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BRONCHIAL INFECTION AND B.S.R. IN
ASTHMA WITH A DESCRIPTION OF A METHOD
FOR STERILE REMOVAL OF BRONCHIAL
SECRETION

By

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In the treatment of asthma it is of value to know whether or not bronchial infection exists and usually this has been investigated by bacteriological examination of the sputum. In some cases the samples of sputum have been rinsed to eliminate mouth and pharyngeal bacteria, as described by Mulder (1937). With this treatment Mulder has especially succeeded in showing the significance of hemophilus influenzae as the cause of acute as well as of chronic bronchitis. May (1953) has recently stated, that if in cases of chronic bronchitis samples are taken from different parts of the sputum, growth of different bacteria will be found in each. By studying the effect of chemotherapy on bacteria in sputum, the appearance of the sputum and the patient's condition, May saw that hemophilus influenzae and pneumococci especially play an important causal rôle in chronic bronchitis. Despite the existence of the above indirect methods to determine bronchial infection, we have considered a direct method desirable to verify the presence of bacteria in bronchial secretion.

In this investigation we have compared the bacteria in

sputum with the various ways in which the bronchial secretion was collected, both in direct tests and by means of culture. Two methods have principally been employed to obtain the secretion, by bronchoscopy in local anaesthesia and by introducing a sterile catheter through a tracheal tube after intravenous narcosis with Evipan and Scoline. The results of a series using the former method were reported in brief in a preliminary publication in 1953. This paper includes a more complete account of these as well as the results of cultivations of bronchial secretion from asthmatic patients, when the secretion was collected in accordance with the latter method, which will be more fully described.

METHODS

Bronchoscopy: This was performed in the usual manner and, as a rule, only Phenemal was administered as pretreatment. The bronchial specimens were collected with the aid of a special irrigation—suction device. The instrument is passed down the bronchoscope and bronchial secretion is sucked-up into a closed sterile container. The samples were immediately sent for cultivation. The bronchoscopy took place at the Ear, Nose and Throat Clinic of the Lund University Hospital and we tender our thanks to the medical staff for their help.

The sputum samples were generally taken the same morning prior to the collection of the bronchial secretion, direct in sterile tubes.

Catheterization through a tracheal tube was done fasting. For a few days before the secretion was sucked up, the patients were given Antasten, one tablet three times daily, and immediately preceding the anaesthesia 3 ml adrenalin were administered subcutaneously. Dosage with Evipan-Natrium (Bayer) and Scoline (Allen & Hanbury, Ltd.), followed. The samples were then sucked-up through a sterile catheter that had been introduced through the rubber tube. The catheter was attached to a sterile syringe which contained 1–2 ml saline for irrigation of the bronchial tree. When as much

secretion as possible had been collected, the catheter was drawn up with the aid of a pair of sterile tweezers and its contents evacuated into a sterile tube. Immediately afterwards a new catheter attached to a glass container connected with an electric suction device was lowered down the tracheal tube.

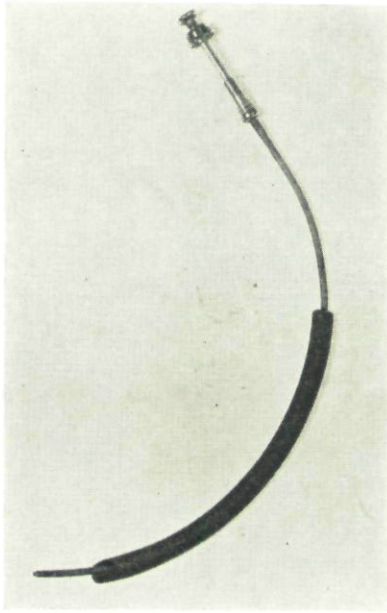


Fig. 1.

All appliances were sterile. By this means the bronchial secretion was sucked-up direct into the container, and the catheter and rubber tubing were closed with clips. Two samples of secretion, independent of each other were thus obtained. Cultivation was performed without delay.

