It should be possible to eradicate completely this variety of ringworm from a community. X-ray epilation should ideally be carried out at the child's first attendance at a dermatological clinic. All contacts in the home and school should be examined with Wood's light.

The importance of *M. canis* ringworm lies in its differentiation from the *M. audouini* variety. X-ray epilation is seldom indicated.

T. sulphureum is likely to cause great anxiety and trouble in the near future, since diagnosis of the non-inflammatory varieties is difficult, and the disease may last for years if untreated. X-ray epilation of the whole scalp is probably the best treatment in most cases.

It is very doubtful whether any procedure can actually shorten the duration of *T. discoides* infections, but symptomatic treatment is appreciated by the patient.

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ATELECTASIS AS A COMPLICATION IN ARTIFICIAL PNEUMOTHORAX

BY

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Since 1920 therapeutic pneumothorax has had a vogue which was certainly excessive at first, but lately the balance has swung the other way and some authorities seem to regard it as a dangerous procedure which should be used only in exceptional cases (Harris *et al.*, 1952; Jackson, 1952; Simmonds *et al.*, 1952).

Young (1949) believes that the cause of this trend of opinion is the fact that the technique seems so easy that it has been carried out by workers inexperienced in the proper selection of cases or in the finer points of its conduct. In the management of artificial pneumothorax (A.P.) cases the physician must be experienced enough to recognize the circumstances that demand the immediate termination of the pneumothorax treatment. Also, to give the best chance to his patients who need the help of an A.P., he must know what "complications" may be disregarded with reasonable safety. One such complication often appearing in an otherwise perfect pneumothorax is the occurrence of an area of atelectasis; and the object of the present investigation is to try to decide whether or not such an occurrence is an indication for suspending this type of collapse therapy.

Some writers have associated atelectasis occurring in an A.P. with such sequelae as progressive tuberculous disease (Rafferty and Shields, 1943), with relapse (Maher-Loughnan, 1950), and with tuberculous pleural effusions and empyemata (Houghton, 1950). On the other hand, Scadding *et al.* (1952), Foster-Carter *et al.* (1952), and Beric Wright (1952) have recorded satisfactory results in small groups of cases with atelectatic lobes or segments, while earlier writers (Brooks, 1938; Erwin, 1939) regarded its occurrence as a favourable event.

At the Cheshire Joint Sanatorium the clinical impression has long been that the occurrence of lobar or segmental atelectasis does not of itself warrant the interruption of the course of an A.P. Adequate material is therefore available at this institution for the numerical examination of the prognostic effects of such atelectasis.

Data

Data for this investigation were obtained from consecutive cases of A.P. induced at the Cheshire Joint Sanatorium between early 1935 and the end of 1945. That all these cases were finally complete was shown by thoroscopic examination as well as by x-ray films. In all cases sputum was either negative throughout or converted to negative by effect of the A.P.

The collecting of data from earlier sanatorium cases has the advantage of allowing a long period of follow-up—of five years in all cases and of ten years in about half of them. Also, in earlier years case selection for therapeutic pneumothorax, and the subsequent management, were less informed than at the present day. We are thus able to collect for assessment groups of cases which would not be seen in current practice, such as those in which there is a persistent cavity in an anatomically complete A.P. One disadvantage of collecting data from earlier cases is the absence of information from routine bronchoscopic examinations.

Where disease in the contralateral lung was regarded as a possible factor in life prognosis the case was excluded—for instance, if on the contralateral side there was an incomplete A.P., or if an attempt at induction of an A.P. had failed on the contralateral side. With regard to contralateral disease, the cases included had (a) no radiological evidence of disease; (b) disease controlled by an uncontroversial A.P.; or (c) disease of moderate extent, healing, and not sufficient to warrant active intervention and not producing a positive sputum.

Disease in the pneumothorax lung, as it appeared prior to A.P. induction, was classified according to its type and its extent.

The type of disease was dealt with under three headings. (1) Cavitated disease: the cavity was at least 5 cm. in diameter, or multiple cavities had a total diameter of at least 5 cm. (2) Exudative disease: the disease was predominantly of a type with a confluent and ground-glass radiographic appearance. (3) Productive disease: cases not classified under (1) or (2) appeared under this heading, so that a variety of radiographic appearances of tuberculous infiltration are included.

