supervised drug administration. There were few instances of significant drug toxicity among these patients.

Based on these studies, the following generalizations regarding SCC can be made:

(A) INH and RIF given regularly for 9 to 12 months result in highly acceptable initial response and relapse rates among patients with drug-susceptible organisms.

(B) A substantial portion of this therapy may be given on a twice-weekly basis. This may be either fully supervised (11) or selectively supervised (12).

(C) The initial phase of daily therapy may be as short as 2 to 4 weeks (11,12).

(D) While SCC may prove effective in some patients with INH-resistant organisms, the overall response rates are not good enough to justify widespread use of SCC in this context.

(E) While there may be a modestly increased risk of toxicity with RIF given twice weekly, if the dose is proper the incidence of adverse reactions appears quite acceptable (11,12).

# Recommendations

Based on the foregoing considerations, the following recommendations for SCC in the United States are offered:

(1) A chemotherapy regimen using a "core" of INH and RIF for a minimum of 9 months' duration is an acceptable alternative to regimens now being used for adults with uncomplicated pulmonary tuberculosis. Although extensive data are not available for children, the regimen would probably be suitable for children as well. At this time, recommendations for shortened treatment cannot be made for patients with extrapulmonary tuberculosis, for drug-resistant cases, or for patients with complicating medical conditions (diabetes, silicosis, or drug- or disease-induced immunosuppression).

(2) For the initial phase of treatment, the patient may or may not be hospitalized, depending on the severity of symptoms, public health considerations of infectiousness, and the ability to ingest medications and provide self-care.

(3) Treatment for the adult patient should begin with INH (300 mg) and RIF (600 mg) daily. In children, give INH 10 mg/kg up to 300 mg and RIF 10-20 mg/kg up to 600 mg daily. EMB (15 mg/kg daily) should be added if the patient resides in or has emigrated from an area with a high level of initial drug resistance, or if a history of previous antituberculosis chemotherapy is obtained. Drug-susceptibility testing should be carried out under these circumstances because of the increased chance of initial drug resistance, especially to INH. If used, EMB should be continued until initial drug-susceptibility studies

#### Tuberculosis Chemotherapy – Continued

confirm susceptibility to INH and RIF. If resistance is found, a revision of the chemotherapy regimen and the length of treatment will be required.

(4) After an initial daily phase of chemotherapy ranging from 2 weeks to 2 months, treatment should be continued, employing either daily (if self-given) or twice-weekly (supervised) INH and RIF. If drugs are self-administered, adherence to the regimen should be carefully monitored by such indicators as clinic attendance, pill counts, urine tests, and bacteriologic examinations of the sputum. If a patient is judged to be unreliable in self-administering medication, therapy should be switched to directly administered, twice-weekly INH (15 mg/kg) and RIF (600 mg). Patients who are receiving RIF intermittently should be regularly monitored by history for possible manifestations of thrombocy-topenia (purpura, petechiae, hematuria) or the "flu syndrome."

(5) Treatment should be continued for no less than 9 months and longer if necessary (until at least 6 months have elapsed from conversion of sputum to culture negativity). Since over 90% of the patients taking INH and RIF can be expected to become sputum negative within 3 months of starting treatment, total treatment for more than 9 months should be exceptional. If there are serious questions regarding the regularity of drug ingestion, if there have been complicating medical conditions, or if there is evidence of disseminated disease, it may be advisable to extend the duration of treatment even beyond 6 months of sputum negativity.

(6) Patients should remain under surveillance for 12 months after completion of therapy. This practice should be continued until sufficient data are accumulated to assure the efficacy of the SCC regimen(s) under field conditions in the United States.

and the state of the second present of the second	Sth W	EEK ENDING		CUMU	ATIVE, FIRST	WEEKS	
DISEASE	March 1, 1980	March 3, 1979*	MEDIAN 1975-1979	March 1, 1968	March 3, 1979*	MEDIAN 1975-1979	
Aseptic meningitis	75	37	33	578	435	335	
Brucellosis	1	2	2	31	13	27	
Chickenpox	6,122	7.606	6.183	42.220	51,414	47,104	
Diphtheria	1	-	3	1	33	33	
Encephalitis: Primary (arthropod-borne & unspec.)	13	12	12	109	87	109	
Post-infectious	3	7	3	20	26	20	
Hepatitis, Viral: Type B	271	288	288	2,534	2.211	2,230	
Type A	574	672	672	4,518	5,074	5,70	
Type unspecified	203	220	192	1,858	1,692	1,441	
Malaria	28	3	5	217	69	44	
Measles (rubeola)	288	452	615	1,379	2,189	3,147	
Meningococcal infections: Total	81	89	52	505	594	362	
Civilian Military	79	89	51	501	594	360	
Mumps	287	474	537	2,241	2,917	5,286	
Pertussis	14	26	23	182	255	224	
Rubella (German measles)	114	314	314	633	1,657	2,216	
Tetanus	1	1.000		5	5		
Tuberculosis	576	547	624	4,025	4,391	4,69	
Tularemia	71.01-110	4	2	12	23	13	
Typhoid faver	10	11	9	39	62	62	
Typhus fever, tick-barne (Rky. Mt. spotted)		-	-	6	11	10	
Veneral diseases:							
Gonorrhea: Civilian	19.558	17,304	17,304	161,490	163.060	162.87	
Military	394	716	465	4,597	4.895	4.895	
Syphilis, primary & secondary: Civilian	512	495	495	4,470	4,169	4.169	
Military	8	10	8	76	53	54	
Rabies in animals	90	81	48	744	496	384	