Fig. 1 shows how the catheter lies in the tracheal tube which must be lowered without contamination of the upper end. The catheter, that had been kept in a box, is passed down with tweezers, and all articles are sterile. The bend of the tracheal tube prevents the catheter from contacting the lower orifice of the tube, which may have been polluted in its

passage through the larynx. The control material from persons with healthy lungs reveals that the samples of bronchial secretion are sterile in 90 % of the cases. This would seem to imply that an infection of the trachea with bacteria from pharynx or larynx must thus be of rare occurrence and involves no hindrance to the method's fitness for use. Roentgen control revealed the point of the catheter lying either in the lower part of the trachea or in the larger bronchi.

The removal of the bronchial secretion was only performed when the asthmatic condition was fairly calm, and there were no complications worthy of mention. Only once did a moderate bronchospasm develop, but after the administration of a small dose of ether with the usual narcosis, the patient was relieved. The investigation caused the patients little discomfort whereas many suffered when undergoing bronchoscopy. All removals under anaesthesia were made at the narcosis department.

After dilution in placenta broth 1 : 10, 1 : 100 and 1 : 1000, specimens of sputum and the sucked-up material from the bronchi were homogenized by repeated suction into a pipette. The dilution was made partly to better distinguish the different kinds of bacteria and partly to obtain an approximate estimation of the quantity of bacteria. The inoculation was made by a standard platinum loop on blood-plates, chocolate plates, sabourand and in anaerobic tubes.

All the samples were gram-stained and observed microscopically direct. After 24 hours inoculation, reading, and in certain cases isolation and drug-resistance tests were performed.

Differential staining of leucocytes from the sputum and secretion also took place.

RESULTS

1. *Bronchoscopic examination of asthmatic patients.*

The asthmatic patients treated with bronchoscopy are shown in Table 1, as also are their ages, BSR and reactions

TABLE 1

Initials and age	Samp. no.	Date of samp. of sput. + bronch. secr.	B. S. R.	Growth in bronch. secre. + or —	Skin tests: at least one pos. = + Skin tests: all neg. = —
A.E. 36	1	20. 3.52	5/12 ¹	—	+
E.N. 49	2	5. 3.52	5/13	+	+
M.N. 50	3	13. 7.51	5/	+	—
N.A. 58	4	26. 5.52	7/16	+	+
B.O. 36	{ 5	7. 2.52	2/5	+	+
" "		10. 4.52	2/5	+	+
A.A. 48	7	2. 4.52	58	+	—
N.L. 55	{ 8	2. 4.52	58/82	+	+
" "		2. 5.52	70/97	+	+
A-S.R. 46	10	24. 3.52	78/115	+	—
L.L. 50	11	20.10.52	10/28	+	+
N.J. 56	12	7. 4.52	3/5	+	+
A.B. 51	{ 13	24. 3.52	8/20	+	+
" "		3. 9.51	13/36	+	+
J.E. 18	15	21. 4.53	2/5	—	+
A.L. 61	16	10. 1.52	15/40	—	—
I.H. 65	17	19. 2.52	31/49	—	+
A.K. 58	18	10. 4.52	36/66	—	+
K.T. 18	{ 19	14.11.51	5/17	+	+
" "		29.11.51	3/6	+	+
G.P. 57	{ 21	26. 9.52	20/43	+	—
" "		29.11.51	23/43	+	—
G.S. 46	23	30. 9.52	2/6	+	+

¹ The blood sedimentation rate was 5 mm in the first hour and 12 in the second.

positive or negative, to skin tests. In this series 18 patients underwent the treatment on 23 occasions.

Table 2 shows which bacteria were found in the sputum and bronchial samples and indicates their resistance. The figures refer to the number the patient in question has in Table 1. For instance, the Figure 2 denotes the patient E.N. in Table 1. In Table 2 it is seen that this patient had alpha and gamma streptococci in the sputum, whereas in the bronchial sample only gram negative rods were observed. Thus there was no coincidence between the sputum and bronchial flora

which is specified in the last column of Table 2 with the indication—, preceded by the patient's number in Table 1 when the cultivation referred to took place, accordingly in this case 2—.

As Table 2 reveals, at the 23 comparative cultivations of sputum and bronchial samples, the same find was obtained on 7 occasions while the remaining 16 showed no coincidence.

Moreover, from Tables 1 and 2 is seen that with the method employed, 5 of 18 patients proved to be free from bronchial infection. When such occurred it consisted of alpha, gamma, plate-haemolyzing streptococci and gram negative rods.

