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Pulmonary Resection for Tuberculosis:

A Review of 1257 Operations

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IT HAS now been 17 years since the first resection for pulmonary tuberculosis was carried out at the Nova Scotia Sanatorium. In the early days, excisional surgery because of its high mortality and complication rate was considered a measure of last resort, to be tried only with misgiving when all other procedures had failed to bring the disease under control. It is rather astonishing to note how it rapidly supplanted the older operations which, in the past decade, have been relegated to a position of relative obscurity. In the period since 1952, lung resection has been an essential component of the therapeutic regimen. It is true that in the past three or four years a decrease in the amount of excisional surgery being performed is evident. It is felt that this in no way reflects on the excellence of the procedure, but indicates that the disease is being discovered at a stage of its development where it is now much more vulnerable to the antimicrobial agents.

It is the purpose of this presentation to relate what has happened to 1155 patients who underwent 1257 lung resections for tuberculosis at the Nova Scotia Sanatorium from November 14, 1944, to December 18, 1959.

TABLE I.—DISTRIBUTION OF PULMONARY RESECTION OPERATIONS

	Number of patients	Number of operations
Single resections	1054	1054
Bilateral resections	88	176
Multiple unilateral resections Bilateral resection plus multiple	12	24
unilateral resection	1	3
Total	1155	1257

From the Nova Scotia Sanatorium, Kentville, N.S. Presented at the Annual Meeting of the Nova Scotia Branch, Canadian Public Health Association, Sydney, N.S., September 28 1961. As noted in Table I, 1054 individuals had a single resection, 88 underwent bilateral resection, 12 had multiple unilateral resection, and in one patient it was necessary to perform bilateral resection together with a later unilateral operation.

TABLE II.—Age and Sex Distribution at Time of First Operation of Persons Undergoing Pulmonary Resection

	Both	h sexes		
Age group	No.	%	Male	Female
0 - 9	12	1.0	8	4
10 - 19	137	11.9	58	79
20 - 29	403	34.9	157	246
30 - 39	317	27.4	138	179
40 - 49	222	19.2	128	94
50 - 59	59	5.1	39	20
60+	5	0.4	3	2
All ages	1155	100.0	531	624

In this series, there were 531 males (46%) and 624 females (54%). The age distribution, shown in Table II, indicates that by far the greatest proportion of patients was in the 20-39 age group. The youngest individual in the series was a female aged 4 years and 10 months, and the oldest, a female aged 65 years.

TABLE III.—Total Operations* Performed Related to Age Groups and Extent of the Pulmonary Lesion

		All fications		M - l t - l	F.c.	
$egin{array}{c} Age \ -group \end{array}$	No.	%	Minimal	Moderately advanced	$Far \ advanced$	Other
0 - 9	12	1.0	1	8	2	1
	151	12.0	33	87	- 30	1
20 - 29		34.9	53	260	126	
30 - 39		27.5	33	217	95	1
	240	19.1	13	142	84	1
50 - 59	64	5.1	i	40	23	
60 - 69	5	9.4		2	2	1
All ages 15	257	100.0	134	756	362	5

*Number of operations (1257) differs from number of persons (1155) involved as indicated in subsequent tables.

TABLE IV.—Type of Operation Performed Related to Extent of the Pulmonary Lesion

Type of operation	All classifications	Minimal	Moderately advanced	Far advanced	Other
Pneumonectomy	130		32	98	
Bilobectomy + segmentectomy	1			1	
Bilobectomy	26		14	12	
Lobectomy + multiple segmentectomy	3		2	1	
Lobectomy + segmentectomy + wedge resection	6		4	${f 2}$	
Lobectomy + segmentectomy	56	1	26	29	
obectomy + multiple wedge resection	5		3	${f 2}$	
obectomy + wedge resection	29		22	7	
obectomy	475	12	305	155	3
Multiple segmentectomy	26	3	10	12	1
egmentectomy + wedge resection	17 17	·	12	5	
egmentectomy	85	6	$\tilde{62}$	17	
Multiple wedge resection	43	7	$\ddot{32}$	4	
Wedge resection	355	105	232	17	1
All operations	1257	134	756	362	5

In evaluating the final results, it was thought to be of considerable importance to determine the extent of the disease at the time of operation. Table III indicates that by far the largest group was in the moderately advanced stage, slightly over one-quarter were in the far advanced category and there were some 134 patients with a minimal lesion. Five patients could not be classified as minimal, moderately advanced or far advanced, their surgical lesions being considered secondary to the evolution of a primary complex.

