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OFFICE OF PUBLIC HEALTH STATISTICS

NEW CONCEPTS IN THE CARE OF TUBERCULOSIS

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In the 32 years since the introduction of streptomycin, modern chemotherapy has revolutionized the treatment of tuberculosis. Whereas in the pre-antibiotic era, treatment was long and uncertain, necessitating long periods of hospitalization in tuberculosis sanatoria to remove contagious individuals from the community, therapy is now highly effective both in rendering the patient non-contagious and in achieving ultimate cure. Prolonged sanatorium style hospitalization, therefore, no longer has a place in the treatment of tuberculosis, and for that reason, the Louisiana State Department of Health and Human Resources is closing its sanatorium, thus joining the 37 other states which have closed their tuberculosis sanatoria.

While emphasis will now be on out-patient treatment, those patients needing hospitalization will be treated in the general hospitals until it is medically safe to the patient and the community to release them to out-patient care. The following conditions must be satisfied before a hospital can safely admit tuberculosis patients: (1) bed space for tuberculosis patients in a room or rooms with exhaust ventilation with or without ultraviolet lights, (2) physicians with expertise in modern management of tuberculosis and awareness of community services and facilities for tuberculosis care, (3) laboratory services for tuberculosis smears and cultures, (4) a nursing staff informed in the modern management of tuberculosis, and (5) out-patient services and follow-up necessary to complete the patients' chemotherapy.² (See enclosed reprint, *Treatment of Mycobacterial Disease*, by the American Thoracic Society, 1977).

Some patients do not require hospitalization at all. The major reasons for hospitalization are symptomatic illness that prevents the patient from caring for himself, illness complicated by other major medical problems, diagnostic problems, especially those that require hospital based procedures such as bronchoscopy for resolution, and therapeutic problems in patients who present difficulties in the selection and maintenance of chemotherapy.

Since the bulk of the patient's course of therapy

will occur out of the hospital, coordination of in-patient and out-patient care is vital. Reporting the case to the parish health unit as soon as a presumptive diagnosis (i.e. positive smear and/or clinical or X-Ray evidence) is made initiates the cooperative process that will ensure successful completion of therapy. It is essential that the diagnosis be confirmed by culture wherever possible and the health unit notified of the culture results. Discharge planning should begin long before the discharge date to guarantee continuation of medications and follow-up. Input from the local public health nurse operating out of the health unit will be aimed at these objectives. The hospital should establish procedures for furnishing a discharge summary and prescriptions to the facility which will continue the patient's care when he leaves the hospital. This follow-up can be through the private physician's office or through one of the eight regional tuberculosis clinics, four parish tuberculosis clinics, or hospital out-patient tuberculosis clinics. In any case medication can be supplied at no charge to the patient through the regional clinics or the parish health units.

The tuberculosis program administrators are hopeful that general hospital care will serve the purposes of prompt diagnosis and initiation of treatment, coordination of plans for completion of therapy with the local health unit, and establishment of positive attitudes in the patient that will motivate him to complete treatment and re-establish his role in the community with minimum disruption. We request the cooperation of physicians throughout the state, and are available to discuss any problems that arise (504-568-5015).

REFERENCES

- ¹ National Tuberculosis and Respiratory Disease Association: Guidelines for the general hospital in the admission and care of tuberculosis patients, *Amer. Rev. Res. Dis.*, 102:992, Dec. 1970.
- ² American Hospital Association: Statement on care of patients with pulmonary tuberculosis in general hospitals, 1972.

SELECTED REPORTABLE DISEASES

(By Place of Residence)

