1968

Atypical mycobacteriosis : the new challenge : a case report and discussion

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ATYPICAL MYCOBACTERIOSIS : THE NEW CHALLENGE

A CASE REPORT AND DISCUSSION

By

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A THESIS

Presented to the Faculty of

The College of Medicine in the University of Nebraska

In Partial Fulfillment of Requirements

For the Degree of Doctor of Medicine

Under the Supervision of Dr. Irving Kass

Omaha, Nebraska

February 1, 1968

INTRODUCTION

The most venerable member of the family Mycobacteriaceae, Mycobacterium tuberculosis, is today a well recognized pulmonary pathogen. But what of the other members of the Mycobacterial family? These organisms, known from the time of Koch, have been recognized as pulmonary pathogens of major import only within the last ten years and remain a largely unknown clinical entity even today. With the relative efficacy in diagnosis and treatment of its ancient brethren, the more prevalent, less well recognized, diagnosed and treated atypical organisms are assuming an ever more important role inthe evolution of human pulmonary disease.

Just how important is the problem of atypical mycobacteriosis? Smith[1] estimates that 3 to 5% of all infections previously diagnosed as typical tuberculosis may in truth be due to an unrecognized atypical organism. By the use of skin testing with specific antigens, the atypical variants have been found to cause many more cases of subclinical infection than does the human tubercle bacillus. The atypical organisms are ubiquitous in nature, primarily in the soil. This finding correlates well with the observed higher incidence of atypical infection around construction sites, as was shown in Lincoln, Nebraska, in 1966[11]. Skin testing of eighth and twelfth graders, a population of about 1500 children, gave an incidence of positive reactions (5 mm or more of induration) to PPD of 3%, up from the 1% recorded annually during the previous decade. The number positive to 10 mm plus of induration showed a ten-fold increase. The construction season immediately prior to testing had been unusually heavy

in southeastern Lincoln and most of the positive reactors were found to live in this part of town. Specific skin testing using atypical mycobacterial antigens on some of the positive reactors residing in this area showed most had a larger reaction to atypical antigen than to PPD, probably due to the phenomenon of "cross-reaction" between typical and atypical tuberculin proteins.

To emphasize the nationwide and statewide prevalence of atypical mycobacteriosis, this paper will present a case of M. kansasii disease apparently contracted in Nebraska and correlate its salient findings with a brief review of the leterature.

CASE PRESENTATION

The patient, a 60 year old white male, was born in Wahoo, Nebraska in 1907. He lived and worked until 1923 on his father's farm near Nebraska City. During this time he took a job in an alfalfa mill for about 9 months, where he described the atmosphere as "choking" with dust and debris. Next, he drove a truck over the unpaved and dusty roads of Nebraska for a brief period. Subsequently, he left rural life and entered administrative work.

The patient has resided in the eastern Nebraska area all of his life with only occasional trips to other areas.

He smoked cigars from 1922 until 1940; he then smoked 2 packs of cigarettes until late in 1965 when he quit on the advice of his physician. He tended to relate the onset of a somewhat persistent cough to his cigarette smoking. He admitted to a family history of

"bronchial troubles" which he could describe only as a deep heavy non-productive coughing.

He complained of a periodic "dragging" sensation when trying to catch his breath and shortness of breath on exertion, most pronounced in the late summer months of July and August, not associated with rhinitis or watery eyes. Also, he complained of wheezing in times of stress and exertional dyspnea which first troubled him in 1956 and has grown gradually worse. In 1960 he sought help from an allergist, and noted subsequent improvement in his seasonal shortness of breath but only slight improvement in his exertional dyspnea. He remained under treatment until 1966.

In 1966 a routine chest film prompted the patients private physician to an investigation and in its course, sputum samples were obtained. Prior to this the patient had not been aware of sputum production, but now that his attention had been called to it, he noted a thick, dark greenish, non-purulent, mucous type of discharge that was heaviest in the morning, and required about one tissue to dispose of. Mycobacterium kansasii was isolated and the patient entered Clarkson Hospital on June 19, 1967. While there and under treatment, he suffered his first of two episodes of hemoptysis, coughing up 2 to 3 cups of blood. Six weeks, later, at home, he coughed up a small amount of pinkish sputum.

The patient denied knowledge of night sweats, fever or weightloss.

Physical examination revealed a blood pressure of 130/70 mm Hg, pulse of 108 per min. and regular, and respirations of 20 per min.

and regular. The patient was an elderly, moderately obese white male who was in no distress. His respirations were noted to be audibly wheezing in character, however he did not appear to be short of breath. Signific nt findings were limited to the respiratory system. The thoracic cage had the typical barrel chested configuration of chronic obstructive lung disease, measuring 40 inches at rest in the fourth intercostal space and 41 inches with maximal inspiration. Percussion gave clear hyperresonant tones. The diaphragms were percussed at T 11 and descended 1½ cm with deep inspiration. Auscultation revealed diffuse inspiratory and expiratory wheezes loudest at the apices bilaterally. Heart tones were distant and obscured by the wheezing. The liver, although of normal length, was pushed down 5 cm below the right costal margin in the mid-clavicular line.

Drug susceptibility studies at the time of organism isolation suggested that his mycobacteria were susceptible to the following anti-tuberculosis agents, and on June 17, 1967, the following treatment was started:

Isoniazid (INH), 300 mg twice a day (8:00 am and 2:00 pm) Trecator (ETH), 250 mg tid (8:00 am, 11:00 am, and 2:00 pm) Streptomycin (SM), 1 gm administered at 8:00 am, 7 days a week for a brief period and then 1 gm given at 8:00am, 5 days a week (Monday through Friday) until he received a total of 90 injections.

Pyridoxine, 50 mg twice a day (8:00 am and 2:00 pm)

In September, 1967, he complained of mental sluggishness and an inability to cerebrate, and for that reason, the INH was decreased to 500 mg/day, (300 mg at 8:00a , 200 mg at 2:00 pm).