(Continued on page 105)

	CUM, 1990		CUM, 1980
Anthrax	-	Poliomyelitis: Total	-
Botulism †	4	Paralytic	
Congenital rubella syndrome (III. 1)	12	Psittacosis (Ala, 1, Calif, 1)	15
Leprosy (Tex. 1, Calif. 4)	28	Rabies in man	1000
Laptospirosis (Hawaii 4)	9	Trichinosis	8
Plague	in rules i un the	Typhus fever, flea-borne (endemic, murine) (Texas 2)	4

\*Delayed reports received for calendar year 1979 are used to update last year's weekly and cumulative totals. †Delayed reports: Botulism: Ohio +1, Wash. +1 (1980).

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REPORTING AREA	ASEPTIC MENIN- GITIS	BRU	CHICKEN	10	10	E	NCEPHALI	TIS	HEPATI	TIS (VIRA			
		CEL- Losis	POX	DIPHT	HERIA	Pri	mary	Post-in- fectious	В	A	Unspecified	MAI	ARIA
	1980	1980	1980	1980	CUM. 1980	1980	1979*	1980	1980	1980	1980	1980	CUM. 1980
UNITED STATES	75	1	6,122	1	1	13	12	3	271	574	20.3	28	217
NEW ENGLAND	3	-	574	-		-	1	-	4	9	5	4	18
NH	_		60							-			
Vt.		-	35	-	-		_	-		-	-	_	
Mass.	1	-	128	-	-	1	-	-	1	2	5	- 1	10
R.I.	2	-	20	-	-	-	-	-	1	2	-	-	1
Conn.	-	-	136	-	- 1	- 1	1	-	1	1	-	1	3
MID. ATLANTIC	24	1	426	1	1	1	3	-	31	36	20	11	33
Upstate N.Y.	3	1	156	-		1	1	-	10	14	8	-	1
N. F. City	17		107	1	1	-	2	-	8	12	2	5	17
Pa.t	4	115	163		2 E C	1	1.1	1.1	13	-	-	-	5
E.N. CENTRAL	7		2.999		12 - N	5			37		20		
Ohio	-	_	396	-		í	-	1.1	11	20	17		1
Ind.t	-	_	152	-	-		-	-	5	5	2	-	-
111. †	4	-	1,086	-	-	-	-	-	7	30	6		-
Mich.	3	-	875			4	1	-	a	11	5	1	1
Wis.	-	-	490	-	-	-	-	-	1	15	-	-	1
W.N. CENTRAL	1	-	747		- 1	1	1	-	14	23	4	1	6
Minn.	-	-	2	-	-			-	3	4	-	1	5
Mo	- E -		175	-		1	1	1 Tel.	10	.5	1		1
N. Dak 1		-	20					- 2 -	10	12	5	-	1.2
S. Dak.	-	_	19	-		-	-	-	-	1	-	-	
Nebr.	-	-	30	-	-	-	-	-	1	ī	-	-	-
Kans.	1	-	166	-	- 1	-		-	-	-		-	-
S. ATLANTIC	10	-	624		1 A 1	2	2	2	55	85	26	2	24
Del.	5	- E	13	-					2	16			-
Ma.	-		1	-				1.1	1	12		1	1
Va t	_	_	5	-	-	1	1		10	4	3		7
W. Va.	1	-	129	-	-	1		-	-	4		-	1
N.C.	2	-	NN	-	- 1		1	-	6	7	3	-	3
S.C.	-	-	12	-		-	-	-	2	1	2	- 7	-
Ga. Fla	6	- 2	401	- 1	1.1	- 1	1.1	2	17	31	11	1	5
E.C. OCATO AL			47					i. an	16	4.7	,		
E.S. GENIMAL	4		47			1		1.1	13	94	-	1	- î
Tenn	10	_	NN	-		-	-	S 14	12	12	1. 1. 1.		
Ala.	-	-	32	-	<b>.</b>		- I	-		10	ī	-	-
Miss.	-	-	10	-	-				2	11	N. 200	-	-
W.S. CENTRAL	з	-	298			1	1		25	85	33	2	24
Ark.	1	-		-		-		-	6	8	2		1
La.	2	-	NN					-	2	8	- 7	-	14
Okla.† Tex.	-	_	298	-		1	1	11	12	61	26	-	4
MOUNTAIN	10	1.0	10					Sec.	10	46			
MOUNTAIN	1		10	-		- 11	- 2 -	12	10	11		_	-
Idaho	-		2			-			-	2	-	-	-
Wyo.	-		-	-			-					-	1
Colo.t	-	-	56	-			-	-	7	18	3		4
N. Mex.	-	-		-		-	-	-	1			-	-
Ariz.	-	-	NN	-		-	-	-	-	28	18	-	3
Utah Nev.	ī	1	2	- 1		- 2 -	1.1	- <u>-</u>	2	4	ž	-	1
PACIFIC	2.4		200						PE	14.0	64	4	
Wash.	24	-	289		1	-	-	1	7	12	4	-	9
Oreg.	-	-	- 1	-		-	1		4	12	-1	1	7
Calif.t	18	-		-		1	2		68	119	51	5	82
Alaska	1		4			1.7.1		-		7			1
* 10 14/21	2	-	36	-	-	1	-	-	6	,		-	
Guamt	NA	NA	NA	NA	1.	NA			NA	NA	NA	NA	
P.R.	2	-	28	-	-	-	-	1	1	3	3		-
V.I.	-	-	1	-		-		100	-				-
Pac. Trust Terr.	NA	NA	NA	NA		NA	-	-	NA	NA	NA	NA	-

