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STUDIES IN BRONCHIAL ASTHMA

III.

A Comparative Examination between Patients with Endogenous and Exogenous Bronchial Asthma with Respect to Blood Sedimentation Rate.

By

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A considerable part of the literature concerning allergy does not at all or very briefly touch upon blood sedimentation rate (BSR) in bronchial asthma, e.g. *Criep* (1945), *Feinberg* (1946), *Cooke* (1947), *Rackemann* (1951), *Hansel* (1953), *Vaughan* (1954), *Hansen* (1957).

Other authors have considered in somewhat more detail the BSR in asthma and other allergic complaints but common to the literature is, however, the fact that the data as a rule are based on very limited patient material and without detailed account of its composition. The conclusions which can be drawn from the available literature are that BSR is low, normal or only insignificantly increased in uncomplicated asthma and that a rise of BSR means a complication of some kind: *Katz & Leffkowitz* (1928), *Cutler* (1932), *Uffe* (1933), *Ellis* (1935), *Tuft* (1937), *Coke* (1939), *Salén* (1943), *Parsons* (1946), *Livingston* (1948), *Westergren* (1952), *Sheldon et al.* (1953), *Colldahl* (1956).

According to *Unger* (1945) the determination of the BSR in asthma may be important, particularly in older patients with negative or doubtful positive skin tests. An increased BSR would indicate antibiotic treatment.

Urbach (1946) tried by help of BSR to differentiate between infectious and non-infectious asthma; however in 158 cases he did not obtain results uniform enough to permit this approach to be used for differentiating between the two types of asthma.

Henriksen (1951) examined 715 asthma patients, the majority of whom were over 16 years of age. He came to the same conclusion that the BSR could not be used to differentiate between asthma with or without infection.

Westcott & Spain (1933) found in 10 asthma patients without signs of infection that the BSR was normal, while in 10 patients with infective asthma it was 4 times as high as in purely allergic cases.

Schulhof (1933) found in 12 asthma patients that 9 had a sub-normal BSR. He came to the conclusion that not only an increased but also a normal BSR in allergic diseases could be indicative of complicating infection.

Gay (1946) made a comparison between pollen asthma and asthmatic bronchitis. Amongst 32 patients with pollen asthma only 4 had a BSR more than 14 mm/hour, but amongst 44 patients with asthmatic bronchitis 17 had a BSR more than 15 mm/hour. An increased BSR therefore suggested an infection but could not be used for differentiating between the different types of asthma.

Möller & Wahlgren (1933) published different results in 6 patients who had died of asthma. Among other things they found a considerable rise of BSR in 5 of the cases. The authors could not prove the cause in the majority of the cases. They pointed out, however, that the discovery was of interest, because it has been claimed that asthma in general is accompanied by a sub-normal BSR.

Only a few examinations have been carried out with the intention of comparing BSR in a symptom-free interval and when symptoms are present. Thus *Storm van Leeuwen & van Niekerk* (1930) examined 61 men and 24 women during periods free from distress. 56 of the men had a normal BSR and 5 a slightly increased BSR. 21 of the women had a nor-

mal BSR and 3 a slightly increased BSR. The conclusion was that the allergic disposition is usually combined with a normal BSR. Besides 59 of the patients were examined during asthma attacks. Of these only 13 had a normal BSR. In 31 cases it was at least 15 mm. The authors' conclusion was that with severe asthma BSR can be normal but that as a rule it is increased, in most cases depending on chronic bronchitis and bronchiectasis.

Gelfand & Victor (1934) examined BSR in patients with hay fever before and during the hay fever season. They could not find any differences.

Sullivan & Vaughan (1937) found among patients with allergic diseases, which were not more closely specified, that BSR was not pathologically altered whether in distress-free intervals or after provocation tests.

Knott (1939) examined 55 cases with bronchial asthma. Between the attacks the BSR was normal. A rise "suggests a search for an infection in the respiratory tract or warns that an attack is coming".

THE AUTHOR'S INVESTIGATIONS

Normal Values and Classification into Different Groups.

As a rule, the BSR of the hospitalized cases was taken the day after their entry into the hospital and then once a week. In the majority of the hospitalized cases many observations could be made on each patient. In the majority of the out-patients on the other hand, the BSR was noted only once, that is to say on the occasion of the patient's first visit to the hospital¹.