The extent of the disease was classified according to the total number of zones in the P.A. x-ray film of the chest which showed infiltration of tuberculous infection. The zones are demarcated by two horizontal lines passing through the second and fourth costal cartilages, thus dividing each lung field into three zones. This classification of disease extent was used by Hartley *et al.* (1935).

Atelectasis is recorded only if it persisted for three months or more. Transient atelectasis following thoracoscopy (Hess, 1951; Penman and Miller, 1952) is thus excluded. In regard to the extent of atelectasis, the cases were classified into four groups—total, lobar, segmental, and nil. Lobar atelectasis includes that of an upper or a lower lobe, there being

no case of a solitary middle-lobe atelectasis. Segmental atelectasis includes cases in which a recognizable segment is collapsed, but cases with more than one atelectatic segment are also included under this heading.

Pleural effusions were recorded only if they were large enough to cover the diaphragm, and if persistent enough to require aspiration. Small or transient effusions are thus excluded. A proportion of these effusions occurred in the later course of the artificial pneumothorax, and some of the data of this complication were obtained from a questionnaire sent to the chest physicians of clinics. Details of survival and duration of the pneumothorax were also available from this source.

Data concerning the occurrence of contralateral spreads, and the activity of disease in the pneumothorax lung, or the degree of re-expansion of the pneumothorax lung after termination of the A.P., were less readily obtained. This part of the investigation entailed use of records and x-ray films at many clinics, and in some cases these records were inadequate for the purpose. For this and other reasons, only 159 cases of the original 266 were available for this part of the inquiry.

Results are tabulated and analysed according to the four groups of atelectasis, and are considered under the following headings: pleural effusions; re-expansion of the A.P. lung, and re-aeration of the atelectatic area; reactivation of disease in the A.P. lung at the termination of pneumothorax; contralateral spread of disease; and mortality rates.

Pleural Effusions

As already stated, only persistent effusions are recorded. They are classified according to whether purulent or non-purulent and according to culture reports into T.B.-negative effusions, T.B.-positive effusions, and empyemata. All the empyemata were positive for the tubercle bacillus. As in the tables below, it is usually convenient to group all three types of effusion together as "persistent effusions," and the last two types together under the heading of "all positive effusions."

A comparatively high death rate has been associated with groups of A.P. cases having persistent pleural effusions (Edwards *et al.*, 1944; Morriss, 1942). Brock *et al.* (1937) believe that in such cases of pleural effusion the active disease in the underlying lung is the detrimental factor rather than the effusion itself. In considering the subject of the prognosis of atelectasis, however, it is obviously important to note any association between atelectasis and pleural effusion.

Houghton (1950) believes atelectasis in the A.P. to be a direct causative factor of T.B.-positive effusions. In his own words, "atelectasis of a grossly diseased lobe with or without cavitation will be followed almost inevitably by pleural effusion, tubercle bacilli will appear in the fluid and sooner or later an empyema will develop." In support of this view he quotes 50 consecutive A.P. cases in which tubercle bacilli had been demonstrated in the pleural fluid—many cases were empyemic. In 86% of these 50 cases a black

lobe or lung was prominent in the x-ray picture. A corresponding group of T.B.-negative effusions did not show such atelectasis, or showed it only as a transitory phenomenon.

In Table I the occurrence of effusions among the cases of the present investigation is shown. The cases having a persistent cavity in the pneumothorax lung are dealt with separately, and effusions of the three types are shown in relation to the extent of atelectasis. Of the 28 cases with T.B.-positive and the 20 cases with T.B.-negative effusions, 25 (90%) and 12 (60%) respectively had some degree of atelectasis. The former finding is similar to the one quoted from Houghton. However, there seems good reason to analyse the matter further before accepting the view that atelectasis is the causative factor of such pleural effusions.

First of all, the persistent cavity group, which includes atelectatic and non-atelectatic cases, has a significantly higher incidence of effusions than the group of cases without persistent cavitation (Table II).