#### TABLE III. Cases of specified notifiable diseases, United States, weeks ending March 1, 1980, and March 3, 1979 (9th week)

NN: Not notifiable. NA: Not available.
\*Delayed reports received for 1979 are not shown below but are used to update last year's weekly and cumulative totals.
\*Delayed reports received for 1979 are not shown below but are used to update last year's weekly and cumulative totals.

1The following delayed reports will be reflected in next week's cumulative totals: Asep. meng.: Pa. -2, Ind. +2; Chickenpox: Ind. +6, III. +13, Calif. +51; Hep. B: Pa. +26, N.Dak. +1; Hep.A: Pa. +24, III. +2, Va. +1, Okla. -3, Colo. -2; Hep. unsp.: Pa. +3, N.Dak. +1, Va. -2, Guam +1.

	м	EASLES (RU	BEOLA)	MENING	OCOCCAL IN Total	FECTIONS	A	AUMPS	PERTUSSIS	RUBELLA		TETANUS	
REPORTING ANEA	1980	CUM. 1980	CUM. 1979*	1980	CUM. 1980	CUM. 1979*	1980	CUM. 1980	1980	1980	CUM. 1980	CUM. 1980	
UNITED STATES	288	1, 379	2,189	81	505	594	287	2,241	14	114	633	5	
NEW ENGLAND	42	114	108	3	19	15	21	206	1	6	- 44	1.0	
Maine	-	-	3	-	1	1	17	83	1	4	11	-	
N.H.†	23	66	2	1	з	2	-	2	-	1	15	-	
VLT	19	46	Э	-	1			-	-	-		-	
Mass. T			100		8	1	-		1.1.1	1		-	
Conn.	-	î	-	2	5	5	3	73		-	7	- 0	
MID. ATLANTIC	60	264	100	15	86	88	61	221	2	4	38	1	
Upstata N.Y.	12	78	48	6	38	32	- 4	23	2	2	19	-	
N.Y. City	23	74	45	5	23	24	4	22	-	<b>'2</b>	12	-	
N.J. Pa	16	23	-	5	11	20	42	42			6		
EN CENTRAL	27	171	553	5	50	52	122	766	5	49	185		
Ohio 1	-1	18	4	1	18	16	51	332		12	1	-	
ind.t	з	16	39	1	9	14	9	35		15	16	-	
10.1	9	37	227	3	6	-	21	99	1	17	30		
Mich.	11	57	201	1	13	16	28	191	1	14	57	-	
Wis.	4	43	82	_		6	13	139	3	3	21	51.0	
W.N. CENTRAL	66	187	274	3	17	19	10	94	1	16	71	1	
Minn.	47	131	100	- <u>-</u>	6	د		12	-	-	1	1	
Mo.	12	34	162	- i	6	10	7	44	1	2	19	-	
N. Dak.	-	-	2	-	ĩ	1	-	3		-	3		
S. Dak.	-	-	1	1	2	1	-	-	-	-		-	
Nebr. Kans.	7	3 18	8			1	3	25	- D	14	44	12	
S ATLANTIC	73	389	273	16	117	158	26	267	,	12	73	,	
Del.	-	- 1° 1				2	2	24		-			
Md.	9	10	5		10	8	6	82		-	=	-	
D.C.	-	-	-		-		-	1	-	-		-	
Vii.T W.V.	- !-	15	18	1	12	22	2	20		-	3	1	
N.C.	28	29	40	1	22	22		40	1	7	15		
S.C.	-		25	3	14	23	ĩ	8		i	33	1	
Ga.	16	190	2	4	27	25	-	-	1	-	-	-	
Fia.T	12	79	154	5	29	53	6	39	-	2	15	-	
E.S. CENTRAL	Э	48	38	6	50	47	13	350	-	1	28	-	
Ky.t	1	29	8	2	14	11	9	321	-	1	10	-	
Tenn.	2	6	4	1	14	13	3	12		-	17	-	
Ala. Miss.	- E -	12	20	2	14	12	ī	13	-	-	-	-	
WS CENTRAL	2	60	250	14	62	1.00	4	69	100	4	25	1000	
Ark.1	ĩ	2	5	2		11		10	-	-	1	-	
Lat	-	6	61	9	23	48	2	9	-	1	2	-	
Okla.		1	3		4	13			-			-	
Tex.	1	51	181	× *	31	28	2	50		3	22	1.00	
MOUNTAIN	2	33	56	2	22	29	2	65	1	1.5	16		
Mont	-	_	14			2	1	20	1	-	-	1.7	
Idano		- C -			1		- 2			1.21	ī 2		
Colo.	-	1	3		â	1	1	14	-	-	÷		
N. Mex.	-	_	10	-	-	2		-	-	-	-	-	
Ariz.	2	12	11	1	5	18	-	9	-	-	4	-	
Utah Nev.	- 2	18	13	ī	1	2	- 2	15	1	1	9	- 2	
PACIEIC	1.2		6 3 7				20	143			15-		
Wash.1	3	21	337	4	16	9	18	55	1	22	123	1	
Oreg.	1		2	4	10	i	ĩ	26	1.141-	11	20	-	
Calif.	9	89	169	3	55	66	9	11	1	8	116	1	
Alaska	-	-		1	1	1	-	3		-	1	100	
riawan	1	3	29	-	-	3	-	2		-	-	-	
GuamT	NA	12	52	1.1	2	1.2.1	NA	24	NA	NA	-		
V.L	3		1	- E -	1.1	2	í		-	_	-	-	
Pac. Trust Terr.	NA	-	3		1000	1	NA		NA	NA	-	-	