Of the patients in this series 12 had no apparent enhanced BSR (if up to 15 may be included) whereas 6 manifested increase. Of the former, 10 had positive reactions in skin tests (and hence skin allergy), but in the latter group, with similar tests, 3 had positive and 3 negative. Likewise as Table 1 illustrates, in the bronchial secretion of 9 patients in the first group there was growth, but none in the secretion of 3; in the second group 4 had bronchial infection whereas 2 had not.

2. Examination of bacteria in the bronchi of healthy persons when the bronchial secretion was collected by catheterization through a tracheal tube.

This method is suitable for investigating persons with healthy lungs. Unlimited control material can be easily obtained by taking samples from patients about to be operated for something other than a pulmonary disease, and in such cases where the narcosis is to be introduced by Evipan-Natrium and Scoline. Samples collected in this way inform as to the occurrence of bacteria in the bronchi of healthy persons and can be employed as control series in corresponding investigations among asthmatic patients.

Bronchial samples from 20 patients who were to be operated for gallbladder or kidney complaints were investigated.

The patients had no apparent lung disease and no antibiotics had been administered preoperatively.

Of 20 patients with no sign of pulmonary disease culture gave growth in only two. In one of these cases the samples from the bronchial tree gave growth of sarcina—a contamination. In the other case culture gave growth of haemophilus influenzae and of alpha streptococci. The postoperative temperature curve was higher than usual, so that the patient may have had a respiratory tract infection already before the operation. This control-material proves that, normally, bacteria seldom inhabit the bronchi.

3. *Examination of bacteria in the bronchial secretion of asthmatic patients when the secretion was collected by catheterization through a tracheal tube.*

A series of 16 asthmatic patients was examined in the above manner. These patients had received no antibiotics the last few weeks prior to the investigation.

The results of cultures are given in Table 3. Of the 16 patients 12 had sterile bronchi, and 4 had growth.

As Table 3 indicates, both the sucked-up secretion and the rinsing liquid from the bronchi of 9 of the 16 cases were cultured. Similar results were obtained from 7 of the 9. The 2 cases which differed are of interest and therefore deserve to be further described. Culture of the rinsing-liquid in Case V.P. disclosed alpha streptococci and the secretion sucked-up direct gave growth of both alpha and gamma streptococci. The sputum gave alpha streptococci and pneumococci. It may be argued that bacteria vary in different parts of the secretion in the same way May demonstrated that cultures from different parts of the sputum reveal bacterial variants. But it may also be that the living-conditions are better for the bacteria in undiluted bronchial secretion than in rinsing-liquid (NaCl). The rinsing-water of the second case gave no growth, whereas haemophilus influenzae were found in the sucked-up secretion. This may be due to the same cause as was men-

TABLE 3

Initials and age	B. S. R.	Quantity of sputum ml.	¹ Appearance of sputum	Bacterial flora in ²			Neutrophilic leucocytes/ Eosinophilic leucocytes			Diagn. ⁴	Skin test ⁵
				Sputum	Bronc.-rins. liquid.	Sucked up bronc. secr.	Sputum	Bronc.-rins. liquid	Sucked-up bronc. secr.		
V. P. 33 years	9/20	20	mp	α-str. c. pneumoc.	α-str. c.	α-str. c.			56/5	A.	+
J. E. 18 years	3/8	20	s	staph. alb. pneumoc.	o	γ-str. c	9/8 ³		55/11	A.	+
V. S. 49 years	3/5	50-100	smp	α-str. c. staph. aur.	o	o	13/79 26/58	13/86	52/21	A.	+
G. N. 41 years	2/5	30	m	pneumoc. pneumoc.	o		17/14		39/11	A.	±
B. N. 59 years	11/24	40-90	mp	γ-str. c. staph. alb. staph. aur.	o	o	18/73	5/48	74/9	A.	-
S. M. 74 years	3/7	30-40	mp	pneumoc.		o	71/16	8/41		A.	-
B. O. 38 years	6/14	80-180	m(p)	γ-str. c. α-str. c. candida	o	o	39/48	5/86	72/7	A.	±
G. F. 58 years	15/35	100	mp	staph. alb. pneumoc.	o	o	16/13	17/81	56/9	A.	-
N. H. 51 years	2/5	70	p	staph. aur. g-neg. rods, g-neg. rods,	o		0/95		87/0	A.	-
J. J. 58 years	3/8	40	mp	pneumoc. α-str. c. I α-str. c. II	o					A.	-