TABLE II.—Persistence of Cavitation and Effusion Incidence

Cases	No.	T.B.-positive Effusions	All Persistent Effusions
Persistent cavity	20	8 (40%)	9 (45%)
No persistent cavity	246	20 (8.1%)	39 (15.8%)
Difference		31.9% ± 11%	29.2% ± 11%

It is therefore justifiable to omit for the time being the cases with persistent cavitation and inspect the incidence of effusion in the remaining cases. Among the latter it is seen (Table III) that a positive correlation exists between incidence of persistent effusions or of T.B.-positive effusions, and extent of atelectasis. A similar correlation is observed between extent of disease by zones in the A.P. lung and the incidence of persistent or T.B.-positive effusions (Table IV).

TABLE III.—Atelectasis and Effusion Incidence (Persistent Cavity Cases Omitted)

Atelectasis	No.	T.B.-positive Effusions	All Persistent Effusions
Total	13	4 (31%)	7 (54%)
Lobar	44	8 (18%)	12 (27%)
Segmental	102	6 (6%)	11 (10.8%)
Nil	87	2 (2.3%)	9 (10.3%)
	246	20 (8.1%)	39 (15.8%)
	χ^2 :	$p < 0.01$	$p < 0.01$

TABLE IV.—Extent of Homolateral Disease and Effusion Incidence (Persistent Cavity Cases Omitted)

Zones of Disease	No.	T.B.-positive Effusions	All Persistent Effusions
1	45	0	1 (2.2%)
2	154	9 (5.8%)	22 (14.2%)
3	47	11 (42.6%)	16 (34%)
	246	20 (8.1%)	39 (15.8%)
	χ^2 :	$p < 0.01$	$p < 0.01$

On the other hand, between the type of initial disease in the pneumothorax lung and the incidence of pleural effusions there is little or no correlation. Indeed, the differences of incidence of effusion among the three types of disease (Table V) are no greater than could occur by chance.

TABLE V.—Type of Homolateral Disease and Effusion Incidence (Persistent Cavity Cases Omitted)

Type of Disease	No.	T.B.-positive Effusions	All Persistent Effusions
Cavitated	85	8 (9.4%)	17 (20%)
Exudative	36	5 (14%)	7 (19.5%)
Productive	125	7 (5.6%)	15 (12%)
	246	20 (8.1%)	39 (15.8%)
	χ^2 :	$p = 0.25$	$p = 0.25$

TABLE I.—Effusions and Atelectasis

Atelectasis	No.	T.B.-negative Effusions	Non-purulent T.B.-positive Effusions	Empyemata
<i>Persistent Cavity Cases</i>				
Total	1	—	—	—
Lobar	8	—	3	1
Segmental	6	—	1	2
Nil	5	1	1	—
	20	1	5	3
<i>Non-cavity Cases</i>				
Total	13	3	4	—
Lobar	44	4	6	2
Segmental	102	5	3	3
Nil	87	7	2	—
	246	19	15	5

It should be noted that the χ^2 test quoted in the tables above does not measure the strength of an association or indicate whether or not a correlation is statistically significant. It serves to show, however, where differences are no greater than might occur by chance.

The findings in Table V seem to disagree with the views of Rafferty (1947), who states that there is a higher incidence of pleural effusions where the pneumothorax lung originally showed pneumonic tuberculosis or giant cavitation.

The extent of the initial disease and the extent of atelectasis are both correlated with the incidence of pleural effusions. That the first-named two variables are themselves associated is demonstrated in Table VI. The question therefore arises, Which of the two variables is primarily associated with the occurrence of pleural effusion?

TABLE VI.—*Distribution of Extent of Disease and of Atelectasis (Persistent Cavity Cases Omitted)*

Atelectasis Extent	One Zone Infiltrated	Two Zones Infiltrated	Three Zones Infiltrated
Total	0	4	9
Lobar	1	28	15
Segmental	16	71	15
Nil	28	51	8
	45	154	47

It should be possible to deduce the answer, given sufficient cases. The cases under consideration should be grouped according to the extent of atelectasis, and each such group should be examined to find if the incidence of effusion is still proportional to the extent of the disease by zones and vice versa. With the present number of cases the best that can be done is to analyse the subgroups containing the greatest numbers—that is, "segmental atelectasis" (Table VII) and "two zones of disease" (Table VIII)—for the incidence of persistent effusions.