## TABLE III (Cont.'d). Cases of specified notifiable diseases, United States, weeks ending March 1 1980 and March 3 1979 (9th week)

NA: Not available. \*Delayed reports received for 1979 are not shown below but are used to update last year's weekly and cumulative totals.

The following delayed reports will be reflected in next week's cumulative totals: Measles: N.H. +4, Vt. +3, Ind. -3, Ill. +8, Va. -3, Fla. +1, Ky. -1, Ark. -1, La. -1, P.R. -1; Men, inf.: Ohio +4, Wash. -1; Mumps: Guam +2; Rubella: Mass. -1, Ark. -1.

REPORTING AREA	TUBE	RCULOSIS	TULA-	ULA- TYPHOID		TYPHUS FEVER (Tick-borne)		8	VENE	VENEREAL DISEASES				RABIES (in	
	CUM		REMIA	FE	CUM	(R	MSF)		GONORRHEA	CUM	S	PHILIS (P	ri. & Sec.)	Animals	
	1980	1980	1980	1980	1980	1980	1980	1980	1980	1979*	1980	1980	1979*	1980	
UNITED STATES	576	4,025	12	10	39	-7	6	19,558	161,490	163,060	512	4.470	4,169	744	
NEW ENGLAND	19	118	-	1	4	-		548	4,548	4,385	14	129	77	8	
Maine 1	-	1	-	-	-	-	-	33	301	297	-	-	1	8	
N.H.	1	2	-	-	-	-	-	14	149	132		-	4	-	
Vt	-	4	-	-	-	-		11	136	72		1	-		
Mass.	8	45	-	-	2	-	-	275	1,784	1.777	11	78	49	-	
K.I.	6	19	-		3 <u>-</u>	-	-	45	265	397		40	2		
ourn.			100	•	1	-		170	11913	11100	,	40			
MID. ATLANTIC	104	735	-	1	4	-	Ł	1,962	17,738	16,971	76	648	632	2	
Upstate N.Y.	23	134	-	-	-	-	-	371	2,745	2,306	3	- 47	42	-	
N.Y. City	37.	279	-	-	3	-	-	1.000	7,487	0,538	43	432	431		
N.J.	16	150	-	ı	1	-		80	2,933	3,233	12	83	81	2	
<b>n</b> .	28	172	1.1		_	-	1	511	4,573	4,894	18	86	78		
E.N. CENTRAL	90	5. 542	1	2	4	-	_	3.492	24.528	24.938	50	303	575	84	
Ohio	14	92	-	-		-	-	950	7.457	6.534		63	114	2	
Ind.	13	73	-	-	-	-	-	799	3.090	1,711	4	42	25	8	
111, t	34	217	-	2	2		-	817	5,261	8,550	25	84	343	49	
Mich.†	24	122	1	-	2	-	-	630	5,862	5,993	14	94	72	-	
Wis. T	5	38	-		-		-	296	2,858	2,150	7	20	21	25	
WALCENTRAL	16	132	4		-		,	895	7.178	7.892	7	46	54	214	
Minn t	10	25	1	-	-	-	-	1 3.8	1.276	1.384	2	13	19	32	
lowa		ĩĩ	-	_	-	-	-	63	813	1.028	-	3	6	51	
Mo.	7	60	2	-	-	-	2	476	2,953	3,285	5	28	18	64	
N. Dak.	-	2	-	-	-	-		12	97	127	-	-	-	16	
S. Dak.	2	6	-	-	-	-	-	31	250	279		- X -	-	36	
Nebr.†	-	6	1		-	-	-	66	616	508	-	2	-	1	
Kans.	3	22	-	-	_	-	-	109	1,173	1.281	2 -		11	14	
S ATLANTIC	134	935	3	1	13	-	3	4.308	40.233	39.355	129	1.092	1.012	70	
Del,	-	15		-	i	-	-	43	602	575	2	5	7	-	
Md.	17	117	1	-	2	-	-	418	3,823	4,594	7	82	67	-	
D.C.	6	49	-	-	2	-	-	346	3,005	2,389	3	70	69	-	
Va.	16	96	-	1	2	-	-	447	3,507	3,759	10	99	110	1	
W. Va.t	5	42	-	-	1	-		79	494	576	1	4	18	-	
N.C.	31	176		-	- <u>†</u> -	- 2 -	2	720	0,300	0,330	- 16	78	55	13	
Ge	11	12	5		-	_	- Ţ	714	7.126	7,287	51	222	260	40	
Flat	23	249	-	-	3	_		1.265	11.395	10.613	36	377	323	16	
								A		- 1	14			100	
E.S. CENTRAL	47	386	-1	-	1	-	-	2,145	13,252	14,556	32	356	291	39	
Ky.	15	80	- T	-	1	-	-	238	1,955	2,000	6	21	30	20	
Ale	21	129	1	-	-	-	-	122	4,739	5,090	19	1 50	53		
Miss.	6	60		- 21				372	2.837	3,110	12	126	76	-	
	-														
W.S. CENTRAL	40	313	-	-	-		-	2,357	20,817	21,965	130	875	705	238	
Ark.	5	13	-	-	-	-	-	187	1,595	1.786	1	30	22	30	
La.	3	82	-	-	-	-	-	441	3,290	3+748	31	148	158	20	
Okla		37	-			-	-	210	2,146	1,931	88	6 36	516	177	
lex,	32	101		1.01			1.1	11313	151/00	141,500		0.11	210		
MOUNTAIN	11	113	1	2	3	-	-	734	6,268	6,449	31	113	59	17	
Mont.	-	5	-	-	1	-	-	32	231	357	-		4	1	
ldaho t	-	5	-	-	-	-	-	15	288	269	2	5	3	-	
Wyo.	-	9	-	-			-	11	175	168		3	3	1977	
Colo.†	1	10	-	1	1			137	1,535	1.750	5	32	23	100	
N. Mex.	3	24				-	_	220	1 702	633	20	40		14	
Ariz.	2	21		1	1		12	323	215	307	20	40		17	
Nev.	i.	5		- 21	_	-	-	75	1.080	926	1	- ti	ì	-	
													1.00		
PACIFIC	115	751	2	3	10	-	-	3,117	26,928	26,549	43	908	764	72	
wash.	10	64	-		-		_	NA	1.9/7	2:344	NA .	72	40	100	
Cult	2	39	1	1	12	-		2.015	22 320	21 001	20	792	440		
Alaska	101	634	2	-	10	-		72	£ 2 1 £ 2 C	201901 850	-	2	2	12	
Hawaii	,	12		_	_		-	61	369	471	-	11	10	-	
	-	.,											-	-	
Mark Same	100	1000		1.17				0.1 11	10.2						
Guam 1	NA	1	-	NA		NA	2	NA 0.2	12	19	NA 14	-		-	
Vi	4	20			- 2 -	- 2 -	- 2	43	214	203	17	60	74		
Par. Truet Terr	NA		-	NA	_	NA	-	NA		69	NA		_	-	