The SM was discontinued on October 17, 1967, because he had received 90 injections. He was instructed to take INH, 300 mg at 8:00 am, 200 mg at 2:00 pm and there was no change in the schedule for taking ETH and pyridoxin. In addition, he was given Ethambutol-Myambutol (EMB), 2,000 mg (25 mg/kg/day which he was instructed to take in one dose at 8:00 am in the morning). After 60 days the dosage for EMB was reduced to 15 mg/kg/day.

Before the EMB was administered, the patient was seen by an opthalmologist who found that he had 20/20 acuity in each eye. His red and green color discrimination as tested by the A-O Plates revealed completely normal color vision and the perimeter of visual field using a 3 mm test object at a 330 mm distance was normal in each eye. The fundus examination was normal and the remainder of the intraocular contents were within normal limits.

On November 13, 1967, the INH was discontinued because of severe right shoulder hand syndrome. The pyridoxin was increased to 100 mg twice a day (8:00 am, 2:00 pm). Ethambutol-Myambutol and Trecator were continued as already prescribed. Following the discontinuing of INH there was a marked improvement in the right shoulder hand sympt

On December 17, 1967, the EMB dosage was decreased to 1,200 mg daily. At this time, the patient is receiving EMB, ETH and pyridoxin and this will be continued for at least 18 months.

Table 1 shows the results of therapy in graphic form.

TABLE 1: Smear, culture and drug susceptibility correlation

	Sputum Smear	Culture*
3/15/67	many	4+
7/05/67	many	4 +, catalase positive, photochromogenic, arylsulfatase negative. The mycobacteria were resistant to INH at 0.2 and 1.0 mcg/ml but susceptible at 5.0 mcg/ml blood level. Resistant to SM at 2 mcg/ml, susceptible at 10.0 mcg/ml. Susceptible to Ethionimide at 5.0 mcg/ml. Resistant to Kanamycin at 5.0 mcg/ml. Resistant to Capreomycin at 5.0 mcg/ml. Resistant to Cycloserine at 10.0 and 25.0 mcg/ml but susceptible to 50 and 100 mcg/ml. Slightly resistant to Ethambutol at 2.5 mcg/ml but susceptible to 5.0 mcg/ml since there were only 16 colonies at this concentration.
8/29/67	many	3 + one
09/26/67	colonies rare	colony
10/18/67	negative rare	negative
10/19/67	negative	5 colonies
11/02/67	negative	negative
11/17/67	negative	negative
12/04/67	negative	negative
12/05/67	negative	negative
12/18/67	negative	negative
12/19/67	negative	negative not
01/02/68		reported

* 4 + = 500 or more colonies; 3 + = 250 to 500 colonies; 2 + = 100 to 250 colonies; 1 + = 50 to 100 colonies; less than 50 colonies is recorded as the number followed by the letter "c". (For example, 10c = 10 colonies).

A film of the chest on 9/12/63, (Figure 1) revealed a small heart size. There was an infiltration of the left upper lobe and also a smaller infiltration in the right upper lobe along with considerable "hiking up" of the left pulmonary artery segment which would suggest that the patient had a long-standing infection in the left upper lobe region. The trachea appeared to be deviated somewhat to the right. There was some tenting on the surfaces of each leaf of the diaphragm, suggesting old pleural adhesions. The patient was asymptomatic at this time, indicating the chronic, low grade nature of his disease.

A chest X-ray taken on March 9, 1967 (Figure 2) and planagrams taken in June, 1967 (Figure 3) exhibited an increase in the infiltration in the left upper lobe. There were small areas of cavitation within the infiltration which may represent areas of focal emphysema. The patient was still asymptomatic and treatment was begun only after his routine chest film revealed the process to be slowly advancing. Note the relatively indolent progression the disease process has shown over the intervening four years.

X-ray taken on November 12, 1967, showed a decrease in the infiltration in the region of the second rib anteriorly on the left. There did not appear to be any significant change in the right infiltration.

The left pulmonary artery was still "hiked up".

About 90 days after the initiation of chemotherapy, the patient noted that the sputum had begun to diminish in amount and that the exertional dyspnea had improved. Presently, there is almost no sputum and the dyspnea continues to improve.

FIGURE 2: Increased infiltration is noted in the left upper lobe since 9/23/63 along with small cavities on the left.