TABLE VII.—*Incidence of Effusion Related to Extent of Disease (Cases with Segmental Atelectasis Only)*

	Extent of Disease in Zones			Total
	1	2	3	
Incidence of persistent effusions	0 (16)	8.5% (71)	33.3% (15)	10.8% (102)
	$\chi^2: p < 0.01$			

Table VII demonstrates a positive correlation between effusion incidence and extent of disease, but in Table VIII (with a larger number of cases included) there seems to be no association between effusion incidence and degree of

TABLE VIII.—*Incidence of Effusion Related to Degree of Atelectasis (154 Cases with Two Zones of Disease Only)*

	Degree of Atelectasis				Total Incidence
	Nil	Segmental	Lobar	Total	
Incidence of persistent effusions	15.7% (51)	8.5% (71)	21.4% (28)	50% (4)	14.3% (154)

atelectasis. This analysis, so far as it goes, suggests that extent of initial disease in the pneumothorax lung is the primary factor in the causation of effusions rather than atelectasis *per se*.

It should be remembered that the classification of the extent of disease in a lung according to the number of zones seen to be infiltrated in a P.A. x-ray film is not an exact method. No allowance is made for the density of involvement of each zone.

Cuthbert and Nagley's (1948) description of the radiological "black lobe" when it is seen at thoracoscopy is of a mixture of collapsed and aerating tissue. The pathological finding associated with this x-ray appearance was of multiple small foci of parenchymal and bronchiolar infection. To

produce the homogeneous radiological appearance of the "atelectatic" lobe or segment, such an infiltration would be expected to be dense in character within the related lobe or segment.

Erwin (1939) notes that lobes which collapse in an A.P. and fail to expand early are extensively diseased ones; and Morland and Price Thomas (1952) state that when atelectasis appears in an A.P. the lobe or segment so affected is usually the part of the lung most seriously diseased.

The extent of the disease as seen in a P.A. film is one factor in the incidence of pleural effusions, and it is logical to assume that the density of infiltration might also contribute to its causation. Both extent and density of infiltration are apparently associated with the occurrence of atelectasis in a pneumothorax. An incidence of effusions in proportion to the extent of atelectasis in the A.P. (Maher-Loughnan, 1950; Farquharson, 1951) may well be accounted for by the extent and density of parenchymatous infiltration initially present in the lung.

Re-expansion of the Pneumothorax Lung

Re-expansion of the pneumothorax lung was noted from its radiological appearance at least one year after cessation of refills. The appearance of the lung and also of the adjacent structures—diaphragm, chest wall, and mediastinal organs—was then observed. Cases were classified into three groups. (1) Full re-expansion. The lung appeared expanded and normal apart from healed disease; no atelectasis was apparent; and there was no displacement of adjacent structures. (2) Incomplete re-expansion. This group included cases in which the lung itself was not fully expanded—commonly an apical space remained. Also included are a few cases in which the lung was expanded except for a persistent atelectatic lobe or segment. Cases in which the lung seemed to be expanded but in which moderate displacement of the mediastinum or other chest structures occurred also appear in this group. (3) Unexpandable lung. In this group either the lung failed appreciably to re-expand and a dead space remained or there was gross displacement of mediastinal structures and contraction of the chest wall and diaphragm.

Of the original 20 in the persistent cavity group and the 246 in the non-cavity group, only 3 of the former and 156 of the latter are available by which to assess re-expansion. These are the numbers of cases which can be followed up radiologically until at least one year after termination of the pneumothorax. Of the 246 cases, 90 are thus excluded for various reasons—A.P.s not abandoned at the time of assessment, adequate records not available, patients moved to inaccessible areas, etc. That the 156 cases are, practically speaking, an "unselected" sample of the original consecutive group of cases is, however, indicated by the fact that the incidence of mortality and of pleural effusion occurs at approximately the same rates as in the original group of 246.

Only six cases which left the sanatorium with a total atelectasis and only three that were discharged with persistent cavitation in the A.P. have been followed up. There was no case with a full re-expansion among these nine, and it is thought reasonable to consider them separately from the main group of 150 cases.

Among these 150 cases a full re-expansion of the A.P. lung occurred in approximately half, while an unexpandable lung was seen in 10%. The distribution of expansion in relation to atelectasis is seen in Table IX.