Table IV illustrates the extent of the surgical undertaking relative to the amount of disease at the time of operation. It will be demonstrated in a later table that the good results of surgery vary inversely with the quantity of lung resected. By and large, throughout the years, this depended on the amount of disease found at the time of operation. It must be emphasized, however, that the limited excisional techniques of segmentectomy and wedge resection are rather recent innovations and that in the earlier years a much higher proportion of pneumonectomies and lobectomies was carried out. In this group of patients, the first segmental resection was not performed until 1951, and the first wedge resection in 1952. Lobectomy was the most frequently performed procedure, with

wedge resection in second place. As stated in a previous report, a wedge resection is preferred whenever possible. This type of limited resection has an extremely low complication rate, has practically no adverse effect on pulmonary function, and has produced excellent final results.

While it is not the purpose of this report to present a detailed account of operative complications, it may be of interest to tabulate these briefly. They have been related to the type of operation performed and have been divided as to whether they occurred before or after a six-month postoperative interval in relation to the type of operation performed but with those groups eliminated which were too small to be statistically significant. Of the patients undergoing pneumonectomy, 54% were without complications. Of those subjected to lobectomy, 79% manifested no complications, while in the wedge resection group no complications developed in 90%. Segmental resection has not been found to produce an excessively high complication rate, but rather it is felt that, at least in part, the incidence of complications will increase directly with the increasing amounts of lung resected. This statement should be qualified in comparing wedge and segmental resections. The amount of lung resected in each of these procedures

TABLE V.—Type of Operation Performed in Relation to Presence or Absence of Postoperative Complications

Type of operation	All cases	No complications	Complications evident within six months of operation	Complications not evident until six months after operation
Pneumonectomy.	130	70 (54%)	60 (46%)	
Bilobectomy + segmentectomy. Bilobectomy + multiple segmentectomy. Lobectomy + multiple segmentectomy.	26 3	17 (65%) 3 (100%)	1 (100%) 7 (27%)	2 (8%)
Lobectomy + segmentectomy + wedge resection	6 56	5 (83%) 32 (57%)	1 (17%) 22 (39%)	2 (4%)
Lobectomy + multiple wedge resection	5 29	5 (100%) 24 (83%)	5 (17%)	, , , ,
Lobectomy. Multiple segmentectomy. Segmentectomy + wedge resection.	26	337 (79%) 19 (73%) 14 (82%)	90 (19%) 7 (27%)	8 (2%)
Multiple wedge resection	85 43	14 (82%) 71 (84%) 41 (95%)	$egin{array}{c} 3 \ (18\%) \ 14 \ (16\%) \ 2 \ (5\%) \end{array}$	
wedge resection	355	321 (90%)	34 (10%)	
All types of operations	1257	999 (79.4%)	246 (19.6%)	12 (1.0%)

TABLE VI.—Mortality Record, as of December 31, 1959, of all Persons as Related to the Time of Death and the AGE GROUP AT TIME OF FINAL OPERATION