STATE AND PARISH TOTALS	ASEPTIC MENINGITIS	DIPHTHERIA	ENCEPHALITIS	ENCEPHALITIS, POST INFECTION	HEPATITIS A AND UNSPECIFIED	HEPATITIS B	TUBERCULOSIS, PULMONARY	MENINGOCOCCAL INFECTIONS	PERTUSSIS	RABIES IN ANIMALS	RUBELLA*	SEVERE UNDERNUTRITION	SIGELLOSIS	TYPHOID FEVER	OTHER SALMONELLOSIS	TETANUS	MEASLES	GONORRHEA	SYPHILIS, PRIMARY AND SECONDARY
REPORTED MORBIDITY APRIL, 1977																			
TOTAL TO DATE 19 76	17	0	5	3	150	42	183	17	1	0	71	5	18	0	26	1	111	6401	191
TOTAL TO DATE 19 77	2	0	4	0	212	41	199	44	0	4	9	4	14	0	20	1	56	5514	192
TOTAL THIS MONTH	2	0	2	0	51	8	56	2	0	3	1	2	3	0	6	0	1	1364	48
ACADIA					1		2					1						15	
ALLEN																		1	
ASCENSION																		4	
ASSUMPTION							1											2	
AVOUELLES																		2	
BEAUREGARD																		8	
BIENVILLE																			
BOSSIER					1					3								14	
CADDO			1			1	5											122	5
CALCASIEU					3								2					60	1
CALDWELL																			
CAMERON																		1	
CATAHOULA																		2	
CLAIBORNE						1													
CONCORDIA																		8	
DESOTO																		5	
EAST BATON ROUGE	2				5										3			138	7
EAST CARROLL																		5	
EAST FELICIANA																			
EVANGELINE					1		1											1	
FRANKLIN																		6	
GRANT																		3	
IBERIA																		3	
IBERVILLE																		10	
JACKSON																			
JEFFERSON					20			1									1	68	6
JEFFERSON DAVIS																		2	
LAFAYETTE							1											38	2
LAFOURCHE							1											7	
LASALLE																		3	
LINCOLN							1											21	
LIVINGSTON																			
MADISON					1		1											5	
MOREHOUSE							1											10	
NATCHITOCHES																		8	
ORLEANS					8	6	27	1					1		2			498	13
OUACHITA					1		4											44	
PLAQUEMINES																		3	
POINTE COUPEE																		1	
RAPIDES					1													58	
RED RIVER																		2	
RICHLAND																		2	1
SABINE					1													7	
ST. BERNARD							3											1	
ST. CHARLES																		5	
ST. HELENA																		2	
ST. JAMES																		5	1
ST. JOHN																		5	
ST. LANDRY																		5	
ST. MARTIN					1		2											3	
ST. MARY			1		3													3	
ST. TAMMANY																		13	
TANGIPAHOA					1		2					1						19	
TENSAS																			
TERREBONNE							1											4	
UNION							1											9	
VERMILION																		2	1
VERNON					2						1				1			50	9
WASHINGTON							2											7	
WEBSTER					1													4	1
WEST BATON ROUGE																		16	1
WEST CARROLL																		1	
WEST FELICIANA																		17	
WINN																		6	
OUT OF STATE																			

* Includes Rubella, Congenital Syndrome

American Thoracic Society

Medical Section of the American Lung Association

Treatment of Mycobacterial Disease*

THIS IS AN OFFICIAL STATEMENT OF ATS.

This brief statement is intended to be a guide for physicians and health workers who are not totally familiar with the details of chemotherapy for mycobacterial disease; it is not meant to be exhaustive. Those interested in a more detailed review are referred to the "State of the Art" review by Johnston and Wildrick (1). The classification system revised in 1974 (2), greatly simplifying categorization of all persons with mycobacterial exposure, infection, or disease, will be the framework of this statement. Doses are listed in the accompanying table, and the principles of drug use are discussed in the text.

Treatment of Infection or Disease Caused by *Mycobacterium tuberculosis*

Category 0—No tuberculosis exposure, not infected

No therapy necessary.

Category I—Tuberculosis exposure, no evidence of infection

Some contacts not yet proved to be infected are candidates for so-called "primary prophylaxis" because the tuberculin skin test may be in the process of conversion. All household contacts should be considered for such treatment. Primary prophylaxis is standard for children, being especially important for those less than 5 years of age and absolutely essential for neonates. Isoniazid is the only drug with demonstrated effectiveness. The usual duration of treatment is until approximately 3 months after the contact has been broken, unless the patient changes to Category II (3, 4).

Category II—Tuberculous infection, without disease

The treatment of persons who are infected but do not have disease is based on the concept that the lifetime risk of developing tuberculosis for an untreated infected person exceeds the risk of therapy with one year of isoniazid. Most agree that positive reactors who are less than 35 years of age are candidates for therapy. Persons older than 35 who have an additional risk factor such as corticosteroid therapy, immunosuppressive therapy, or disease state that impairs the immune response should also be treated. For additional details concerning treatment

of infection, see "Preventive Therapy of Tuberculous Infection" (3).