TABLE IX.—*Re-expansion and Atelectasis (Persistent Cavity and Total Atelectasis Cases Excluded)*

Atelectasis	Total	Full Re-expansion	Partial Re-expansion	No Re-expansion
Lobar	33	15 (45%)	15	3 (9%)
Segmental	63	31 (50%)	23	9 (14%)
Nil	54	32 (63%)	19	3 (6%)
	150	78	57	15

Table IX shows that a diminished proportion of full re-expansion occurs in relation to the extent of atelectasis. On the other hand, atelectasis is not associated with unexpandable lung.

TABLE X.—*Re-expansion According to Effusion Present (Persistent Cavity and Total Atelectasis Cases Excluded)*

Pleural Effusion	Total Cases	Full Re-expansion	No Re-expansion
T.B.-positive	12	1 (8%)	5 (42%)
T.B.-negative	11	4 (36%)	2 (18%)
No effusion	127	73 (57%)	8 (6%)
	150	78	15
	χ^2 :	$p < 0.01$	$p < 0.01$

Two factors which could be expected to restrict the proportion of cases showing full re-expansion in a group of atelectasis cases (Jackson, 1952), as compared with a group with no atelectasis, are: (a) persistence of atelectatic lobe or segment; and (b) a higher incidence of pleural effusions which accompany (though, as previously reasoned, are not caused by) atelectasis.

A lower incidence of full re-expansion among cases having effusions, particularly effusions positive for tubercle bacilli, is shown in Table X.

The importance of effusion, especially empyemata, in hindering lung re-expansion is well known, and has been mentioned, among others, by Mitchell (1951) and Heaton and Ogden (1950).

Persistence of an atelectatic lobe was seen in only two of the 150 cases and of an atelectatic segment in only four cases. So that persistent atelectasis is not here a factor of any great importance in limiting the proportion of cases having a full re-expansion. Incidentally these six cases were not associated with any untoward final result. Erwin (1939) reports that the few lobes which fail to re-expand are always extensively diseased, and permanent atelectasis is to be regarded as a selective collapse maintained automatically; this coincides with my own impression of these six cases.

The duration of the pneumothorax has been shown (Heaton and Ogden, 1950; Mitchell, 1951) to influence pleural thickening, and therefore lung re-expansion. It is worthy of note that 11 out of the 15 cases of unexpandable lung had had an A.P. for over six years. In fact, all of the unexpandable lung cases had either an over-prolonged A.P. or a T.B.-positive pleural effusion, or both. This suggests that pleural thickening is the cause of this undesirable sequel—which is the view of Rafferty (1947)—rather than a possible bronchial factor (Farber, 1942; Mitchell, 1951).

Duration of the A.P. in the cases of this investigation has a "chance distribution," being largely dependent upon the preference of the various physicians working at 15 different clinics.

It may be that a bronchial factor limits re-expansion in the total-atelectasis group, for in four out of six such cases followed up a persisting partial atelectasis was the reason for failure of full expansion. The other two cases exhibited an unexpandable lung. Of the persistent-cavity group only three cases were followed up completely, and these showed partial re-expansion.

Groups of cases with lobar or segmental atelectasis (with no persistent cavitation) may therefore be expected to have a smaller proportion of cases exhibiting a complete re-expansion. This is chiefly on account of the incidence of pleural effusions in such groups. It has already been reasoned that the extent and density of the original lung disease, and not the atelectasis itself, is the underlying factor in effusion incidence.

Reactivation of Disease

The occurrence of active tuberculous disease in the re-expanded pneumothorax lung was investigated in the 156 cases without persistent cavitation which were followed up until one year after the termination of pneumothorax.

Activity of disease was determined by sputum reports and other clinical evidence, as well as by the radiological appearance of the re-expanded lung. Three out of the six cases with total atelectasis showed reactivation. The remaining 150 cases are grouped separately, and in Table XI the in-

TABLE XI.—*Reactivation and A.P. Duration (Total Atelectasis Cases Excluded)*

A.P. Duration	Cases	Reactivation Cases
Less than 1 year	5	4 (80%)
1 to 2 years	16	1 (6.2%)
2 to 3 "	14	1 (7.3%)
3 or more years	115	9 (7.8%)

cidence of reactivation is shown according to the duration in years of the pneumothorax. It is apparent that the incidence of reactivation in these cases is independent of A.P. duration if those of under one year are first excluded. For this reason, in examining the incidence of reactivation in relation to lobar and segmental atelectasis, cases in which the A.P. is of longer duration than one year are grouped together (Table XII). It is apparent that there is no association between lobar and segmental atelectasis and the incidence of reactivation.