	Cumulative percentage of deaths	All ages	0 - 9	10 - 19	20 - 29	30 - 39	40 - 49	50 - 59	60
Died on operating table	4.5%	4	0	1	2	0	0	1	0
Died less than one week after operation	25.8%	19	1	1	4	4	6	3	0
Died 8 - 60 days	43.8%	16	0	1	5	2	7	1	0
Died 61 days to one year	60.7%	15	0	0	7	2	4	${f 2}$	0
Died in 2nd year	74.2%	12	0	2	3	2	5	0	0
Died in 3rd year	80.9%	6	0	0	2	0	3	1	0
Died in 4th year	82.0%	1	0	0	0	0	1	0	0
Died in 5th year	86.5%	4	0	1	0	2	1	0	0
Died in 6 - 10th year	97.7%	10	0	1	${f 2}$	2	5	0	0
Died in 11th year or later	100.0%	2	0	0	1	1	0	0	0
Still alive		1002	10	113	347	285	191	51	5
Not known		64	0	14	31	15	3	1	0
All persons		1155	11	134	404	315	226	60	5

may be approximately the same, but the complication rate of segmental resections is about twice that of wedge resections.

Mortality statistics for the entire series are shown in Table VI. It will be noted that over 60% of the deaths occurred during the first year postoperatively. It has been the custom, in reporting results of studies such as this, to regard fatalities in the first 60 days after operation as operative mortality. On this basis, it is noted that 39 patients died during this period. This, reckoned on the basis of 1257 operations, represents an operative mortality of approximately 3.2%. The total deaths amounted to 89. Disregarding the 64 patients who have not been traced, this signifies a case fatality rate of 7.7%. Almost half of the deaths occurred in those 291 people who were over 40 years of age. Fortyfive per cent of the total mortality therefore occurred in this group of 291 older people who represented only 25% of the entire series of cases.

Table VII relates the mortality figures to the amount of lung resected. Again, if the three groups large enough to be statistically significant are studied, it is found that the highest mortality rate is in the pneumonectomy group and the lowest in the wedge resection patients. Also, the patients undergoing lobectomy had a significantly higher mortality than the average for the entire group. This would suggest that the danger of the operative procedure is in direct proportion to the amount of lung removed and, by the same token, to the extent of the disease present.

Of considerably more importance to the mortality statistics than the roentgenographic extent of the disease is the type of lesion for which the operation is performed. Table VIII lists the indications for operation related to the mortality. The terms used in this table to describe the pathology are self-explanatory. The expressions "destroyed lung" and "destroyed lobe" have been used in their literal meaning. By "residual disease" is meant the solid lesion or lesions remaining after optimum medical therapy. By "coin lesion" is meant the round dense asymptomatic lesion found on a routine roentgenogram. In these last-named cases, exploration of the chest is undertaken with the

TABLE VII.—Deaths from All Causes Recorded as of December 31, 1959, Related to Time of Death and Type of OPERATIONS PERFORMED

Time of death postoperatively	All types of operation	Whole or balance of lung	Two lobes and segment	Two lobes	Lobe and two or more segments	Lobe and segment and wedge	Lobe and segment	Lobe and two or more wedges	Lobe and wedge	Lobe	Two or more segments	Segment and wedge	Segment	Two or more wedges	Wedge
On operating table Less than one week after operation 8th to 60th day	19 16 17 14 7 2 4	3 6 3 7 5 2		2			2 1 2		1	1 8 8 8 6 2 2 1 6	•	1	2 1 1		2 1
In 6th to 10th year	1094 65	96 3 130	1 1	18 2 26	3	6	49 1 56	5 5	27 29	2 403 28 475	26 26	15 1 17	78 3 85	42 1 43	325 26 355
Per cent mortality	8.2	24.4	0	25.0	0	0	10.9	0	6.9	9.9	0	6.2	4.9	0	1.2