Category III—Tuberculous infection, with disease

Past tuberculosis previously untreated. Persons who have had tuberculosis but who have not previously received adequate chemotherapy or persons who are tuberculin skin test reactors with roentgenographic findings consistent with tuberculous scarring should receive isoniazid preventive therapy for one year (3).

Current tuberculosis. Isoniazid, ethambutol, rifampin, and streptomycin are generally considered to be first-line or primary drugs. The most frequently used regimen is isoniazid and ethambutol for 18 months. When the bacterial population is thought to be particularly large (extensive cavitary lesions) or the patient is from an area where drug-resistant tuberculosis is prevalent, daily streptomycin may be included in the regimen, usually not longer than 3 months, until the bacterial population is reduced.

Rifampin combined with isoniazid is as effective as any 3-drug regimen in the treatment of extensive cavitary disease. Therapy using a combination of isoniazid and rifampin for periods of time as short as 6 months is being evaluated in this country. Results are encouraging, but it should be used only under carefully controlled circumstances until the data are confirmatory.

Para-aminosalicylic acid may be preferable to ethambutol as a companion drug to isoniazid for the treatment of young children because of the difficulty in monitoring visual changes that rarely occur with ethambutol. Streptomycin may be used as a companion drug to isoniazid, usually for only 3 months, particularly when oral drugs cannot be administered.

Isoniazid and ethambutol are the preferred combination when treatment during pregnancy is necessary.

Disease caused by drug-resistant bacilli. Second-line drugs are used only to treat disease caused by *M. tuberculosis* resistant to first-line drugs or to replace first-line drugs in patients for whom they are contraindicated. These are listed in the table. Viomycin, capreomycin, kanamycin, and streptomycin should generally not be used together because of possible eighth nerve damage and nephrotoxicity. Second-line drugs are definitely more toxic and in

* Reprints may be requested from your state or local Lung Association.

TREATMENT OF MYCOBACTERIAL DISEASE IN ADULTS AND CHILDREN

First-Line Drugs	Dosage*		Most Common Side Effects*	Tests for Side Effects*	Remarks*
	Daily	Twice Weekly			
Isoniazid	5-10 mg/kg up to 300 mg PO or IM	15 mg/kg PO or IM	Peripheral neuritis, hepatitis, hypersensitivity	SGOT/SGPT (not as a routine)	Bactericidal. Pyridoxine 10 mg as prophylaxis for neuritis; 50-100 mg as treatment
Ethambutol	15-25 mg/kg PO	50 mg/kg PO	Optic neuritis (reversible with discontinuation of drug; very rare at 15 mg/kg), skin rash	Red-green color discrimination and visual acuity†	Use with caution with renal disease or when eye testing is not feasible
Rifampin	10-20 mg/kg up to 600 mg PO	Not recommended	Hepatitis, febrile reaction, purpura (rare)	SGOT/SGPT (not as a routine)	Bactericidal. Orange-urine color. Negates effect of birth control pills
Streptomycin	15-20 mg/kg up to 1 g IM	25-30 mg/kg	8th nerve damage, nephrotoxicity	Vestibular function, audiograms;† BUN and creatinine	Use with caution in older patients or those with renal disease
Second-Line Drugs					
Viomycin	15-30 mg/kg up to 1 g IM		Auditory toxicity, nephrotoxicity, vestibular toxicity (rare)	Vestibular function, audiograms;† BUN and creatinine	Use with caution in older patients. Rarely used with renal disease
Capreomycin	15-30 mg/kg up to 1 g IM		8th nerve damage, nephrotoxicity	Vestibular function, audiograms;† BUN and creatinine	Use with caution in older patients. Rarely used with renal disease
Kanamycin	15-30 mg/kg up to 1 g IM		Auditory toxicity, nephrotoxicity, vestibular toxicity (rare)	Vestibular function, audiograms;† BUN and creatinine	Use with caution in older patients. Rarely used with renal disease
Ethionamide	15-30 mg/kg up to 1 g PO		GI disturbance, hepatotoxicity, hypersensitivity	SGOT/SGPT	Divided dose may help GI side effects
Pyrazinamide	15-30 mg/kg up to 2 g PO		Hyperuricemia, hepatotoxicity	Uric acid, SGOT/SGPT	Combination with an aminoglycoside is bactericidal
Para-aminosalicylic acid (aminosalicylic acid)	150 mg/kg up to 12 g PO		GI disturbance, hypersensitivity, hepatotoxicity, sodium load	SGOT/SGPT	GI side effects very frequent making cooperation difficult
Cycloserine	10-20 mg/kg up to 1 g PO		Psychosis, personality changes, convulsions, rash	Psychologic testing	Very difficult drug to use. Side effects may be blocked by pyridoxine, ataractic agents or anticonvulsant drugs

* Check product labelling for detailed information on dose, contraindications, drug interaction, adverse reactions, and monitoring.