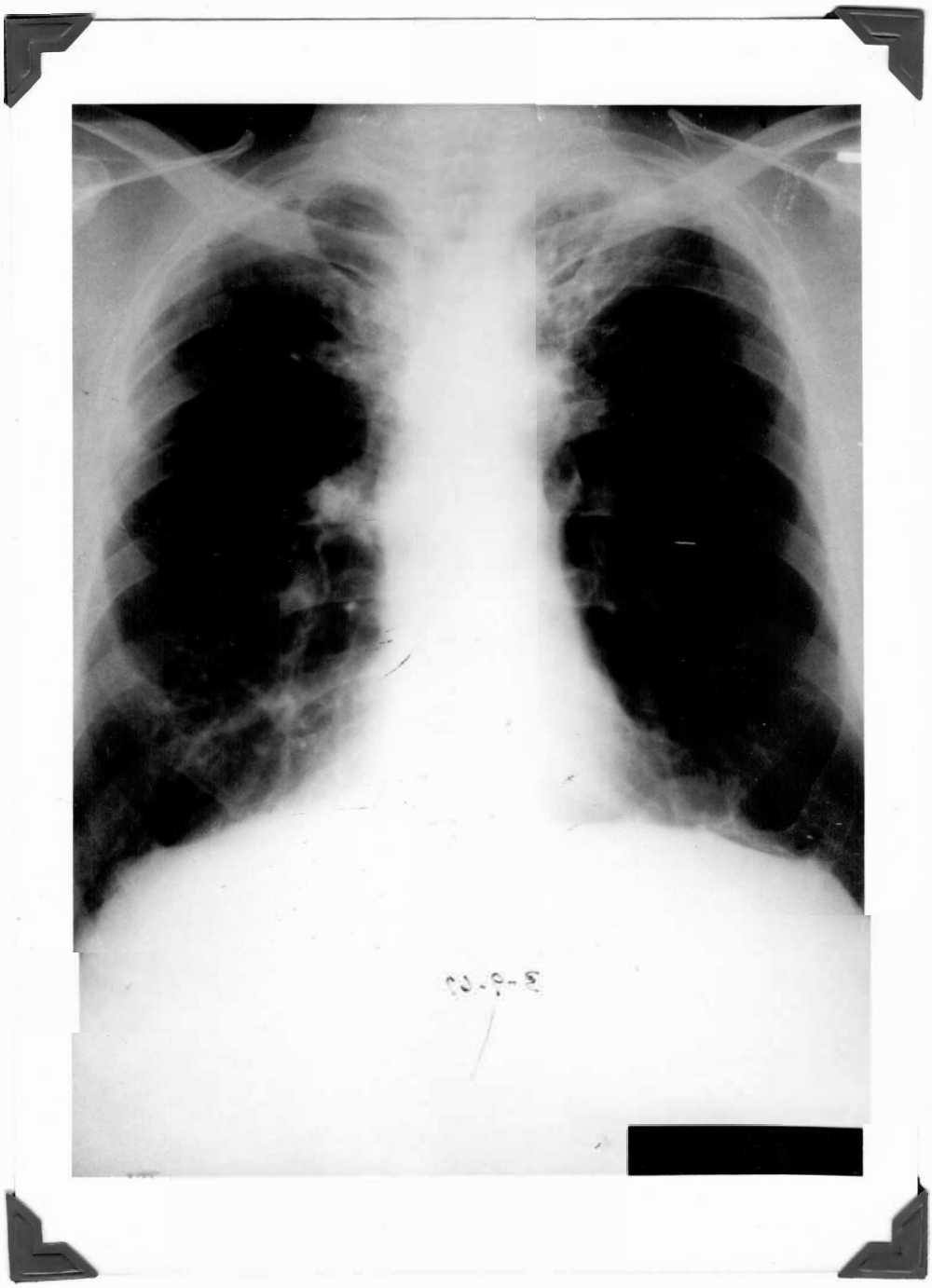


FIGURE 1: An infiltration is noted in each apex, largest on the left, along with a "hiking-up" of the left pulmonary artery segment and evidence of old pleural adhesions.