# TABLE III (Cont.'d). Cases of specified notifiable diseases, United States, weeks ending March 1, 1980, and March 3, 1979 (9th week)

NA: Not available. \*Delayed reports received for 1979 are not shown below but are used to update last year's weekly and cumulative totals.

The following delayed reports will be reflected in next week's cumulative totals: TB: Idsho -1, Guam +1; T. Fever: III. +1; GC: Maine +1 civ. -1 mil., III. +484 civ., Wis. -1 civ., Colo. -2 civ., Guam +8 mil.; Syphilis: III. +25, Mich. -1, Minn. +3; An. rabies: Nebr. +2, W. Va. +1, Fla. +2.

# TABLE IV. Deaths in 121 U.S. cities,\* week ending March 1, 1980 (9th week)

			_							_			
Looper-		ALL CAUS	SES, BY AG	E (YEARS)		1000	- AND LOW-	ALL CAUSES, BY AGE (YEARS)					
REPORTING AREA	ALL	>65	45-64	25-44	<1	P&I** TOTAL	REPORTING AREA	ALL	>65	45-64	25-44	<1	P&I** TOTAL
NEW ENGLAND	815	567	168	41	16	90	& ATLANTIC	1,244	752	315	80	50	75
Boston, Mass.	217	128	54	17	8	24	Atlanta, Ga	137	79	34	14		4
Bridgeport, Conn.	4/	10	2	2	1.2	2	Baltimore, Md.	88	52	20	12	1	ś
Cambridge, wass. Fall River Mass.	34	28	6	-		1	Jacksprille, Fla.	107	68	33	2	2	á
Hartford, Conn.	74	48	17	5	2	4	Miami, Fla.	124	67	38	12	4	6
Lowell, Mass.	45	31	12	1	-	3	Norfolk, Va.	76	44	26	1	- 4	11
Lynn, Mass.	28	19	5	3	-	1	Richmond, Va.	109	69	31	3	3	10
New Bedford, Mass.	29	22		-	-	2	Savannah, Ga. St. Patemburg, Ela	123	29	18	-	_	5
Providence R.I.	98	72	1.6		- 1	16	Tampa, Fia.	76	50	15	4	2	- 7
Somerville, Mass.	16	14	2	-	-	2	Washington, D.C.	184	110	45	12	12	11
Springfield, Mass.	53	37	11	2	3	8	Wilmington, Del.	49	28	10	- 4	5	-
Waterbury, Conn.	36	33	3	-		3	510 101						
Worcester, Mass.	74	52	16	3	1	14	E C CENTRAL	690	4.21	180	43	1.8	32
							Birmingham Ala	108	60	32	8	4	2
MID. ATLANTIC	2, 948	2,034	639	156	60	220	Chattanooga, Tenn.	64	40	14	5	2	6
Albany, N.Y.	63	41	16	2	2	3	Knoxville, Tenn.	50	30	18	2	-	-
Allentown, Pa.	25	17	8	1. 11			Louisville, Ky.	106	66	27	6	2	10
Buffalo, N.Y.	142	101	33	5	1	11	Memphis, Tenn.	131	91	25	9	1	3
Camden, N.J.	67	40	13	2	1	1	Mobile, Ala.	63	28	1.9	2	5	2
Frie Pat	20	29	5	2	1	1	Nontgomery, Ala.	114	65	32	7	5	6
Jarsey City, N.J.	61	39	15	3	2	5		- 70		100			
Newark, N.J.	43	33	5	1	3	4							
N.Y. City, N.Y.	1,635	1,138	330	101	35	112	W.S. CENTRAL	1,316	762	344	101	53	65
Patanson, N.J.	39	26	9	2	2	5	Austin, Tex.	56	31	15	6	3	3
Pittsburgh Pa t	298	185	79	15	9	26	Baton Rouge, La.	50	27	10	4		2
Reading, Pa.	45	38		2	1.2	12	Dollar Ter	214	119	65	19	3	8