¹ The present investigation includes 748 patients, namely 400 hospitalized and 348 out-patients, all at least 18 years old. With the help of anamnesis, skin tests, and provocation tests the author has shown above that 133 patients (17.9 %) had the type of asthma where allergens of different kinds could be proved to be the cause of the asthma, while in the remaining 615 cases such a cause could not be found. In this work the first group is entitled *exogenous*, and the latter group *endogenous* asthma. See further chapter I.

The BSR was taken and estimated according to Westergren's method with the reading taken after 1 hour. Also it would have been valuable to have readings of BSR after 2 and 24 hours. The examined patients were, however, nursed at the hospital long before any scientific examination of the material had been started and therefore only 1-hour BSR has been observed.

According to Westergren the following normal limits of the BSR are applicable: In men up to 5–10 mm/hour, and in women up to 10–15 mm/hour. He points out, however, that strictly speaking a normal BSR in men should be at most 4–7 mm/hour, and in women at most 8–11 mm/hour. However, it can fairly often be increased without provable cause, for which reason the first mentioned values above can reasonably be used in working up clinical material. These figures apply to persons up to 50 years of age. In persons more than 50 years old the above limit "still for purely practical reasons" might be raised to 15 mm/hour for men and 25 mm/hour for women even although among others *Eckerström* (1949) has shown that merely a higher age in itself does not cause a rise in BSR.

After discussion with Westergren other bases for age classifications and for limits have been used in this investigation, as will be seen below. The material has been divided into two main groups, one where the patients were under 35 years of age, and another where they were more than 35 years old at the time of examination. As a normal value for men under 35 years BSR has been given at the most 5 mm/hour and for women under 35 years at the most 10 mm/hour. For men over 35 years the corresponding limit has been 10 mm/hour and for women over 35 years 20 mm/hour. Further, a classification has been made in this way, that the values in a second group have been noted from the above-stated normal limits to 15 mm/hour, in a third group, from 15 to 35 mm/hour, and in a fourth group more than 35 mm/hour. The age classifications and limits are seen in the tables enclosed.

RESULTS OF THE AUTHORS' INVESTIGATIONS

Hospitalized patients (tables 14 to 15).

As has already been mentioned, these include 400, namely 148 men and 252 women. Of these, 37 men and 28 women had exogenous asthma while 111 men and 224 women had endogenous asthma.

Endogenous Asthma (tables 14 A-14 B).

Of the 111 men with endogenous asthma only 10 were under 35 and 101 more than 35 years old when examined. From table 14 A it is seen that of all the patients 35 (31.5 %) had a normal BSR, 16 (14.4 %) an insignificantly increased BSR and 60 (54.1 %) a definitely increased BSR.

TABLE 14 A
Blood Sedimentation Rate.
Hospitalized Males with Endogenous Asthma.

BSR in 1 hour	Number of patients	Number of patients		
		With fever	With infection only in the respiratory tract	With other illnesses causing a raised BSR
<i>Age of the Patients when examined ≤ 35 years.</i>				
0-5	5			
6-15	3			
16-35	2			
> 35	0			
Total	10			
<i>Age of the Patients when examined > 35 years.</i>				
0-10	30	5	4	
11-15	13	1	1	3
16-35	39	17	11	13
> 35	19	12	8	7
Total	101	35	24	23

TABLE 14 B
Blood Sedimentation Rate.
Hospitalized Females with Exogenous Asthma.

BSR in 1 hour	Number of patients	Number of patients		
		With fever	With infection only in the respiratory tract	With other illnesses causing a raised BSR
<i>Age of the Patients when examined ≤ 35 years.</i>				
0-10	8	1	1	
11-15	6	3	3	1
16-35	14	5	8	4
> 35	4	1	1	1
Total	32	10	13	6
<i>Age of the Patients when examined > 35 years.</i>				
0-20	74	32	15	
21-35	55	25	20	14
> 35	63	46	34	16
Total	192	103	69	30

Of the 224 women with endogenous asthma, only 32 were under 35, and 192 more than 35 years old when examined. Of all these 224 82 (36.6 %) had a normal, 6 (2.7 %) an insignificantly increased, and 136 (60.7 %) a definitely increased BSR (table 14 B).