TABLE XII.—*Incidence of Reactivation According to Atelectasis (Total Atelectasis Cases and Cases with A.P. Duration Under One Year Excluded)*

Atelectasis	Cases	Cases with Reactivation
Lobar	32	3 (9%)
Segmental	60	4 (6.6%)
Nil	53	4 (7.5%)
	145	11 (7.6%)

It is worth noting that the total incidence of reactivation is of the same order as that found by some other observers of A.P. series—Potter (1942) gives 7½%, Morriss (1942) 6%, Aycock and Keller (1942) 5½%, and Hurst and Schwartz (1942) 10%.

In the persistent-cavity group there is insufficient data for consideration from the point of view of reactivation or of contralateral spread of disease.

Contralateral Spread

The occurrence of a bronchogenic spread of disease into the contralateral lung in A.P. cases is given a varying incidence by different observers. Potter (1942), for instance, noted an incidence of 6%, while Morriss (1942) found it in 30% of his cases. In the present 156 cases, followed up in detail, the total incidence seems to be 12%. How this is distributed in relation to atelectasis is shown in Table XIII.

TABLE XIII.—*Incidence of Contralateral Spread and Atelectasis*

Atelectasis	Total Cases	Cases with Spreads
Total	6	2 (33%)
Lobar	34	2 (6%)
Segmental	62	9 (14.5%)
Nil	54	5 (9%)
	156	18 (11.5%)

With the possible exception of the cases with total atelectasis, the number of which is too small for assessment, the incidence of contralateral spread is not associated with atelectasis (Table XIII).

Mortality Rates

Cedric Shaw (1933) discusses prognosis in artificial pneumothorax cases and says, "The one real ponderable in pulmonary tuberculosis is mortality." But to each death from tuberculosis, sociological and immunological as well as clinical factors make their contribution. Deductions therefore cannot be made from differences in mortality rates

between one group of tuberculous subjects and another unless such differences are obvious and significant. In Table XIV such a significant difference in mortality rates is seen when the cases with and without persistent cavitation are compared.

TABLE XIV.—*Mortality Rates in Relation to Persistence of Cavitation*

Cases	No. at Risk, 5 Years	Dead at 5 Years	No. at Risk, 10 Years	Dead at 10 Years
Persistent cavity . .	20	8 (40%)	13	11 (85%)
No persistent cavity	246	13 (5.25%)	122	19 (15.6%)
Difference . .		34.75%±11%		69.4%±11%

Farquharson's (1951) results of survival among A.P. cases with atelectasis are in accordance with those of Table XIV. Of 25 cases with cavitated and 75 cases with non-cavitated atelectasis, she reports 19 (76%) and 13 (17.3%) respectively as ill or dead. Also, among the good A.P. cases in the series of Foster-Carter *et al.* (1952) 7 out of 10 with persistent cavitation died within eight years.

In non-cavitated atelectatic cases, evidence of a mortality rate in relation to the extent of atelectasis might well be expected. The association between the extent of atelectasis and that of disease by zones has already been demonstrated (Table VI); and a remarkable correlation between life expectation and disease extent by zones has been demonstrated by Hartley *et al.* (1935) and more recently by Foster-Carter *et al.* (1952). The latter investigators show that the law "Expectation of survival in pulmonary tuberculosis varies inversely as the radiological extent of the disease" applies equally to groups of collapse or non-collapse cases.

In fact, there seems to be a slight trend of association between extent of atelectasis and mortality rates (Table XV). So small a trend, however, argues against atelectasis *per se* being a factor in life prognosis, having regard to the influential factor of disease extent by zones.