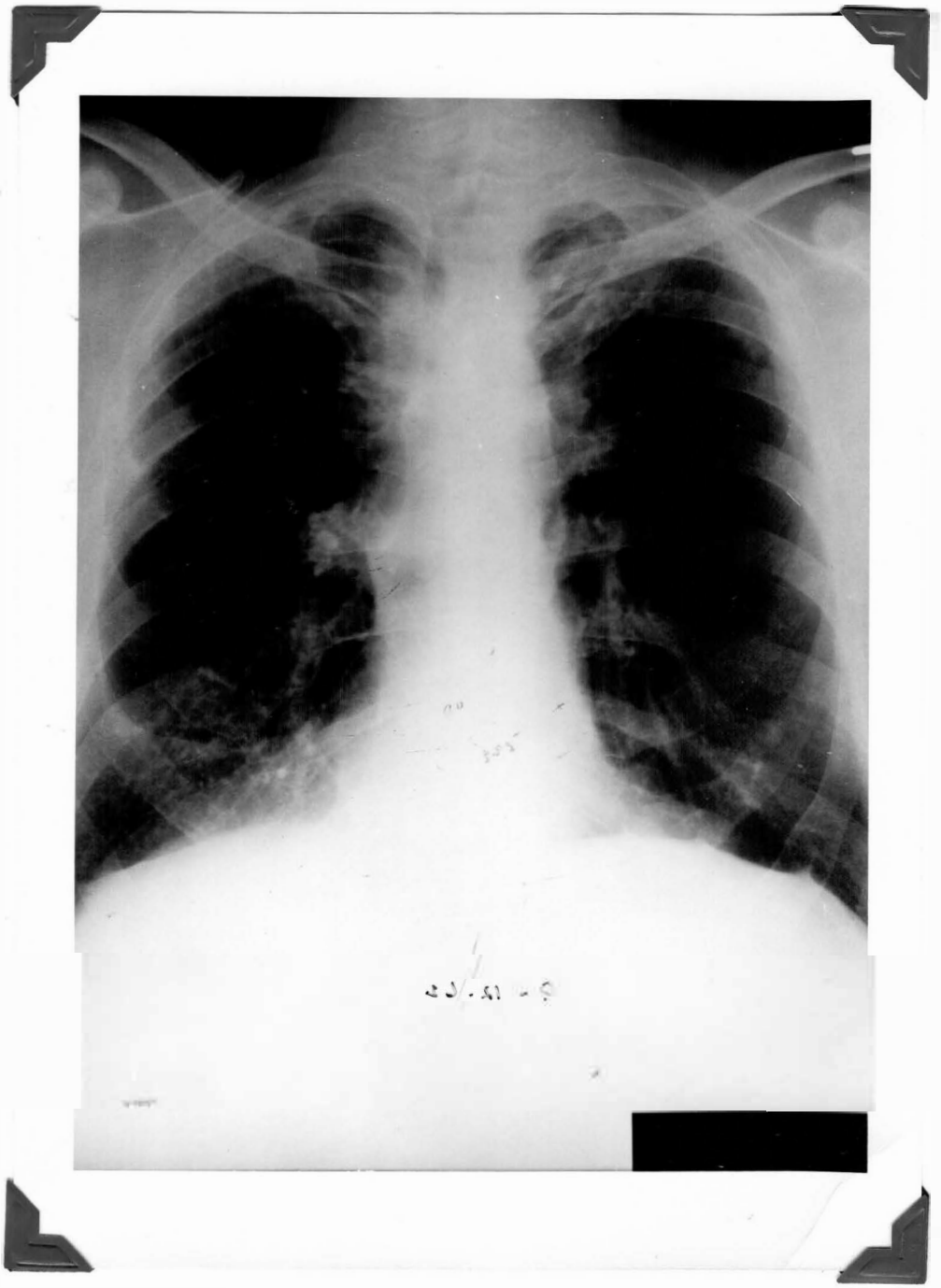
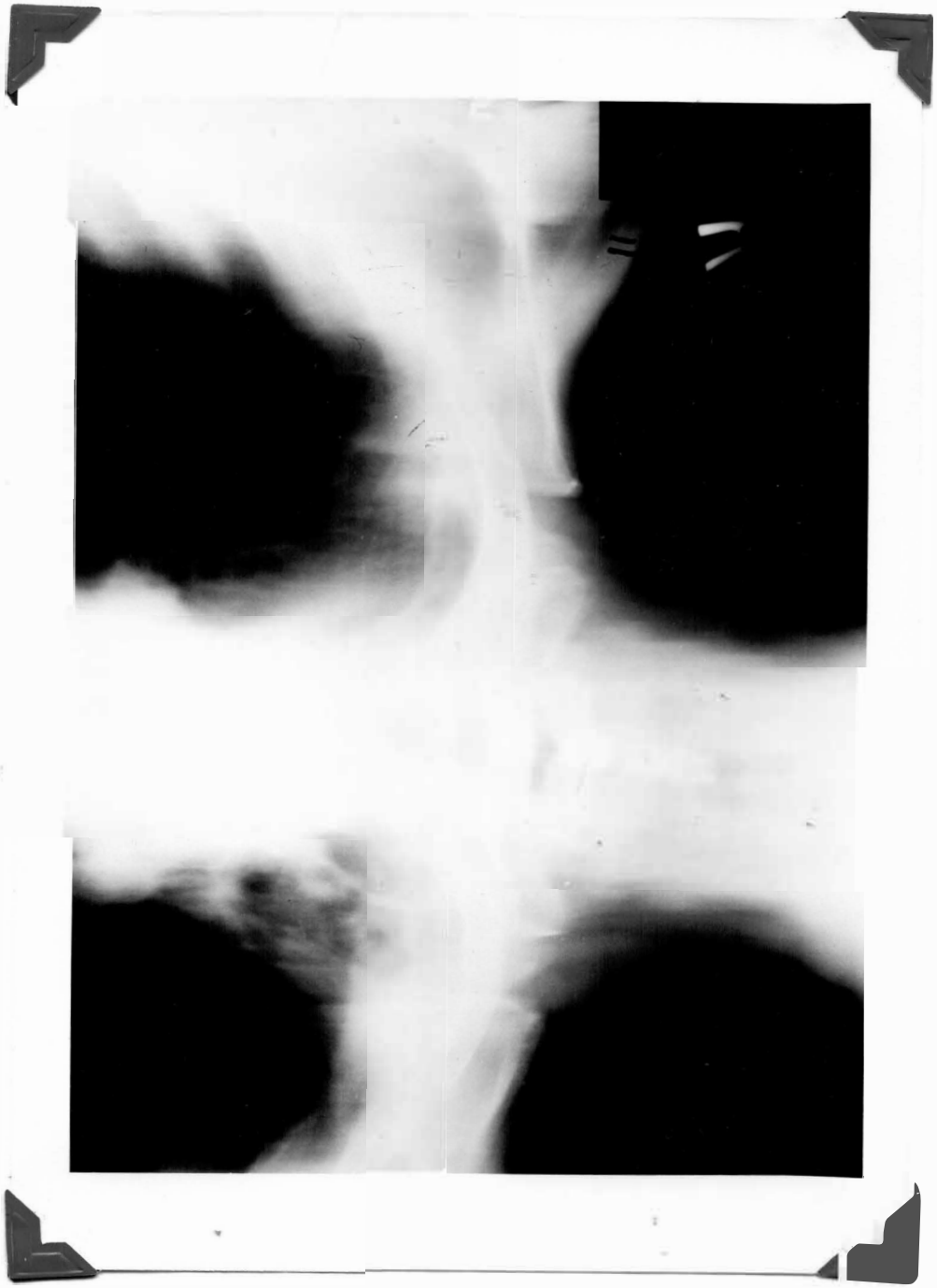


FIGURE 3: Planagrams of the left apex taken in June, 1967, showing the infiltration and cavitation in greater detail.



DISCUSSION

In the urban and heavily industrialized areas of England and the United States fifty years ago, almost everyone over the age of twenty years was infected with a tubercle bacillus as indicated by strong positive reaction to standard doses of tuberculin (1). Opie, Landis and McPhedran (cited by #1) in 1929 noted that 70.4% of 1,422 Philadelphia school children reacted to a 1:1,000 dilution of OT (10 TU, i.e. Tuberculin Units). They also noted, in passing, that 12.6% of their population was positive only to a 1:100 (100 TU) dilution of tuberculin. Similar figures outlining the marked prevalence of infection with typical tuberculosis as indicated by reaction to 10 TU and 5 TU (1:2,000) were published by other authors of the time.

However, ever since reliable morbidity and mortality figures have been kept, the incidence of disease caused by tuberculosis has been in a steady decline, apparently unrelated to medical efforts. The reason for this fall is not known, though undoubtedly the extensive tuberculosis control program in the United States has augmented the trend.

As would be expected, as the opportunity for infection and reinfection with typical tuberculosis was reduced, the number of strong 10 TU reactors fell; unexpectedly, the previously low number of weak 100 TU reactors rose. A Duke University study (cited by #1) between 1930 and 1940 found that 60% of their medical students reacted to 10 TU but only 20% were positive to 100 TU. In 1956-57, conversly, only

24.3% of their medical students were positive to 10 TU while 37.5% reacted to the 100 TU dose. Other investigators also observed this shift.