A raised BSR is found in both the above mentioned age groups.

Exogenous Asthma (tables 15 A-15 B).

Of the 37 hospitalized men with exogenous asthma not less than 27 were under 35 and only 10 over 35 years when examined. Of all 37, 20 (54.1 %) had a normal, 8 (21.6 %) a slightly increased, and 9 (24.3 %) a definitely increased BSR. In these patients with exogenous asthma the increased BSR occurred above all in the age groups over 35 years of age (table 15 A).

Of the hospitalized women with exogenous asthma, 12 were under 35 years and 16 over 35 years at the time of the examination. Of all these 17 (60.7 %) had a normal and 11 (39.3 %) a definitely increased BSR. The increased BSR occurred in both age groups (table 15 B).

TABLE 15 A
Blood Sedimentation Rate.
Hospitalized Males with Exogenous Asthma.

BSR in 1 hour	Number of patients	Number of patients		
		With fever	With infection only in the respiratory tract	With other illnesses causing a raised BSR
<i>Age of the Patients when examined $\leq$ 35 years.</i>				
0-5	17		1	
6-15	6		1	1
16-35	3	1	1	
> 35	1		1	
Total	27	1	4	1
<i>Age of the Patients when examined $>$ 35 years.</i>				
0-10	3	1		
11-15	2			
16-35	2	1	2	
> 35	3	1		1
Total	10	3	2	1

In the material studied there is, accordingly, a large percentage of increased BSR, particularly in cases of endogenous asthma. The question then naturally arises, whether it is possible to show the existence of a larger percentage of infections in the cases of increased BSR than in those of normal BSR and primarily then in the lungs, bronchi or sinuses (respiratory tract). Special columns in the tables 14 and 15 show the number of patients with only such infections and the number of patients with other complications, which have been considered

to be the cause of an increased BSR. The estimate as whether infections in the respiratory tract have existed or not was based on a comparison between hospital records data concerning fever, auscultation of the lungs, X-ray of the lungs and sinuses, otolaryngologic examination, and the character of the expectoration. For this purpose a sputum showing thick yellow clots has been labelled "purulent".

TABLE 15 B
Blood Sedimentation Rate.
Hospitalized Females with Exogenous Asthma.

BSR in 1 hour	Number of patients	Number of patients		
		With fever	With infection only in the respiratory tract	With other illnesses causing a raised BSR
<i>Age of the Patients when examined ≤ 35 years.</i>				
0-10	7	2		
11-15				
16-35	3			3
> 35	2	1		1
Total	12	3		4
<i>Age of the Patients when examined > 35 years.</i>				
0-20	10	1		
21-35	2			2
> 35	4	1	1	2
Total	16	2	1	4

If those cases are excluded that had a raised BSR of other causes than an infection in the respiratory tract, it will be seen that these last-mentioned infections are considered to exist in the following number of the cases: in 11.4 % at a normal BSR and in 37.7 % at an increased BSR in male patients with endogenous asthma; in 19.5 % at a normal BSR and in 62.2 % at an increased BSR in female patients with endogenous

asthma. In cases of exogenous asthma such infections existed in 5 % of the cases of male patients with a normal BSR and in 33.3 % with an increased BSR. The corresponding figures for female patients were 0 % and 33.3 % respectively.

Other indices of an acute and, even more so, of a chronic infection are rises of the anti-streptolysin (AS) and anti-staphylosin titres (ASt). These titres were examined in the majority of patients hospitalized. As titre rises were regarded for AS rates of 200 units or more and for ASt 1.4 units or more.

TABLE 15 C

Percentage Distribution of Raised AS and ASt in 335 Hospitalized Patients with Endogenous Asthma and in 65 Hospitalized Patients with Exogenous Asthma.