G. P.	31/55	15-100	mp	pneumoc. staph. aur. I + II	0	haem. infl.	84/13	93/6	57/13	A.	—
58 years				staph. alb. γ-str. c.							
S. G.	34/53	60	mp	γ-str. c. neiss. candida	pneumoc.	pneumoc.	74/25	80/13	74/9	A.	—
33 years				α-str. c. β-str. c.	0	0	65/27 37/55		61/13	A.	—
E. J.	37/54	30	mp	en. c.			93/3		54/2	A. + S.	—
39 years	28/48	80	mp	pneumoc. α-str. c. staph. alb.	0				65/0	A. + S.	—
H. N.	27/66	30-70	mp	α-str. c. pneumoc. neiss.	α-str. c.	α-str. c.	92/4	45/49	71/5	A. + Chol.	—
66 years											
O. N.	21/14	45	mp	pneumoc. α-st. c. staph. alb. neiss.	0		2/97	0/97			—
56 years											

¹ s = serous, m = mucous, p = purulent.

² α-str. c. = α-streptococci (I + II = two different types).

γ-str. c. = γ-streptococci.

pneumoc. = pneumococci.

staph. alb. = staphylococci alb.

staph. aur. = staphylococci aur.

g. neg. rods = gram negative rods.

neiss. = neisseria.

0 = sterile.

³ 9/86 = 9 % neutrophils and 86 % eosinophils in the differential count of the sputum.

⁴ A = asthma, S = sinusitis, Chol. = cholecystopathia.

⁵ + = one or more positive reactions in the skin test.

± = one or more questionable reactions in the skin test.

— = no positive reactions in the skin test.

tioned in the former case, namely, that owing to its sensitiveness, the *haemophilus influenzae* might easily be injured in the common salt solution. From the culture viewpoint, these two cases would seem to indicate the advantage of employing secretion sucked-up direct, when results showed the possibility of thus obtaining more bacterial variants than did culture from bronchial rinsing-water.

None of the bacteria found in 2 of the 4 cases with growth in the bronchial secretion were observed in the corresponding sputum sample.

Ten of the 16 patients in this group had no apparent increase of BSR, but the remaining 6 had. BSR up to, and inclusive of 15, has not been looked upon as apparent increase. It is of interest to note that of the 10 patients with no such increase, only one had growth in the bronchial secretion. Among the 6 with enhancement were 3 whose secretion gave growth.

Table 3 reveals the fact that conclusions cannot be drawn from the appearance of the sputum as to whether or not there is bronchial infection. In all the infected cases there was mucopurulent sputum, but in 10 of the 12 cases without infection the sputum was of the same appearance. Increase of blood-eosinophils was found in 11 of the 14 of the investigated cases. Of the 4 with bronchial infection, 3 had increase of blood-eosinophils. Differential counts of the sputum were made in 13 cases, in 11 of which eosinophils were frequently pronounced. In the differential counts of bronchial secretion or rinsing-liquid in 9 cases, bronchial infection was present in 3. In the remaining 6, eosinophils were preponderant in the secretion. In the 3 cases with infection the neutrophils were most often in excess, even if a marked increase of eosinophils was present. Thus, there is a decided difference in the distribution of white blood corpuscles in the bronchial secretion whether infection exists or not. But it is of importance to point out that even when there is positive proof of a bronchial infection and simultaneous increase of the neutrophilic leucocytes in the secretion, there nevertheless occurs an enhance-

ment of the eosinophilic leucocytes. This indicates that, in all probability allergic factors are of significance, although the skin reaction is negative in tests with the customary antigens. As Table 3 illustrates, the diagnosis of the 16 patients in this series was as follows: Bronchial asthma in 13 cases, bronchial asthma + maxillary sinusitis in 2 and bronchial asthma + cholecystopathia in one.