TABLE XV.—*Mortality Rates in Relation to Atelectasis (Persistent Cavity Cases Omitted)*

	Atelectasis			
	Total	Lobar	Segmental	Nil
Dead in 5 years . .	15.4% (13)	6.8% (44)	5.9% (102)	2.3% (87)
" " 10 " . .	28.6% (7)	18.5% (27)	14.3% (49)	12.8% (39)

The figures in parentheses show the number of cases followed up.

Foster-Carter *et al.* also note the mortality in 45 of their A.P. cases with lobar or segmental atelectasis but no persistent cavitation. The survival rate in this group was exactly the same as that of the group of A.P.s as a whole.

Discussion

In the group of cases having persistent cavitation in the pneumothorax lung, the comparatively high rates of death and incidence of pleural effusions are striking. It is instructive to note that these mortality and effusion rates are quite similar to those reported in some series of pneumothoraces in which there was demonstrable endobronchial tuberculosis (Chamberlain and Gordon, 1942; Tuttle *et al.*, 1942; Rafferty and Shields, 1943). Most of the cases of the present investigation were treated before routine bronchoscopy became available, but these findings suggest that where there is persistent cavitation in a pneumothorax lung there is concomitant endobronchial tuberculosis.

On the other hand, in the group without persistent cavitation, judging by the course and prognosis, the presence of lobar or segmental atelectasis would not appear to indicate an underlying endobronchial disease. The prognosis regarding life and the occurrence of effusions, as well as the incidence of contralateral spread and ipsilateral reactivation of disease, are no worse than among cases with no atelectasis.

The small number of cases with total atelectasis, however, seem to share the grave prognosis of the persistent-cavity group.

As a result of the work of Coryllos (1933) atelectasis in adult pulmonary tuberculosis was for a long period believed to be synonymous with endobronchial tuberculosis (Pinner, 1945). More recently, alternative mechanisms of lobar and segmental atelectasis have been described—for example, by Cuthbert and Nagley (1948) and Coello and Nagley (1948). According to these writers the aetiology of atelectasis (as defined in the present investigation) can lie peripheral to the major bronchi. Moreover, observance of the recognized tenets in prescribing A.P. therapy, such as withholding it in the presence of "hot" disease, of a "wheeze," or of a tension cavity, will serve to avoid many cases in which tuberculous bronchitis might be present. The fact of sputum conversion by the A.P. also serves to exclude from this series cases of endobronchial tuberculosis (Davies, 1943).

Lobar and segmental atelectasis may thus be observed radiologically in the pneumothorax lung in the absence of endobronchial tuberculosis, and in such cases its occurrence seems to be a benign circumstance.

Summary

Consecutive anatomically complete A.P. cases with sputum conversion were followed up for at least five years. They were grouped according to the presence of persistent cavitation (20 cases) and, in those without persistent cavitation (246 cases), according to the presence of total, lobar, segmental, or no atelectasis in the A.P. lung.

Cases with persistent cavitation showed significantly higher mortality rates and incidence of pleural effusions than the remaining group.

Cases without persistent cavitation showed an incidence of pleural effusion which was in proportion to the extent of atelectasis. There is evidence, however, that this was because of the concomitant extent of initial disease in the pneumothorax lung rather than a result of atelectasis *per se*.

In 156 of the cases without persistent cavitation it was possible to evaluate the incidence of contralateral spreads, of disease reactivation in the A.P. lung, and the completeness of re-expansion after termination of the A.P.

The great majority of atelectatic lobes and segments (excluding cases with total atelectasis) re-aerated at the termination of the A.P. Full re-expansion depended largely on whether or not pleural effusion had been present.

If cases with total atelectasis are excluded there was no connexion between the presence of atelectasis and the occurrence of contralateral spreads or the occurrence of disease reactivation in the A.P. lung.

Mortality rates in the group with no persistent cavitation showed no significant relationship with the occurrence of lobar or segmental atelectasis.

In the light of these findings, alternative aetiologies of atelectasis in a pneumothorax lung are discussed.

It is concluded that the occurrence of persistent cavitation or of total atelectasis in an A.P. lung carries a grave prognosis. The occurrence of lobar or segmental atelectasis, however, does not, of itself, appear to worsen prognosis.

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FATAL CASE OF MARROW APLASIA AFTER TREATMENT WITH CARBIMAZOLE

THE EFFECT OF A.C.T.H.