The explanation for such a change was not clear, and a controversy arose. The logical explanation, and the one accepted by most workers in the field during the mid-1950's, lay in the concept of a gradually decreasing degree of sensitivity to tuberculin ski test material in the absence of repeated subclinical superinfections. That this can occur is realized today; a complete loss of reactivity to 5 TU of human tuberculin will take place after 26 to 36 years when a large proportion of the active cases are removed from the population [2]. (cited by #1) At that time, however, Dr. Carroll Palmer postulated the existance of a massive soil based infection most prominent in the southeastern United States by an atypical variant of the well recogn zed human tubercle bacillus, capable of inducing low grade allergy in the infected person. This allergy caused a cross reaction to tuberculin skin test material. Much later, Smith [1] concurred, stating that the marked decrease in active untreated tuberculosis which decresed the total number of new reactors had uncovered many patients with a low grade allergy from infection with an unclassified or atypical mycobacteria.

That such organisms exist and are capable of infecting man has been known since Koch. Mycobacterium balnei was the first atypical variant to be a recognized cause of human disease; it was isolated from elbow lesions and a swimming pool in 1952 by Linell and Norden [3].

Mycobacterium kansasii, later designated the prototype of Runyon's photochromogenic Group I, was isolated at necropsy in 1953 by Buhler and Pollak (cited by 1). The scotochromogenic Group II was isolated from the lymph nodes of a group of children suffering from cervical adenitis by Schaefer and Riggiardo (cited by 1). Group III, the Battey organism, was discovered in the sputum of a patient in a southern hospital in 1957 (cited by 1). Runyon's Group IV, the Rapid Growers such as M. fortuitum, was isolated in 1938 from a human abscess by deCosta and Cruz (cited by 1).

Although existence of the atypical mycobacteria was appreciated, their role as pulmonary pathogens causing a relatively high incidence of infection has not previously been realized for reasons which will be discussed, and even today their true prevalence is unknown because it appears that the vast majority of them give rise to only chronic, low grade subclinical infections. However, Smith (1) has estimated that 3 to 5% of all clinical infections originally diagnosed as typical tuberculosis are probably the result of an atypical strain. Lester, Botkin and Colton in 1958 found that of 929 cases culture positive for acid fast bacilli, 300 or 32% were positive for an atypical acid fast bacillus[4]. Smith and Johnston (2) felt in 1964 that the atypical mycobacteria are more frequent in children and young adults than is typical tuberculosis. Edwards (cited by 1), in 1963, found that four of the five types of atypical mycobacteria, with the sole exception of M. fortuitum, had a higher percentage of reactors than typical mycobacterium (Table 2). In addition, as Palmer postulated, by far the largest number of skin test reactors were found to be in the southeastern United States. Smith (1) noted 70% to 80% of the population in this area reacted to Battey and Scotochromogen antigen, as opposed to only 20% to 30% at the northern borders (Figure 4 and 5).

TABLE 2: Frequency and mean size of reactions among Navy recruits from all parts of the country to 0.0001 mg (5 TU) of specific PPD antigen. (cited by 1)

PPD Antigen	Prepared From:	# Tested	Reactions of 2 mm or More	
			Percentage	Mean Size in mm
PPD-S	M. tuberculosis H37RV	212,462	8.6	10.3
PPD-F	M. fortuitum	3,415	7.7	4.8
PPD-Y	M. kansasii	13,913	13.1	6.2
PPD-A	M. avium	10,060	30.5	6.7
PPD-B	Battey	212,462	35.1	7.7
PPD-G	Scotochromogen	29,450	48.7	10.3

FIGURE 4: Geographic variations in the frequency of reactors to PPD-S among U. S. Navy recruits who were lifetime one county residents. (cited by 1)