4. *Some observations of interest in the treatment of patients with bronchial infection.*

Patient S.G. (Table 3) was taken ill in January 1953 with a severe cold and cough, at first accompanied by yellowish green expectoration. After a calmer period, in March, the trouble increased, with wheezing in the chest and difficulty in breathing. This condition went on continuously and was worse at times with colds. For this reason she was taken on 10.9.53 to a hospital and in October 10. was transferred to Lund's Medical Clinic, in a status asthmaticus with a temperature of approximately 38° . Symptomatic treatment, without antibiotics, had a calming effect and the temperature became normal. However, the trouble periodically returned and the sputum continued to be mucopurulent, therefore on Oct. 23. the bronchial secretion was investigated and pneumococci were found to be present (Table 3). Aureomycin was administered from Oct. 24 to Oct. 27 but was exchanged on Oct. 28 for chloromycetin owing to malaise. As the patient was still fairly asthmatic, despite the chloromycetin treatment, on Nov. 10, ACTH was given additionally. The former was discontinued on Nov. 11 and the latter on Dec. 3. A renewed investigation in the middle of December proved the bronchial secretion to be sterile. On Nov. 20, Roentgen had revealed peribronchial changes which, on comparison with earlier roentgenographs were found to have increased in spite of the chloromycetin treatment. New pictures taken Dec. 5 showed that considerable improvement had taken place. Pictures of the nasal cavi-

ties showed varying degrees of swelling in the mucous membrane, but no fluid. Examination at the Ear Department showed the nasal mucous membrane to be typically "allergic".

The conditions of the patient G.P. (Table 3) are similar. The patient was skin-negative and had suffered from asthma 14 years in connection with infections. The last period occurred after an infection and continued for 6 months. On 9.12.53, after the bronchial sample had revealed growth of *haemophilus influenzae*, treatment with chloromycetin began but when during the following days the condition grew worse, ACTH was also administered in doses of 20 U. daily in the beginning, and then less. This happened on Dec. 13 and on Dec. 20 the patient was practically free. The chloromycetin was discontinued on Dec. 28 and ACTH (acton prolongatum, 10 U. per day) on 8.1.54. There was no growth in the bronchial secretion in January 54.

The course was different in the case of patient V. P. (Table 3). She had had asthma for 5 years in connection with colds. Three days prior to admission at the hospital she caught cold and the accompanying asthma developed. Skin tests manifested allergy to dust. Treatment with symptomatica (Quillaja and KJ, adrenaline and theophyllamine) was given. After 10 days the patient was discharged from the hospital, symptom-free. No special treatment for the bronchial infection (alpha and gamma streptococci) was necessary. The patient probably belongs to the not insignificant group of asthmatic patients who are dust-sensitive but where the organism can balance the allergy, until an infection appears. This patient later underwent specific treatment with autodust.

Some patients with bronchial infection thus have very prolonged trouble that becomes enhanced with the administration of antibiotics, but which can be made to disappear with ACTH. In other cases the complaint disappears without special treatment for the infection. The cases in this investigation, which belong to the first group had bronchial infection with pneumococci and *haemophilus influenzae* respectively. They are of interest because, as earlier pointed out by Mulder

and May, these bacteria would seem to be of the greatest causal significance in chronic bronchitis.

TABLE 4

Method	Patient Group	Results of Bacterial culture		Total of investigated patients
		Growth	0 Growth	
Bronchoscopy	Asthma	13	5	18
Catheterization through the tracheal tube	Healthy lungs	2	18	20
	Asthma BSR ≤ 15	1	9	10
	BSR > 15	3	3	6

DISCUSSION

The frequency of bronchial infection found in asthma differs according as to whether it is bronchoscopically collected material that is investigated or sucked-up bronchial secretion in a sterile catheter let down in a tracheal tube. Growth was found in 13 of 18 cases with the former method, but only in 4 of 16 with the latter. This difference between the methods is statistically significant.