		Number of cases	Number of cases with fever	% raised AS and ASt.
Endogenous asthma	≤ 35 years of age	42	10 (23.8 %)	55.3
	> 35 years of age	293	138 (47.1 %)	48.3
Exogenous asthma	≤ 35 years of age	39	4 (10.2 %)	73
	> 35 years of age	26	5 (19.2 %)	45.5
Total		400	157 (39.3 %)	

Table 15 C shows the percentage distribution of increased titres within the two main groups, endogenous and exogenous asthma. Men and women under 35 years of age have been taken together as one group and men and women over 35 as a second group. The table shows that high AS and ASt titres are to be found for 55.3 % of the under-35 cases within the endogenous group and for 48.3 % of the over-35 cases. The corresponding frequency rates within the exogenous group are 73 % and 45.5 % respectively. Consequently, the average rate of increased titres for the whole of the endogenous group is 49.5 %, and for the exogenous one 62.7 %—in other words, fairly similar figures. It is to be noted, however, that one must take into account the influence of the characteristic age

factor implying a lower rate of increase in the titres of old people—a factor demonstrated by *Westergren* (1954, 1956).

The frequency rates in the present investigation do not agree with *Westergren*'s findings. He examined AS and ASt in 202 asthma patients. Only 20.8 % had risen AS titres and 17.9 % risen ASt titres. He considers "that although asthma patients certainly to a great extent must be regarded as "infection sensitive", their resistance to infections, as regards septic conditions more serious in type, on the whole can be deemed good".

Out-Patients (tables 16 to 17).

As has been mentioned above these consist of 140 men and 208 women. Of these 38 men and 30 women had exogenous asthma, while 102 men and 178 women had endogenous asthma.

TABLE 16 A
Blood Sedimentation Rate.
Male Out-patients with Endogenous Asthma.
(data concerning 15 cases missing).

BSR in 1 hour	Number of patients
<i>Age of the Patients when examined $\leq$ 35 years.</i>	
0-5	5
6-15	4
16-35	
> 35	
Total	9

Age of the Patients when examined > 35 years.

0-10	49
11-15	10
16-35	17
> 35	2
Total	78

Endogenous Asthma (tables 16 A–16 B).

Of the 102 men with endogenous asthma, data concerning the BSR are missing in 15 cases. In the remaining 87 cases only 9 patients were at most 35 years old and 78 over 35 years old when first examined. As has already been mentioned, in almost all cases only one BSR has been taken, namely on the occasion of the patient's first visit to the hospital. Such a solitary value is of course a more uncertain basis to draw conclusions on. Of the 87 men 54 (62.1 %) had a normal, 14 (16.1 %) a slightly increased, and 19 (21.8 %) a definitely increased BSR (table 16 A).

Of the 178 women with endogenous asthma, data concerning the BSR are missing in 14 cases. Of the remainder 164, 32 were under 35 years of age, and 132 over 35 years when examined. Of all 164, 108 (65.9 %) had a normal, 6 (3.6 %) a slightly increased, and 50 (30.5 %) a definitely increased BSR (table 16 B).

TABLE 16 B
Blood Sedimentation Rate.
Female Out-patients with Endogenous Asthma.
(data concerning 14 cases missing).

BSR in 1 hour	Number of patients
<i>Age of the Patients when examined $\leq$ 35 years.</i>	
0–10	21
11–15	6
16–35	5
> 35	
Total	32
<i>Age of the Patients when examined > 35 years.</i>	
0–20	87
21–35	28
> 35	17
Total	132

Exogenous Asthma (tables 17 A-17 B).

Of the 38 male out-patients with exogenous asthma data are missing concerning the BSR in 2 cases. Of the remaining 36 patients 23 were under 35 years of age and 13 over 35 years. Of all the cases 29 (80.6 %) had a normal, 3 (8.3 %) a slightly increased, and 4 (11.1 %) a definitely increased BSR (table 17 A).

Of the 30 women with exogenous asthma data are missing in 3 cases. Of the remaining 27 cases 11 were at most 35 years old, and 16 over 35 years. Of all these 27 patients 20 (74.1 %) had a normal, 3 (11.1 %) a slightly increased, and 4 (14.8 %) a definitely increased BSR (table 17 B).

In the out-patients AS and AS_t were not examined, nor the character of the expectoration. Conclusions concerning infections in the respiratory tract can not be drawn in these patients.

TABLE 17 A
Blood Sedimentation Rate.
Male Out-patients with Exogenous Asthma.
(data concerning 2 cases missing).