† Initial levels should be determined on start of treatment.

some cases less effective than the primary drugs, and usually should be employed only by physicians familiar with their use.

Regimens that include second-line drugs should be based on the susceptibility pattern of bacteria and on the potential for toxicity in any given patient. The patient with drug-resistant organisms should always be receiving at least 2 and preferably 3 drugs to which the organisms are known to be susceptible. More than 18 months of therapy may be required in some of these patients, and adjunctive surgery is occasionally indicated.

Treatment of Other Mycobacterial Disease

Treatment of disease caused by mycobacteria other than *M. tuberculosis* is in many ways similar to treatment of drug-resistant tuberculosis. Many mycobacteria that can be grown from soil, food, plants, water, and occasionally from bronchial secretions are not pathogens. Diagnosis of disease requires identifying organisms by culture and satisfying generally accepted diagnostic criteria (2). A single isolate of one of these organisms is common and often is not associated with disease. By drug susceptibility testing, 2, 3, or sometimes 4 drugs that appear effective can be selected. However, *in vivo* and *in vitro* susceptibility test results may not correlate.

M. intracellulare (Battey bacillus) is often resistant *in vitro* to all drugs but cycloserine. However, multiple-drug regimens, usually including both isoniazid and rifampin, may be effective. Resection of localized lesions may be necessary in this mycobacterial disease.

Fortunately, the other fairly common mycobacterial pulmonary disease, that caused by *M. kansasii*, usually responds well to the standard chemotherapy described under Category III. Rifampin added to one or 2 standard drugs makes a substantial difference in response. The use of drug susceptibility testing helps one individualize therapy.

Avoiding Failure

Treatment failures occur either because inappropriate regimens are prescribed or because the patient fails to adhere to the regimen. Mistakes in selecting a regimen are most frequently made with previously treated patients. *Remember: Always use at least 2 drugs to which the patient's organisms are susceptible. Therefore, never add one new drug at a time unless you know the susceptibility pattern of the organisms, so that you are using at least 2 effective drugs.*

Most failures are due to interruption to self-medication by unreliable patients, who are often alcoholics. Ways to deal with irregular adherence to regimens include:

(1) Facilitating cooperation with therapy by flexible systems of delivery with pleasant facilities and understanding personnel who take the patient's life style into account.

(2) Supervising treatment. Directly administered intermittent therapy provides another option for ensuring an adequate regimen. Patients can even be visited at home or at work when treatment is required only twice a week. Two regimens considered effective are isoniazid and streptomycin, or isoniazid and ethambutol, given twice a week (5). Doses are noted in the table. Supervision of daily therapy for as long as 18 months is almost always impractical, but can be done when the patient is already in an institution (e.g., hospital, nursing home, or prison); the patient should not be institutionalized for this purpose. Daily therapy with rifampin and isoniazid for periods as short as 6 months has been used successfully in other countries. Direct supervision of such a regimen would be more feasible than the current 18-month program. Because most patients adhere best to regimens during the early part of therapy, short-term regimens may have greater success even when not directly supervised. Short-term chemotherapy is being used under controlled circumstances at this time in the United States. If the early encouraging results are confirmed, utilization of this form of therapy should increase.

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1. Johnston, R., and Wildrick, K.: The impact of chemotherapy on the care of patients with tuberculosis, *Am Rev Respir Dis*, 1974, 109, 636.
2. Diagnostic Standards and Classification of Tuberculosis and Other Mycobacterial Diseases, American Lung Association/American Thoracic Society, New York, 1974.
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4. American Thoracic Society: Guidelines for the investigation and management of tuberculosis contacts, *Am Rev Respir Dis*, 1976, 114, 459.
5. American Thoracic Society: Intermittent chemotherapy for adults with tuberculosis. A statement of the Program Committee, Scientific Assembly on Tuberculosis, *Am Rev Respir Dis*, 1974, 110, 374.