Rochester, N.Y.	134	95	29	3	4	12	El Paso, Tex.	68	36	19	ŝ	4	6
Schenectady, N.Y.	31	22	9	-	-	1	Fort Worth, Tex.	107	47	37	8	8	6
Scranton, Pa.1	41	36	3	1	-	3	Houston, Tex.	164	94	42	13	7	4
Syracuse, N.Y.	76	48	22	4		4	Little Rock, Ark.	75	48	16	5		- 4
Interior, N.J.	36	23	11	2		2	New Orleans, La.	209	130	47	12		12
Yonkers, N.Y.	37	28	ġ		- E -	4	San Antonio, Tex.	37	27	8	-	2	4
20. 12"							Tulsa, Okla.	111	74	23	8	1	12
E.N. CENTRAL	2.788	1,796	636	162	112	121							
Akron, Ohio	60	41	11	3	3	-	MOUNTAIN	575	368	119	39	32	18
Canton, Ohio	43	31	8	2		4	Albuquerque, N. Mex	. 53	34	9	6		
Chicago, III.	649	391	168	38	33	18	Colo. Springs, Colo.	133	31	30	5	14	7
Cincinnati, Ohio	229	130	62	17	18	10	Let Veret Nev	62	38	19	2	2	-
Columbus Ohio	179	112	34	16	6	5	Ogden, Utah	16	13	1		ī	
Davton, Ohio	140	91	33	6	6	13	Phoenix, Ariz.	143	95	26	15	4	-
Detroit, Mich.	293	181	78	21	10	13	Pueblo, Colo.	22	17	4	1	-	6
Evansville, Ind.	62	44	13	2	2	1	Salt Lake City, Utah	38	16	1	5	8	
Fort Wayne, Ind.	20	35	14	4	2	2	Juction, Ariz.	10	43	10	2	4	-
Gary, Ind. Grand Banide Mich.	74	54	12	ŝ	0.0	11	10.1						
Indianapolis, Ind.	202	129	49	12	7	8	PACIFIC	2,244	1.499	460	136	83	96
Madison, Wis.	50	29	10	4	2	5	Barkeley, Calif.	20	13	4	2	-	-
Milwaukee, Wis.	184	131	28	8	9	6	Fresno, Calif.	69	42	20	3	-	12
Paoria, III.	44	28	. 6	1	9	2	Glendale, Calif.	48	37		1	-	1
Rockford, III.	52	11	10	4		2	Long Beach Calif	119	74	37	5	2	6
Toledo Ohio	107	77	21	5	1.1	2	Los Angeles, Calif.	655	427	133	38	29	20
Youngstown, Ohio	61	39	16	2	-		Oakland, Calif.	67	42	15	7	2	2
							Pasadena, Calif.	31	24	4	1	1	3
19 Mar 19		- 1 ki		AL 43		1.1	Portland, Oreg.	208	152	31	12	8	3
W.N. CENTRAL	8 24	549	169	40	39	51	Sacramento, Calif.	84	51	19	6	1	8
Des Moines, 10wa	35	21	9	2	2	4	San Diego, Lain.	214	145	50	1.0	5	4
Kansas City, Kans	36	18	11	2	4	3	San Jose, Calif.	162	113	26	9	8	3
Kansas City, Mo.	154	94	32	9	11	9	Seattle, Wash	216	151	49	9	4	14
Lincoln, Nebr.	36	30	4	1	1	4	Spokane, Wash.	47	30	7	4	5	5
Minneapolis, Minn.	114	73	26	3	9	6	Tacoma, Wash.	59	44	9	3	2	4
Omana, Nebr.	95	61	19	.1	4	3							
St. Louis, Mo.	204	141	37	13	5	11	ΤΟΤΑΙ	13.444	8.740	3. 030	704	643	74.0
Wichita, Kans.	43	29	10	2	i	1	IGIAL	1 31 444	20140	1030	190	202	100

\*Mortality data in this table are voluntarily reported from 121 cities in the United States, most of which have populations of 100,000 or more. A death is reported by the place of its occurrence and by the week that the death certificate was filed. Fetal deaths are not included.