TABLE VIII.—DEATHS FROM ALL CAUSES RELATED TO TIME OF DEATH AND INDICATION FOR OPERATION

	All indications for operation	Destroyed lung	Destroyed lobe	Residual disease and cavity	Residual disease plus cavity and bronchieclasis	Residual disease and bronchiectasis	Residual disease	Tuberculous bronchiectasis	Tuberculous bronchieclasis and cavity	Tuberculoma or coin lesion	[Other
Died on table. Died less than one week after operation. Died 8 - 60 days. Died 61 days to one year. Died in 2nd year. Died in 3rd year.	16 17 14	0 1 1 1 1	0 1 3 2 1	2 1 5 9 5	0 6 3 2 4	1 7 2 2 2 2	0 3 2 1 0 2	0 0 0 0	0 0 0 0	1 0 0 0	0 0 0 0 1
Died in 4th year Died in 5th year Died in 6 - 10th year Died 11th year or later	$egin{bmatrix} 2\\4\\13 \end{bmatrix}$	0 1 0	0 1 5	0 2 6	0 0	0 0 1	0 0 1	0 0	0 0	1 0 0	0 0
Still alive. Not known. All operations. Per cent mortality (of those traced).	1094 65 1257	12 0 17 29.4	29 3 46 32.6	200 13 246 14.2	137 4 157 10.5	$egin{bmatrix} 224 \\ 12 \\ 254 \\ 7.4 \end{bmatrix}$	30 481 2.0	24 3 27 0	1 0 1 0	8 0 10 20.0	17 0 18 5.6

possibility in mind that the disease may be malignant, tuberculosis being diagnosed only on subsequent pathological examination of the specimen.

The best results were obtained in the so-called residual disease group and the worst results in patients with destroyed lungs and lobes. It is also apparent from this table that the presence of an open cavity at the time of operation had a rather deleterious influence on the eventual result.

This fact becomes even more striking in the data

times that for those in whom no open cavity was demonstrable at the time of operation.

In Table X are listed further details of the fatalities occurring within the first 60 days, previously designated as operative deaths. This table requires little explanation except for the group of 13 patients who succumbed because of hemorrhage into the pleural space postoperatively. Eight of these patients died in the first postoperative week, and the remaining five in the subsequent 53 days.

TABLE IX.—Comparison of Mortality, from all Causes, of Persons with Cavitary and Non-Cavitary Disease at CERTAIN INTERVALS OF TIME AFTER OPERATION

	Number of operations		Dead at end of second year	Dead at end of fifth year	Known dead to December 31, 1959
Destroyed lung or lobe or mention of	400	0= (00()	40 (4004)	F0 (100)	
cavity as an indication		37 (8%)	48 (10%)	56 (12%)	68~(15%)
All other indications	790	19 (2%) .	22~(~3%)	27 (3%)	30 (4%)
All operations	1257	56 (4%)	48 (10%) 22 (3%) 70 (6%)	27 (3%) 83 (7%)	68 (15%) 30 (4%) 98 (8%)

in Table IX, which records the comparative death rates in patients with cavitary and non-cavitary lesions. The death rate in the former is almost four

TABLE X.—Causes of Death Within 60 Days of

Died on operating table:	4
Cardiac arrest 2	
Hemorrhage	
Congenital heart disease (tetralogy of Fallot) 1	
Died in less than one week:	19
Hemorrhage into pleural space	-0
Cor pulmonale 1	
Progression of disease 1	
Pulmonary edema. 5	
Pulmonary infarction	
Transfersion reaction	
Transfusion reaction	
Gastrointestinal hemorrhage,	
cause undetermined 1	
Died from 8 to 60 days after operation:	16
nemorrhage into pleural space 5	
Progression of disease 2	
Empyema or fistula 4	
Pulmonary edema. 1	
Pulmonary infarction 1	
Infactions polynomitis	
Infectious polyneuritis 1 Unknown cause 1	

The source of the bleeding could be determined in only a few of the patients in whom it was due to rupture of the stump of one of the main pulmonary arteries with extremely rapid exsanguination. In the remainder, it was much more insidious, with a slow but constant loss of blood over perhaps several days, a loss that could not be corrected by replacement. In these patients, it was not possible to determine at autopsy the source of the hemorrhage.

Table XI lists the causes of all deaths occurring in the series related to the extent of the surgical procedure. It will be noted that in a considerable proportion death was due to the occurrence of empyema with or without bronchopleural fistula. Thirty-one pneumonectomy patients out of a total of 130, and 44 lobectomy cases out of a total of 475, are dead. This is in marked contrast to the group of wedge resection cases numbering 365, in which there were only four deaths. The other tuberculous and non-tuberculous causes of death are listed in Table XII.

