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DIMINISHED ENDOGENOUS MORNING EOSINOPENIA
IN BLIND SUBJECTS

By
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The diurnal variations of the circulating eosinophils in man have been well established (Rud, 1947; Fisher & Fisher, 1951; Best & Samter, 1951; Halberg et al., 1951; Donato & Strumia, 1952). The night levels of eosinophils are considerably higher than the day levels. The most characteristic phase of this variation is the morning drop of eosinophils and this phenomenon was termed »endogenous morning eosinopenia« (Halberg, Cohen & Flink, 1951). As in the case of any other biological change, it cannot be expected to occur in every single case, but it exists in normal people as a group phenomenon. These variations are related to adrenocortical activity, as increased excretion of 17-ketosteroids and of neutral reducing lipids after awakening have been reported (Pincus, Romanoff & Carlo, 1948).

The endogenous eosinopenia, which was observed in man as well as in animals, was assumed to be related to the initiation of »daily activities« (Halberg, 1953). But the effect on the morning eosinopenia of factors related to daily activities has not been investigated.

In people with normal sleeping habits, the morning light can be considered as one of the most important factors connected with daily activities. In order to assess its effect, we investigated the endogenous morning eosinopenia in blind people.

METHOD AND MATERIAL

Thirty-six completely blind but otherwise healthy subjects, aged from 9 to 30 years (17 males and 19 females) were investigated. These subjects were permanently institutionalised in a home for blind people. Their period of complete blindness ranged
from one to thirty years. On the morning of the examination, the subjects woke up as usual at 6 a.m. The first sample of blood was taken at 6.30 a.m. Their normal activities were not restricted until 9.30 a.m., when the second sample was taken. Breakfast was served at 7.30 a.m.

As a control group, 33 perfectly healthy student nurses aged 17 to 23 years, who were resident in our Nursing School, were examined under the same conditions, except that their breakfast was served shortly after the first blood examination. Stimulation, other than daily routine, was avoided for all subjects of this investigation. Eosinophil counts on freely flowing capillary blood were performed by the same observer. The Randolph propylene glycol aqueous stain was used (Randolph, 1944). Both sides of a 0.9 c. mm. Levy counting chamber of 0.1 mm. depth were counted and the results averaged.

RESULTS

The mean of the absolute number of circulating eosinophils in the blind subjects was 193.7 and 150.0 at 6.30 a.m. and 9.30 a.m. respectively, while in the control group these values were 165.8 and 100.6 at the same hours.

The results are expressed as per cent change from the 6.30 a.m. to the 9.30 a.m. count, with the value obtained at 6.30 equal to 100 %.

In the group of blind people, 17 out of the 36 subjects examined showed a drop of less than 20 % (or a rise) in circulating eosinophils, while in the

54
Table 1.

<table>
<thead>
<tr>
<th>No. of cases</th>
<th>Mean absolute eosinophil count</th>
<th>Mean change %</th>
<th>Standard error</th>
<th>Standard deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>g10</td>
<td>g10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blind subjects</td>
<td>36</td>
<td>193.7</td>
<td>-15.0</td>
<td>± 7.3</td>
</tr>
<tr>
<td>Normal subjects</td>
<td>33</td>
<td>165.8</td>
<td>-38.3</td>
<td>± 4.0</td>
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</tbody>
</table>

Difference between the two mean changes (%)

23.3

Standard error of difference between the drop in the two groups

8.31

control group only 6 of the 33 subjects examined showed a similar change. The mean per cent drop of the circulating eosinophils between 6.30 and 9.30 a.m. in the blind subjects was 15 ± 7.3; the standard deviation was 43.8. In the group of student nurses, the mean per cent drop was 38.3 ± 4.0; the standard deviation was 22.9 (Fig. 1, Table 1). The standard error of difference between the drop in the circulating eosinophils in the two groups was found to be 8.31. As the difference between the two means of the change in per cent in circulating eosinophils between 6.30 and 9.30 a.m., in the blind subjects and in the normal controls, is more than two and a half times the standard error of the difference, this difference is significant.