\*\*Pneumonia and influenza

tBecause of changes in reporting methods in these 4 Pennsylvania cities, these numbers are partial counts for the current week. Complete counts will be available in 4 to 6 weeks.

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Tuberculosis Chemotherapy - Continued

## Conclusion

The time has come for SCC regimens to be introduced in U.S. treatment programs with the stipulation that there be systematic collection of data for assessment of results under *program* conditions, among different populations, and in different geographic areas. Until such data have been collected and analyzed, it is advisable to observe patients who have received SCC for 12 months after stopping drugs, since most relapses are likely to occur in that period.

Close scrutiny of all patients on chemotherapy and directly administered treatment for noncompliant patients will enhance the benefits and minimize the risks of shortening treatment. Therefore, the available resources for patient supervision cannot be reduced and may even have to be augmented for SCC to be successful. With careful implementation and assessment, the introduction of SCC can represent a major step forward in tuberculosis treatment.

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# **National Surveillance Survey**

During April 1979, a questionnaire was distributed to 55 State and Territorial Epidemiologists to examine present disease surveillance efforts and to obtain suggestions for improvement. All but 2 epidemiologists returned the completed questionnaires.

The epidemiologists indicated that both national and state surveillance data were used extensively for disease control efforts while national data was also used for archival

## National Surveillance -- Continued

purposes and for program development. The epidemiologists indicated that data from the MMWR was referred to on a weekly basis in about 60% of the states. When queried about the possibility of indepth surveillance of noncommunicable diseases, about 80% of the epidemiologists responded that such activity could provide useful data for national program policy; approximately two-thirds indicated that such a program would lead to the reduction of morbidity and mortality attributable to these diseases. One-fourth of the respondents expressed willingness to participate in a 3-year surveillance program on environmentally induced or chronic diseases.

More than three-fourths of the epidemiologists stated that automated data processing would be useful in their surveillance efforts. Although fewer than half the states presently use computers for such data analyses, according to survey respondents this technology should be more generally utilized. It was suggested that while current national surveillance efforts were important and should be continued, they should also be modified to take advantage of computerized data-handling systems.

Reported by State and Territorial Epidemiologists; and the Consolidated Surveillance and Communications Activity, Bur of Epidemiology, CDC.

Editorial Note: The Consolidated Surveillance and Communications Activity, Bureau of Epidemiology, is currently evaluating surveillance methodologies in data collection and data analysis. In addition, efforts are being made throughout CDC to develop methods of noncommunicable-disease surveillance, both in chronic and acute disease areas. CDC and the Association of State and Territorial Health Officers are also considering the development of a communications system capable of interacting with state health departments and agencies outside CDC for emergency as well as routine disease-surveillance and control activities.

# Epidemiologic Notes and Reports

# Scombroid Poisoning – New Jersey

On October 4 and 5, 1979, 35 cases of scombroid fish poisoning occurred at 2 Catholic monasteries in New Jersey among nuns who shared tuna fish from a common, non-commercial source.

Illness was first reported on October 4. Following a dinner of broiled tuna fish, 2 sisters from 1 of the monasteries were hospitalized for explosive vomiting and diarrhea. All 23 nuns who ate the fish became ill, while 4 who did not eat the fish experienced no symptoms (p=.0006, Fisher's Exact Test). An unusual bitter or peppery taste was noted immediately by 7 (30%). Onset of symptoms occurred a mean of 39 minutes after eating the fish (range of 5 minutes to 2 hours). Symptoms included facial flushing (82.6%), diarrhea (73.9%), headache (69.6%), erythema other than facial (56.5%), palpitations (43.5%), nausea (43.5%), dizziness (43.5%), prostration (43.5%), chills (39.1%), unusual thirst (30.4%), itching (30.4%), blurred vision (26.1%), cramps (21.7%), and vomiting (17.4%). Conjunctival injection, reported as a common acute occurrence, could not be quantitated. Duration of the major symptom complex was under 6 hours, though weakness and fatigue persisted for 24 hours. The 2 hospitalized patients, ages 65 and 66, were treated with antihistamines and fluid and electrolyte replacement over a 24-hour observation period and then released.