TABLE XI.—Causes of Death Related to Extent and Type of Pulmonary Resection Performed (Includes Nine MULTIPLE OPERATIONS WHICH SHOW AS 18 DEATHS)

	·														
Cause of death	Following all types of operation	Whole or balance of lung	Two lobes and segment	Two lobes	Lobe and two or more segments	Lobe and segment and wedge	Lobe and segment	Lobe and two or more wedges	Lobe and wedge	Lobe	Two or more segments	Segment and wedge	Segment	Two or more wedges	Wedye
Cardiac arrest on operating table Hemorrhage on operating table Hemorrhage into pleural space. Cor pulmonale Progression of disease Empyema or fistula. Other tuberculous. Other non-tuberculous. All deaths.	1 16 9 9 22 19 20	1 1 6 4 3 9 2 5		1 1 3 1 6			1 2 3 6		1 1 2	1 6 4 6 10 9 8		1	1 2 1 4		1 2 1 4

TABLE XII.—Causes of Death Indicated as "Other Tuberculous" and "Other Non-Tuberculous" in Table XI.

Other tuberculous	19
Hemoptysis 1	
Pulmonary edema9	
Pulmonary infarction 5	
Gastrointestinal hemorrhage,	
cause undetermined 1	
Transfusion reaction	
Congenital heart disease	
Cause unknown 1	
Other non-tuberculous	20
Coronary thrombosis	
Cardiac arrest at non-tuberculous operation 1	
Cardiac arrhythmia 1	
Duodenal ulcer 1	
Acute intestinal obstruction	
Pneumonia 5	
Toxic psychosis	
Infectious polyneuritis 1	
Carcinoma 7	
Lung 1	
Breast 1	
Colon 1	
Stomach1	
Site unknown	
Brain tumour 1	

In Table XIII the causes of death are related to the indications for the operations. Probably the most significant point illustrated by this table is the major role that the presence of a cavity plays in those patients who succumbed because of continued activity of their pulmonary tuberculosis as indicated under "progression of disease" and "empyema or fistula". This group numbered 31. Of these, 24 had destroyed lung, destroyed lobe or an open cavity at the time of operation.

In assessing the present status of the survivors, the results were determined two years postoperatively, five years postoperatively and 10 or more years after the date of operation.

The patients in the last-mentioned group had their operations between 1944 and 1949. As shown in Table XIV, they numbered only 58. The overall mortality of this group may seem to be prohibitive, but there may also be cause for satisfaction in the 48% who are well and living a normal life. It must be borne in mind that these cases must be classified, for the most part, as salvage: people for whom no other measure, medical or surgical, was available. Of equal significance is the fact that these patients either had no or, at the most, very inadequate antimicrobial coverage, since streptomycin became available only in 1947 and then in but limited quantities. Moreover, until 1949, it was the only drug available for such cases. Actually, it is rather remarkable that such a large number of seriously ill patients survived what was then a rather dangerous surgical procedure, to be returned

TABLE XIII.—Causes of Death Related to Indication for Pulmonary Resection (Includes Nine Multiple OPERATIONS WHICH SHOW AS 18 DEATHS)

Cause of death	All indications for surgery	Destroyed lung	Destroyed lobe	Residual disease and cavity	Residual disease and tbc. bronchiectasis and cavity	Residual disease and tbc. bronchiectasis	Residual disease	Tuberculous bronchiectasis	Tbc. bronchiectasis and cavity.	Tuberculoma coin lesion	Other
Cardiac arrest on operating table	16	0 0 2	0 0 4	1 0 2	0 0 3	0 1 4	0 0 1	0 0 0	0 0 0	1 0 0	0 0
Cor pulmonale	9 9 22	0 1 0	1 4	5 2 12 6	1 1 3	$\begin{bmatrix} 1\\2\\3\\4 \end{bmatrix}$	0 2 0 3	0 0	0	0 0	0 0
Other tuberculous	19 20 98	0 2 5	3 14	5 33	3 16	3 18	3		0	$\begin{bmatrix} 1\\0\\2 \end{bmatrix}$	1 1

to a useful life with little or no help from the antimicrobial "wonder" drugs.