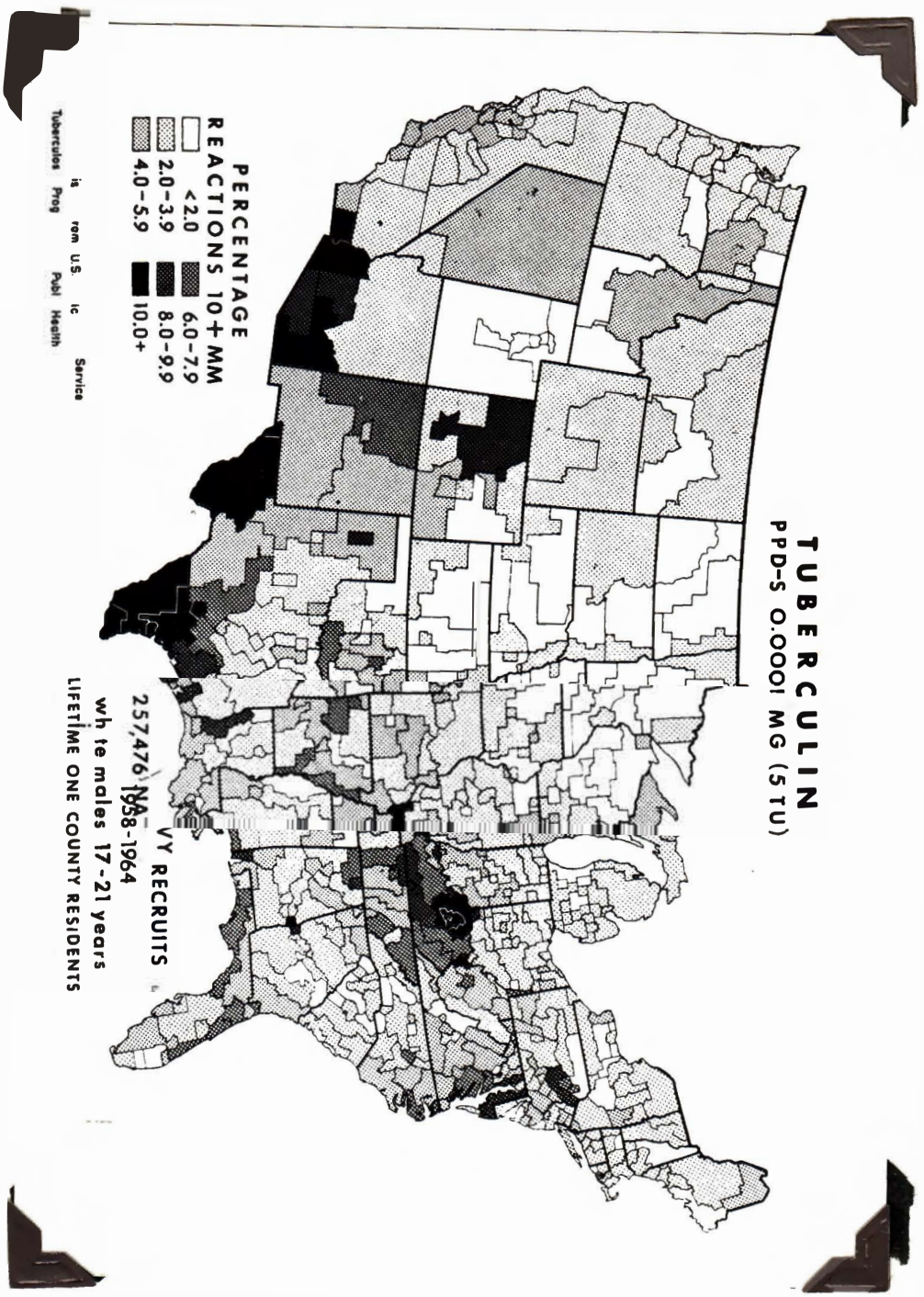
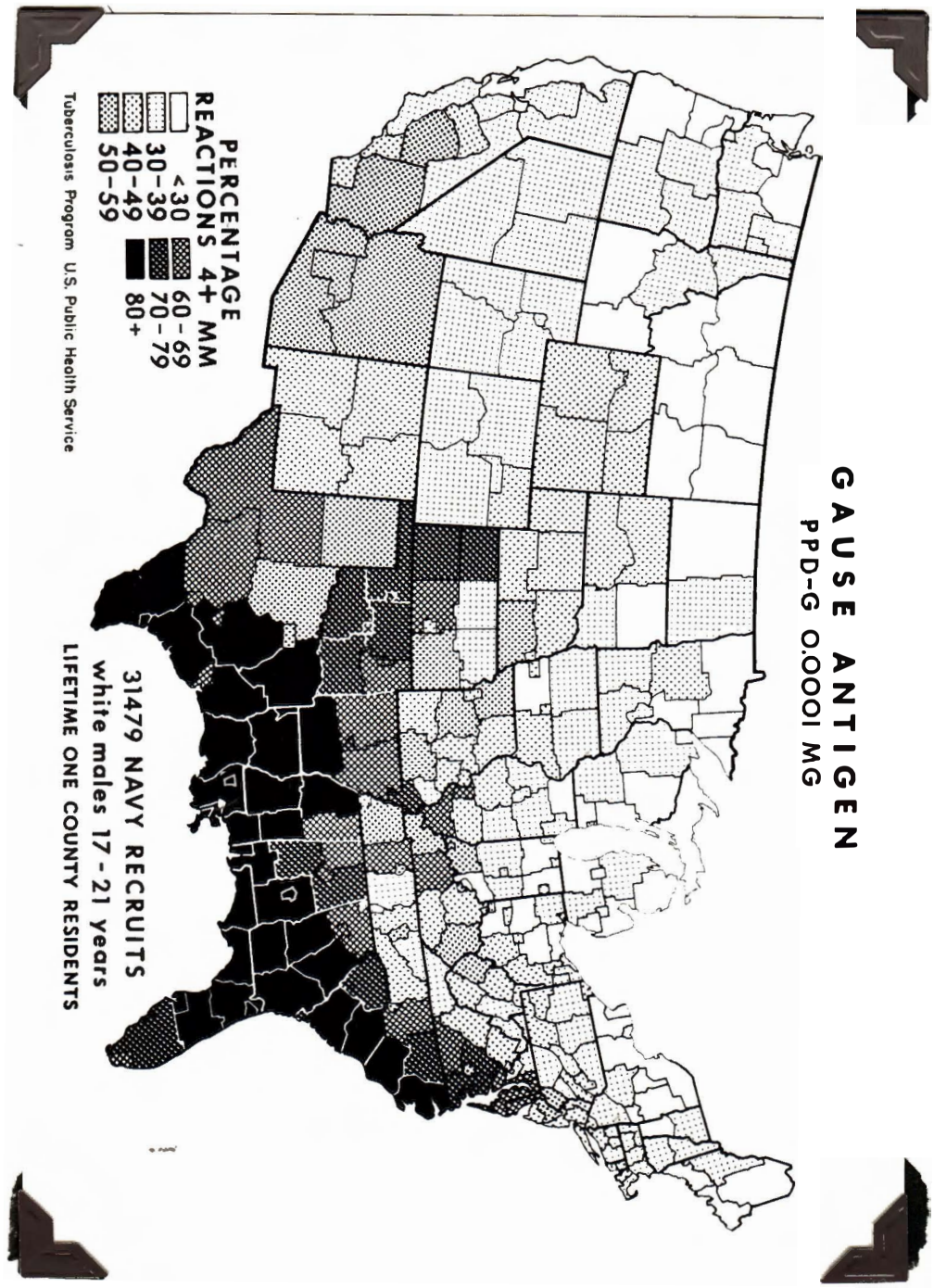


FIGURE 5: Geographic variations in the frequency of reactors to the Gause scotochromogen PPD-G among U. S. Navy recruits who were lifetime one county residents. (cited by 1)



The above data are based on male populations. An interesting, although as yet unexplained finding is that females apparently have a lower incidence of clinical disease (Table 3). (cited by 1)