BY

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Carbimazole ("neo-mercazole"; 2-carbethoxythio-1-methylglyoxaline) must now be added to the long list of drugs that may cause marrow aplasia with depression of all the blood-forming elements.

The incidence of marrow depression due to anti-thyroid drugs is relatively low and is still decreasing as less toxic preparations become available. A report on the treatment of 150 patients with carbimazole by Doniach (1953) stresses the absence of any toxic effects in her cases, and only mild toxic reactions were found to follow treatment of 14 patients with this drug by Lawson and Barry (1951). Poate (1953), in a survey of nine cases, states that carbimazole in therapeutic doses does not interfere with the leucocytes. In a recent study on the clinical effects and toxic reactions of carbimazole, Bartels (1953) found that 3 of his 52 patients treated with this drug developed toxic manifestations. Two of these were skin reactions, the third had agranulocytosis, which however, cleared up within 14 days after discontinuation of the drug.

Rosenbaum and Reveno (1953) reported a case of agranulocytosis and toxic hepatitis secondary to methimazole ("mercazole"), the forerunner of carbimazole, and referred to two instances of agranulocytosis due to this drug (Croke and Berry, 1952; Specht and Boehme, 1952). In the experience of Davidson (1953), who discusses the use of methimazole in 44 patients, this drug is definitely less toxic than methylthiouracil, and, although slightly more toxic than propylthiouracil, the incidence of severe toxic reactions is of the same order of magnitude as with the latter drug. The overall incidence of toxic reactions with methimazole is given by various workers as 4.5–6%, that of agranulocytosis as 0.15%.

The following case is, we believe, the first example of a fatal marrow aplasia following the use of carbimazole.

Clinical History

A married woman aged 23 was admitted to hospital on June 8, 1953, suffering from severe thyrotoxicosis. Her B.M.R. was 74%. As she had suffered from extensive bilateral bronchiectasis for several years, surgical treatment for her thyrotoxicosis was considered undesirable, and she was put on carbimazole, 10 mg. three times a day, on June 19. She was discharged from hospital a fortnight later and continued as an out-patient with carbimazole in the same dosage as her sole medication. When seen a month after discharge her thyrotoxicosis was under control and she felt much better.

On August 12, just under eight weeks after beginning carbimazole she noticed red patches on her skin and was coughing up more blood from her bronchiectatic cavities than ever before. The drug was discontinued and she was admitted to hospital. Purpuric haemorrhages were found over most of her body and on her mucous membranes. There was no soreness of her throat, but she had a pyrexia of between 101 and 103° F. (38.3 and 39.4° C.). Hess's test was strongly positive. A blood count on the day of admission showed: haemoglobin, 64%; red cells, 4,110,000; white cells, 4,000, with a normal differential count; platelets, 61,000; bleeding and clotting times, normal.

Four days later her haemoglobin had fallen to 54%, her white count to 1,000 cells with 29% polymorphs, and her platelets to 25,000. She was transfused with 2 pints (1,140 ml.) of fresh blood. Her bone marrow taken at this time showed marked agranulocytosis and only one megakaryocyte in three films. Electrophoretic examination of the serum, both before and after the first transfusion, failed to reveal the presence of any α_2 -globulin such as may be present in certain cases of purpura (Bernfeld and Stefanini, 1951).

Treatment directed to the control of infection consisted of penicillin for one week, which was then replaced by aureomycin, 500 mg. six-hourly, and this was continued throughout the rest of her illness. She was given approximately 2 pints (1,140 ml.) of fresh blood at weekly intervals for the next eight weeks.

Cortisone was begun on August 23, 11 days after the onset of purpura, the initial dose being 100 mg. six-hourly, followed on the next and subsequent days by 50 mg. six-hourly. As she made no detectable response the cortisone was replaced by adrenocorticotrophic hormone (A.C.T.H.) with a dosage of 40 mg. six-hourly. After starting cortisone the patient's condition was reasonably satisfactory and her temperature settled on aureomycin, but she continued to get crops of petechiae, although Hess's test had become negative before cortisone was started. Her blood picture, which was examined daily, remained unchanged. The platelets were virtually absent, her haemoglobin was maintained in the region of 50% with transfusions, and her white cells remained round about 1,000, with 20 to 30% polymorphs.