Among those for whom at least five years have elapsed since the date of operation, the results are, understandably, considerably better. These are the patients who had their operations in the years 1944 to 1954 inclusive, and they number 573. In the years 1950 to 1954, pulmonary resection for tuberculosis was beginning to come into its own and its forerunner, thoracoplasty, was rapidly fading out of the picture. By 1952, all three of the major antituberculosis drugs were being used, not merely during the immediate preoperative and postoperative days, but for a considerable period before and after operation. Operative techniques had improved, and the indications for excisional surgery had considerably broadened. The size of the "greatly improved" group rose to 60%, and the mortality dropped to 10%.

the total therapeutic regimen of tuberculosis. It is felt now that the tuberculous patient is best served if he is treated in a tuberculosis hospital with modified bed rest and the available antimicrobial drugs. In many cases, either complete resolution or replacement of his tuberculous disease with scar tissue will be achieved. However, frequently significant residual lesions will be left. Whether these be in the form of an open cavity, bronchiectasis, residual disease or a combination of two or three such residua, pulmonary resection should be employed to remove the offending lesion.

In this study it will be noted that no mention has been made of the bacillary status of the patient's sputum. The effect of an open cavity and destroyed lobe or lung on the eventual results have been studied. It is evident from this series that patients with such open cavities at the time of operation had a significantly poorer result than those in whom

TABLE XIV.—Status of Patients at End of Certain Periods from Two to Ten Years after Operation

Years	Number of •	$Greatly \ improved$		Improved		Worse		Dead		Alive—status unknown			Not traced	
	operations	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	
10	58 573 1021	344	(48.3) (60.0) (70.8)	94	(5.2) (16.4) (14.6)	0 8 37	$\frac{\%}{(1.4)}$ (3.6)	58	(36.2) (10.1) (6.0)	5 30 14	(8.6) (5.2) (1.4)	1 39 36	(1.7) (6.9) (3.6)	

By the end of 1957, 1021 pulmonary resections for tuberculosis had been performed, and consequently a two-year follow-up was possible on this large series. We are now into what has been called the "modern era" in the overall management of pulmonary tuberculosis, and the indications for pulmonary resections are well standardized. The gratifying improvement in the full recovery rate to 71% and the decrease in the number of fatalities to 6.0% are shown in Table XIV.

DISCUSSION

Several impressions that we have entertained for some time are confirmed by this study. In the years when the first operations in this series were performed, thoracoplasty was the fashion, and deservedly so at that time. Pulmonary resection for tuberculosis was a formidable procedure and was carried out only for so-called thoracoplasty failures and for those patients in whom thoracoplasty was given no chance whatever to succeed. With the advent of antimicrobial therapy and with the development of newer and better surgical techniques for excision, a dramatic change in the surgical approach came about rather quickly. At the same time, the work of Medlar² and others showed that the so-called stable pulmonary tuberculous lesion was not as innocuous as had been thought previously, and in many cases it should be removed. The indications for lung resection were progressively broadened, and the operation assumed the important position it holds today in

the cavity was either closed or inspissated. If it is at all possible, therefore, it would appear to herald the prospect of a much better final result if the patient's cavity can be closed or inspissated and his sputum rendered non-bacillary before he comes to operation. In a considerable proportion of cases this is not feasible, and excisional surgery must be undertaken to prevent an imminent progression of the tuberculous disease. It is suggested that the age of the patient has considerable bearing on the final result. There would appear to be a considerable increase in the incidence of complications and mortality in people over 40. Today it is patients in this group who are coming more frequently to the attention of chest physicians for treatment of tuberculosis. It is probable that the indication for resection of a residual focus with the object of preventing future reactivation is not as pressing for these individuals as it is in much younger people.