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Why was the recognition of atypical disease delayed so? Youmans explained it by pointing out that the prevalence of human tuberculosis was so great that the relatively few cases of atypical mycobacterial disease discovered went unmarked. The pigmented and non-pigmented atypical organisms, wide spread in nature, were frequently found along with typical tubercle bacilli in gastric washings or sputum samples and so when found alone were often regarded skeptically as etiologic agents. In addition, while typical bacilli caused disease when injected into guinea pigs the atypical variants generally did not, heightening the impression that they were not pathogenic. Laboratories only compounded the state of obscurity by eschewing culture, feeling that smear and Ziehl-Neelson stain were sufficient for diagnosis. As the newer chemotheraputic agents were developed, however, the need for culture and sensitivity was realized, and the large number of atypical organisms thus cultured helped put investigators on the track of the atypical disease types.

Thus far, with the exception of M. kansasii, all of the atypical variants have been isolated from nature. (cited by 10) Kubica found that 45% of 1,200 soil and water samples from the southwestern U. S. grew acid fast bacilli; 48 atypical forms were isolated: 2 photochromogens, 12 scotochromogens, 22 Battey and 12 Group IV strains. Chapman and associates have suggested milk to be a potent and unrecognized source

TABLE 3: Reactions of 5 mm or more in medical students and student nurses to 5 TU of specific PPD antigen. (cited by 1)

	Number	PPD-S	PPD-B	PPD-Y	PPD-Scot.	PPD-F
medical students	164	14.6%	24.3%	14.0%	51.8%	-
medical students	82	12.2%	-	-	-	14.6%
student nurses	80	6.2%	17.5%	7.5%	22.5%	-

of atypical mycobacteria[7]. Of 770 samples of milk obtained and tested, 261 or 33.8% yielded pathogenic atypical organisms. Isolated without doubt were Runyon Groups II, III, and IV; a small minority of the bacteria did show certain characteristics of Group I, but due to the inconsistancy of the photochromogenic trait and other reasons, definitive identification could not be done.

The characteristics of each of Runyon's Groups have been relatively well established and are compiled here in chart form (Table 4)[12]. The atypical strains show, in contrast to the typical, a capacity to grow slowly at lower temperatures, significiently increased selective resistance to SM, PAS and INH, lower pathogenicity for all experimental animals and an absence of progressive disease in guinea pigs, rabbits and fowl, frequently a high catalase activity, pigmentation in two of the groups, and characteristic acylamidase activity.

But what was the actual mechanism behind Palmer's theory? What did cause the rise in the number of 100 TU reactors? Can this great reservoir of latent atypical mycobacteriosis be held in account? It can. It has been shown that each mycobacterial species is a mosaic of protein antigens. Some are specific; most are shared in varying degrees with all other strains, both pathogenic and saprophytic. Therefore, because these atypical species induce low grade allergy and because of cross antigenicity, the PPD specific for each infectious agent will always give a larger reaction in millimeters than a heterologus PPD will in the same individual. In other words, skin testing with one PPD will give a positive, albeit less vigorous reaction in an

TABLE 4 : CHARACTERISTICS OF SOME MYCOBACTERIA CAUSING DISEASE IN MAN

Type of Mycobacteria	Colony Description (7H10 agar)	Pigmentation on Initial Isolation: Grown in dark	Pigmentation on Initial Isolation: Exposed to light	Growth Rate (Minimal Inocula) 30 C.	Growth Rate (Minimal Inocula) 37 C.	Growth Rate (Minimal Inocula) 45 C.	Neutral Red	Niacin	Drug Resistance mcg/ml INH 0.2	Drug Resistance mcg/ml SM 2	Drug Resistance mcg/ml PAS 3	Catalase	Animal Pathogenicity: Guinea pig	Animal Pathogenicity: Chicken	Animal Pathogenicity: Rabbit	Animal Pathogenicity: Mouse (infectivity)
M. tuberculosis	dry, friable, difficult to emulsify	none to buff	none to buff	0	2-4 wk	0	+	+	S R	S S	S S	+++ 0 to +++	++++ +	0 0	+ 0	++++ ++++
M. bovis	dry, friable, more readily emulsified than human type	none to buff	none to buff	0	2-4 wk	0	+	0	S	S	R	+++	++++	0	++++	++++
M. avium*	small, spreading, translucent or drop-like	none or faint yellow, tan or pink	none or faint yellow, tan or pink	0	3-4 wk	2-3 wk	+	0	R	R	R	++++	0	++++	++++	++++
M. balnei*	smooth, butyrous, easily emulsified (rarely rough)	none to buff	deep yellow	1-2 wk	0	0	0	0	R	R	R	+++++	0*	0	0	0*
M. kansasii*	smooth, butyrous, easily emulsified (rarely rough)	none to buff	deep yellow	2-3 wk	2-3 wk	0	0	0	R (sens. to 1 mcg)	R	R	++++	0	0	0	++++
Unclassified* Group II (Scotochromogens)	smooth, butyrous, easily emulsified	yellow to orange	yellow to orange	2-3 wk	2-3 wk	0	0	0	R	S or R	R	+++++	0	0	0	0
Unclassified* Group III (Battey types)	small, spreading, translucent, or opaque, hemispheric	none	none	2-3 wk	3-4 wk	0	0	0	R	R	R	+++	0	0	0	0 or ++++
Unclassified* Group IV Rapid Growers M. fortuitum	rough or smooth	usually buff	usually buff	2-4 days	2-4 days	0 or 2-4 days	0	0	R	S or R	R	+++++	0	0	0	0 or ++++

*These species are serologically distinguishable

From [redacted]tional Jewish Hospital, Denver 6, Colorado

individual sensitized by a heterologus but antigenically similar species. Human and scotochromogen PPD produce the greatest sensitivity in man, while avian, Battey and scotochromogen induce the greatest degree of cross reaction to human PPD. Herein we see the explanation. Individuals infected with atypical organisms develop sensitivity at such low levels that the antigenic challenge of the small heterologus 10 TU dose can not initiate the cross reaction whereas the maximal 100 TU heterologus dose and the small but specific homologus 10 TU dose can.