It would seem that two causes especially are responsible for this divergence. Firstly it is possible that when locally anaesthetizing the larynx and trachea and lowering the bronchoscope, which in this operation was perforated, bacteria from the oral cavity and pharynx may have followed in their wake. The fact that with this method other bacteria are occasionally found in the secretion than those cultured from the pharynx does not necessarily argue against this assumption since, according to May's investigations, bacteria show an irregular distribution throughout the sputum. The other reason of the quite different bacterial growth in bronchial secretion depending on the method employed, may possibly be that a better sample of the secretion would be obtainable with the

aid of bronchoscopy. In bronchial rinsing as well as in the suction-up of secretion, a sufficient supply of the latter can undoubtedly be collected for an investigation of the secretion by staining, with differential counts of the leucocytes. Therefore at the same time a representative idea of eventual bacteria in the secretion must be counted with in both methods. With the last method special arrangements are indeed necessary in order to form an opinion as to whether the sample is from the lower part of the trachea or upper parts of the greater bronchi, but this should play no rôle as a bronchial infection in asthma would generally seem to be of a diffuse nature. Now and again a Roentgen picture has been taken of the trachea while the suction was in process which enabled the position of the catheter to be exactly shown. It may be argued therefore that the difference in the frequency of bronchial infection in asthma with the two methods, should be due to bacteria introduced from the oral cavity and pharynx, on application of bronchoscopy. Bronchial infection would therefore not seem to be so usual in connection with asthma. In the present series bronchial infection is present in 25 %. If this series were divided into two groups, the one with patients who just before and after the sample-taking had no apparent increase of BSR, and the other with apparent enhanced BSR, one finds (Table 4) that the former group would include 10 patients of whom one had bronchial infection, while the other group would consist of 6 patients with 3 cases of infection. In this series the occurrence of bronchial infection is not more frequent among asthmatic patients with no apparent increase of BSR than among patients with healthy lungs (Table 4). If these two groups are put together (patients with healthy lungs and asthmatic patients with apparent normal BSR) there would be 30 patients of whom 3 had bronchial infection. If comparison is made between this combined group and the one which includes 6 patients (of whom 3 had bronchial infection) with asthma and apparent increase of BSR, there is a fairly good statistic difference between them.

To judge from the material in this investigation asthmatic patients with no apparent increase of BSR have no greater frequency of bronchial infection than have patients with healthy lungs, whereas asthmatic patients with enhanced BSR have.

It is of great interest that with the indirect method of Mulder, Orie and Israels (1953) found in a great investigation including 300 patients that one-third of the asthmatic patients had bronchial infection, which means a percentage of the same magnitude as we have found with a direct method. Furthermore it is of interest that these authors also point out that effective antibiotic treatment of a bacterial purulent bronchitis in asthma may cause severe aggravation of asthmatic complaints.

May also states (1953) that in the treatment of chronic bronchitis with effective antibiotic therapy, the sputum, in many instances, was extremely tenacious and difficult to expectorate. The patients complained of increased dyspnoea and were troubled by their unproductive cough.

In prolonged cases of asthma which are difficult to handle, the method described in this paper would seem to offer much valuable enlightenment in respect to the occurrence of bronchial infection, especially if attention be paid to the composition of the white blood corpuscles in the bronchial secretion.

Furthermore, this method is also applicable in cases where sputum is either scarce or absent. It has therefore been possible to obtain a representative idea from patients with healthy lungs. We have not been able to find any reliable information in the literature, pertinent to the occurrence of bacteria in the trachea and greater bronchi of healthy persons.

SUMMARY

A new method is described whereby a bronchial infection can be identified through the direct culture of bronchial secretion collected by sterile suction.

The method implies catheterization through a tracheal tube under anaesthesia, with Evipan and Scoline. It has proved to be of value in difficult cases of asthma, also, it has not been associated with any complications.

Investigations performed with this method have shown that 90 % of the patients with healthy lungs were sterile in the lower part of the trachea and in the larger bronchi.

Asthmatic patients with no apparent increase of BSR were not found to have bronchial infection more frequently than persons with healthy lungs. Comparison with the two earlier mentioned groups shows that asthmatic patients with enhanced BSR had bronchial infection oftener than had these.

In addition to the direct culture-response, differential counts made from the bronchial secretion collected by sterile suction according to the given method indicate whether an infection exists, and in that case the neutrophilic leucocytes are increased. An almost exclusive eosinophilic finding argues against infection.

It has not been possible to draw any conclusion from the macroscopical appearance of the sputum as to the presence of a bronchial infection.

When suitable antibiotics are administered to asthmatic patients with bronchial infection the asthmatic troubles often become aggravated. In such cases a combination with antibiotics and ACTH is indicated.

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