Of late years there is a tendency toward conservatism in regard to the amount of lung tissue removed. The operation of pneumonectomy is performed rather infrequently and is usually restricted to those patients who have a useless lung and whose pulmonary function will probably be considerably improved by total excision. At the other extreme, a larger proportion of wedge resections is being undertaken. Other procedures performed with some frequency are right upper lobectomy, superior segmental resection, and removal of the apical posterior segment on the left side.

SUMMARY .

The present status of 1155 patients who underwent 1257 pulmonary resections for tuberculosis has been presented.

No attempt has been made to analyze the immediate postoperative complications. Rather, the outcome in all undergoing excisional surgery for tuberculosis at the Nova Scotia Sanatorium in the years 1944 to 1959 inclusive has been presented.

The results of resection have greatly improved over the years owing to the broader selection of patients for surgery, improvement in operative technique, and most of all to the assistance of antimicrobial therapy. However, the gratifyingly high salvage rate in those patients who were operated upon in the years 1944 to 1949 is impressive. These people were seriously ill before operation and received either no antimicrobial therapy or at the most what would be considered most inadequate drug coverage by today's standards.

As would be expected, the results of excisional surgery in tuberculosis vary inversely with the amount of lung resected.

The presence of cavitary disease and presumed bacillary sputum at the time of operation affects the eventual outcome of resection adversely. If at all possible, prospective candidates for lung excision should not be subjected to operation until an existing lung cavity becomes closed or inspissated and the sputum is negative for tubercle bacilli.

Pulmonary resection has been, is, and for some time to come will continue to be a valuable adjunct in the overall management of patients with pulmonary tuber-

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Studies of Active Immunization Against Enteropathogenic Escherichia Coli

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K NOWLEDGE of the immunology of gastro-enteritis due to enteropathogenic *E. coli* has not progressed in keeping with clinical, epidemiological and bacteriological studies because laboratory animals are not susceptible to these infections of infancy. In humans, there are two distinct groups of E. coli: those that are enteropathogenic and those that are not. As we have shown in a previous publication,13 such a distinction cannot be demonstrated in the chick embryo, the mouse or the monkey. All strains of E. coli can kill these species provided that the bacterial dosage is adequate. This dosage, which varies from one strain to another, bears no relation to the pathogenic power of these micro-organisms for the gastrointestinal tract of infants. Finally, little is known regarding the protective power of E. coli antibodies which are present both in the infections of infancy and in experimental studies in volunteer adults. We have encountered in the literature several reports of studies on gastroenteritis1-7, 9, 10, 14 both in adults and in infants, but these studies emphasize particularly the enteropathogenic potency of certain types of E. coli and are limited to the in vitro detection of the antibodies formed.

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The problem of immunity has thus to date been barely touched upon, and only two attempts at experimental reinfection in humans have been published. In 1953, Hiroki4 reported two cases of experimental infection in infants, one with E. coli strain 055:B5 and the other with strain 0111:B4. In both cases the test dose, administered several days after the stool cultures had become negative, caused gastroenteritis; however, the clinical symptoms were less severe than during the first infection.

In 1956, Wentworth et al.14 attempted without success to reinfect an adult with a dose of E. coli 0127:B8 which had caused gastroenteritis in the same volunteer 32 days previously.

Active immunization of laboratory animals has been attempted by only three groups of investigators. In 1953, Gorzynski and Neter³ noted that non-lethal doses of E. coli 055:B5 injected intraperitoneally protected the mouse against a lethal dose administered 12 to 30 days after the first injection. These authors, however, do not mention by what route the mice were challenged. In 1955, Minck and Lavillaureix⁸ made similar observations on strain 0111:B4. In these studies the mice were immunized intraperitoneally and the test dose was subsequently administred intracerebrally.

In 1954, Frappier and Sonea¹² immunized mice intraperitoneally with filtrates and concentrated washings of strains 055:B5 and 0111:B4. They observed that these mice were partly protected