In the interpretation of skin test data, it should be kept in mind that an individual may be infected with more than one mycobacterial agent. Smith (1) has suggested a program to follow for most efficient use of the intradermal antigenic material. He advocates the routine intermediate (5 TU) dose of PPD-S. If this is negative, retest with 100 TU of PPD-A to pick up atypical infection. If a positive is observed at any step, specific skin testing must be undertaken.

One incidental asset to atypical infedtion seems to exist; the patient is probably less sensitive to typical infection. Since cross sensitivity occurs, it would be only logical to suppose that cross immunization might also come about, especially in the light of the fact that BCG employs M. avium antigen. Youmans makes an interesting observation in this regard. He wonders if the decline in morbidity and mortality of typical tuberculosis might be due, in part, to low grade immunization over a large population by the atypical variants.

The recognition of atypical mycobacteriosis poses a real problem

because the clinical evidence does not make up a readily identifiable entity. It appears that, in general, atypical infections resemble their typical brethren in most significient features. Symptomatologic, histologic and radiographic findings are practically indistingushable. However, some valid differences do exist. There is a broad base of latent subclinical infection, the true magnitude of which is unknown. The disease process tends to be chronic, without significient inflammatory or exudative components, prone to produce a chronic fibrocavitary disease with indolent thick walled cavities. Acute intrapulmonary dissemination and extra pulmonary hematogenous spread to bone, joint, and viscera occur but rarely. Those manifesting clinical disease often are older white males who show a marked tendency not to communicate the disease to family or close contacts. There is no evidence to firmly relate the process to any particular pre-disposing disease, environment, condition or occupation; emphysema, silicosis, bronchiogenic carcinoma and graphite pneumoconiosis have all been associated, however[8].

Bates[9], in his examination of 199 cases of atypical mycobacteriosis from a clinical aspect, found that his patients were generally over 50 years of age and their disease tended to insidious onset with X-ray evidence of disease several years prior to the onset of symptoms. Only one half sought medical help because of pulmonary symptomatology. Eighty per cent complained of cough, 40% had sputum in an amount described as more than slight, 33% complained of dyspnea at rest or with exertion, 25% experienced weight loss, 25% had hemoptysis with the

majority of these patients suffering Group IV disease) and 10% complained of a chronic, low grade fever. Deaths due to progressive atypical disease occurred in 16%.

Youmans attempts to draw the above observations together by postulating that later in life, when natural body defense mechanisms gradually fail for unknown reasons, the atypical infection acquired in youth might mushroom into clinical disease thereby accounting for the greater prevalence in older people and the low communicability.

The treatment of atypical mycobacteriosis is generally unsatisfactory at this time, primarily because these organisms show selectively greater resistance to the standard anti-tuberculous agents in widespread use today. For instance, human tuberculosis (H37RV) is sensitive to INH at blood levels of 0.2, 1.0 and 5.0 mcg/ml, whereas M. kansasii is sensitive only at the upper two concentration levels. The same situation exists with SM; the human variant is sensitive at 2.0, 10.0 and 25.0 mcg/ml while the Group I variant is resistant at the lowest dose level. So we see that the atypical organisms show a selective resistance. INH and SM may be used, but only at high dosage with concomitantly greater risk of toxicity. It is recommended that INH be administered at the dosage schedule of 16 mg/kg/day with half given at 8:00 a and the remainder at 2:00 pm continuously for 18 months. SM dosage ideally is 20 mg/kg/day, all at 8:00 am, for 90 consecutive injections or until sputums become culture-negative.

Two newer drugs, Viomycin (VM) and Ethionamide (THA) appear to be effective chemotheraputic agents, especially against Group I

organisms. M. kansasii, the commonest and most virulent pulmonary pathogen of the atypical variants, is the most consistently sensitive of the four groups to the above drugs. The other three groups are unpredictable in their drug susceptibilities and drug sensitivity studies are best done in such cases. The program of choice against the Group I mycobacteria has been THA 250 mg tid at 8:00 and 10:00 am and 2:00 pm, or qid at 8:00 and 10:00 am, noon and 2:00 pm for up to 18 months combined with VM 1 gm a day for 5 days a week, Monday through Friday for 90 days or until the sputum is culture negative.

Ethambutol is one new agent that the drug susceptibility studies frequently show as effective against the atypicals. This drug is administered 25 mg/kg/day for 60 days, then 15 mg/kg/day until toxicity occurs or the sputum becomes culture-negative. It may be continued for up to 18 months also.

With such programs as outlined above, Dye and Kass[6] found that thirteen of their fourteen cases of atypical infection became sputum-culture-negative by 37 days and stayed so indefinitely. Four of five patients who had not become sputum-culture-negative with operation did so after VM and THA therapy.

It should be noted that multiple drug attack is the current approach and, if possible, should be combined with lobectomy, segmental resection or pneumonectomy once two consecutive sputum cultures have been negative.

Drug toxicity is usually within an acceptable range. The severe ocular toxicity sometimes seen with Ethambutol should be noted and

diligently watched for.

SUMMARY

The history, physical and clinical course of disease with response to treatment of a patient with M. kansasii atypical mycobacteriosis was presented.

The great frequency of atypical infection was noted, along with the reasons for its delayed recognition.

The environmental source and bacteriological characteristics of the atypical organisms were enumerated.

Host response to atypical mycobacterial infection and disease was discussed, followed by the clinical manifestations of disease.

Principles of therapy in general and programs of chemotherapy in specific were mentioned.

ACKNOWLEDGMENT

The author wishes to make known how gracious, thorough and ungrudging his advisor, Doctor Irving Kass, was with his valuable time and worthy advice.

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