BSR in 1 hour	Number of patients
<i>Age of the Patients when examined $\leq$ 35 years.</i>	
0-5	18
6-15	2
16-35	2
> 35	1
Total	23
<i>Age of the Patients when examined > 35 years.</i>	
0-10	11
11-15	1
16-35	1
> 35	
Total	13

TABLE 17 B
Blood Sedimentation Rate.
Female Out-patients with Exogenous Asthma.
(data concerning 3 cases missing).

BSR in 1 hour	Number of patients
<i>Age of the Patients when examined $\leq$ 35 years.</i>	
0-10	8
11-15	3
16-35	
> 35	
Total	11
<i>Age of the Patients when examined > 35 years.</i>	
0-20	12
21-35	4
> 35	
Total	16

Account of total Material.

1. This examination concerning the BSR in asthma shows that among the patients examined there was an increase of the same order in a significant number of the cases with *endogenous* asthma. This was especially the case with the hospitalized patients, viz. in 68.5 % of the men and 63.4 % of the women. In the out-patients the corresponding figures were only 37.9 % and 34.1 % respectively. It is not very easy to explain what is the reason for the lack of agreement between the two groups. The comparison between hospitalized and out-patients is of course made more difficult by the fact that only one BSR has been noted in the latter while a number of observations have been made on the former.

2. It appears that even with *exogenous* asthma there was an increase in BSR, but not with the same frequency as for endogenous asthma. Even amongst the exogenous cases there were a greater number of increased BSR amongst the hospital-

ized patients as compared with the out-patients, *viz.* in 45.9 % of the men and 39.3 % of the women in the first-mentioned group, in 19.4 % of the men and 25.9 % of the women in the latter group. The differences between the two groups cannot be explained.

3. It appears that in all the endogenous cases an increased BSR occurred in 52.4 %, but in all the exogenous cases in only 32.8 % of the cases. This difference may *partly* be explained by the fact that there was a higher incidence of infections in the respiratory tract and of other illnesses causing a raised BSR in the endogenous than in the exogenous cases—this concerns the hospitalized patients only. But the difference may perhaps also *partly* be due to the fact that there is really a definite *difference* between *endogenous* and *exogenous* asthma which has been pointed to earlier in connection with the age of onset of the complaint, where it could be shown that patients with exogenous asthma were taken ill at a much earlier age and had a lower age distribution than patients with endogenous asthma.

4. If those cases are excluded that had an increased BSR of other causes than an infection in the respiratory tract, the following results were obtained: an infection in the respiratory tract occurred in all the hospitalized patients with endogenous asthma in 17.4 % (*viz.* 11.4 % of the males and 19.5 % of the females) of the cases with a normal BSR and in 54.1 % (*viz.* 37.7 % of the males and 62.2 % of the females) of the cases with an increased BSR. The corresponding figures for exogenous asthma were 2.7 % (*viz.* 5 % of the males and 0 % of the females) and 33.3 % (*viz.* 33.3 % of the males and 33.3 % of the females). Thus an increased BSR is more suspectable for such an infection than a normal BSR.

SUMMARY

A review of the literature shows that the blood sedimentation rate (BSR) in asthma has either not been considered at all or very briefly in a great part of the literature on allergy.

Amongst the authors who have made somewhat more detailed investigations the general opinion is that as a rule the BSR is low, normal or only insignificantly increased in cases of uncomplicated asthma and that an increase means some complication. Individual authors have also shown that the BSR has been higher with the presence of asthmatic distress than with freedom from distress.

In the author's material 51.1 % showed a normal BSR, viz. 19.3 % males and 31.8 % females, while 48.9 % had an increased BSR, viz. 18.6 % males and 30.3 % females. The increased BSR as a rule was found in patients with endogenous asthma, especially those hospitalized. There was a definite difference between endogenous and exogenous asthma. In the first group 52.4 % had increased BSR and in the latter 32.8 %.

In the hospitalized patients of the present material there are signs that infections occur in a great percentage, not only in cases of endogenous but also in cases of exogenous asthma. Indices of such an infective influence are increased antistreptolysin (AS) and antistaphylosin (AS_t) titres, which were found in 49.5 % of the cases with endogenous asthma and in 62.7 % at exogenous asthma.

The investigation has also shown that in the present material BSR cannot be used to differentiate between asthma with and without infections in the air passages, lungs or sinus. An increased BSR, however, renders such an infection more likely than a normal BSR.

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