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#### March 7, 1980

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# Scombroid Poisoning - Continued

The incriminated tuna fish was a gift from a second monastery, which had received a total of 9 "fresh," yellow-fin tuna from a non-commercial fisherman on August 28. Nuns at this monastery had donated 1 fish to their sister convent and had dined on the remaining 8 tuna 5 times. Twice they had experienced the typical scombroid symptom complex, but they attributed it to improper cooking. Just before the New Jersey State Department of Health investigators arrived on October 5, the nuns had prepared frozen tuna fish steaks. They had boiled them for 1 hour in an attempt to eliminate the cause of the illness. Mild nausea, flushing, or dizziness occurred within minutes in 12/20 (60%) who ate the fish. All recovered within 3 hours. Analysis of the tuna fish for free base histamine was conducted by the Food and Drug Administration's Brooklyn Laboratory by the fluorimetric method, yielding results of 370 mg/100 g.

On August 27, 6 amateur sportsmen had caught 28 yellow-fin tuna, weighing 45-105 pounds apiece, off the New Jersey coast. Because of the unusually large catch, only some of the uncleaned fish could be chilled in ice boxes. The remainder were left covered on the deck and periodically hosed with seawater. The catch was divided on shore; 6 of the uncleaned fish were subsequently refrigerated, but not frozen, at the home of the brother of 1 of the nuns. The following day, 5 of these fish plus 4 others were transported with-out refrigeration to the monastery. The sixth uncleaned fish subsequently spoiled and was discarded. All other fish were eaten without illness.

Reported by L Zimmer, MD, St. Mary's Hospital, Orange, New Jersey; R Altman, MD, State Epidemiologist, M Thun, MD, New Jersey State Dept of Health; W Staruszkiewicz, MS, Fishery Technology Br, Bur of Foods, Food and Drug Administration; Field Services Div, and Enteric Diseases Br, Bacterial Diseases Div, Bur of Epidemiology, CDC.

Editorial Note: Scombroid fish poisoning is a continuing problem in the United States: 32 outbreaks involving 207 individuals were reported to CDC between 1975 and 1979. The disease takes its name from the family Scombridae (tuna and related species) because of the frequent association of fish in this family with illness; the most commonly implicated fish for the last 5 years, however, has been mahi mahi (dolphin), which has accounted for 13 (40%) of all outbreaks reported.

Scombroid fish poisoning results from the ingestion of heat-stable toxins produced by bacterial action on dark meat fish (1,2). High levels of histamine in the fish correlate with occurrence of illness; disease usually results when concentrations exceed 20 mg/100 g. The disease is preventable if the fish are properly handled, particularly if they are refrigerated early and adequately.

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The Morbidity and Mortality Weekly Report, circulation 96,486, is published by the Center for Disease Control, Atlanta, Georgia. The data in this report are provisional, based on weekly telegraphs to CDC by state health departments. The reporting week concludes at close of business on Friday; compiled data on a national basis are officially released to the public on the succeeding Friday.

The editor welcomes accounts of interesting cases, outbreaks, environmental hazards, or other public health problems of current interest to health officials. Send reports to: Center for Disease Control, Attn: Editor, Morbidity and Mortality Weekly Report, Atlanta, Georgia 30333.

Send mailing list additions, deletions, and address changes to: Center for Disease Control, Attn: Distribution Services, GSO, 1-SB-36, Atlanta, Georgia 30333. When requesting changes be sure to give your former address, including zip code and mailing list code number, or send an old address label.

# Current Trends

# Influenza – United States

For the period February 17-23, 5 states—Connecticut, Rhode Island, Kansas, Nebraska, and South Dakota—and New York City reported widespread outbreaks of influenza to CDC. Four states (Maine, New Jersey, New York, and Michigan) reported regional outbreaks, and 25 states reported sporadic influenza cases.

For the sixth consecutive week the number of pneumonia and influenza (P&I) deaths reported from 117 U.S. cities remained above the epidemic threshold. For the week ending March 1, P&I deaths increased above the previous week's total.

The majority of influenza isolates in the United States continue to be influenza B viruses. Influenza A (H1N1) viruses, previously isolated in school outbreaks in Maryland (1), were also isolated during February in Delaware from 2 young-adult residents of an institute for the mentally retarded and from 2 children in a family in Houston, Texas. Reference antigenic analysis of the isolates from Maryland and Texas confirms their similarity to A/Brazil/11/78. Influenza A (H3N2) strains continue to be isolated sporadically. One outbreak of influenza A (H3N2) was reported among patients and staff at an Illinois hospital.

As of March 3, 303 cases of Reye syndrome with onset since December 1, 1979, were reported to CDC. Thirty-three states have reported at least 1 case. Ohio has reported 102 cases; Michigan, 40; Minnesota, 19; and Indiana, 17. Ohio's high total is due in part to a pre-existing active surveillance system established by the Ohio State Department of Health. Official state health department figures may not agree with unofficial reports because of delays in official reporting and variations in case ascertainment.

Reported by State Epidemiologists and Laboratory Directors; R Couch, MD, Baylor Medical College, Houston, Texas; L Blouse, PhD, U.S.A.F. School of Medicine, Brooks Air Force Base, Texas; Laboratory of Infectious Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health; Immunization Div, Bur of State Services, Consolidated Surveillance and Communications Activity, Bur of Epidemiology, the World Health Organization Collaborating Center for Influenza, Virology Div, Bur of Laboratories, CDC.

Reference

1. MMWR 1980;29:83-4.

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