DISCUSSION

It has been shown that in any group of normal subjects, there is a significant drop in circulating eosinophils between 6.30 and 9.30 a.m. For control groups, mean values between 27 and 50 % have been reported (Halberg et al., 1951; Halberg & Engel, 1952). In groups of patients with adrenal insufficiency and hypopituitarism, there is no characteristic early morning fall in eosinophils (Halberg et al., 1951, Halberg, Cohen & Flink, 1951, Halberg, Flink & Vissher, 1951). Further, it does not exist in children below the age of 15 months, but in a higher age group, a drop of 39 % has been demonstrated (Halberg & Ulstrom, 1952). Diurnal variations in eosinophils have also been shown to
exist in dogs (Halberg, 1953) and mice (Halberg & Visscher, 1950), but not in lambs which possess a relative deficiency in the pituitary-adrenal mechanism (Zarrow et al., 1952).

These morning changes in the activity of the adrenal cortex are probably influenced by the autonomic nervous system (Halberg, 1953). Purely neurogenic stimuli affect the adrenocortical function. Thus, emotional tension (Dreyfuss & Feldman, 1952) and the neurogenic stimulus of suckling (Bromberg, Feldman & Eliakim, 1952) in man, emotions and sound in dogs (Bonvallet, Morel & Benda, 1951), immobilisation, sound and light in rats (Fortier, 1951) and finally stimulation of hypothalamic centres in cats (Porter, 1953) and dogs (Hume & Wittenstein, 1950), cause increased activity of the adrenal cortex, as evidenced by the drop of the circulating eosinophils.

The pathways and the relations between the hypothalamus – which is the centre of the autonomic nervous system – and the anterior lobe of the pituitary gland have been investigated and a hypophyseal-portal system of veins described (Harris, 1948). It has been shown that the integrity of the hypothalamus is essential for the activation of the adrenal cortex by systemic stimuli. Thus lesions located in different parts of the hypothalamus have prevented the eosinopenia following adrenaline injection in dogs (Hume & Wittenstein, 1950), in cats (Porter, 1953) and in man (Perloff, Levy & Despopoulos, 1952). It has been shown further, that stressed induced changes in the electrical activity of the hypothalamus are correlated with a fall in the circulating eosinophils (Porter, 1952). The integrity of the hypothalamo-hypophyseal pathways is essential for adrenal cortical discharge following neurogenic stimuli, because homo-transplantation of the adeno-hypophysis into the anterior chamber of the eye in rats abolished this discharge (Fortier, 1951).

Light, a purely neurogenic stimulus, causes in intact rats a rapid and intense discharge of ACTH (Fortier, 1950), which would imply a neuroendocrine mechanism. Nervous connections exist between the retina and the supra-optic nuclei of the hypothalamus (Marburg, 1942); the latter is intimately connected with the anterior lobe of the pituitary gland (Harris, 1948). This is probably the neuro-endocrine pathway through which light causes the activation of the adrenal cortex.

The influence of light upon the 24-hour rhythm in the number of eosinophils in mice has been investigated. It has been shown that the reversal of lighting reverses the eosinophil rhythm regardless of availability of food. and it was concluded that light is needed to establish eosinophil rhythmicity in mice (Halberg, 1953).

The results of the present study would seem to indicate that in the group of completely blind, but otherwise healthy subjects, the endogenous morning eosinopenia is diminished as compared with our control group and those reported by others. From Fig. 1 it is evident that in a number of blind subjects,
a marked drop of eosinophils during the morning hours occurred. However, it should be emphasized again at this point that endogenous eosinopenia is a group phenomenon in normal subjects, and therefore the impairment of this drop in blind people should be similarly viewed. Undoubtedly, emotional factors, acoustic stimuli and bodily activity contributed to the morning eosinopenia in both the blind and normal subjects.

Apart from blindness, there were two other minor differences between our two groups. The time of eating breakfast, which was served one hour earlier in the case of our controls, and the different distribution of the ages in the two groups. With regard to food, it has been emphasized that the effect of meals can be disregarded as far as eosinophil count is concerned (Swanson, Bauer & Ropes, 1952). The difference in ages can also be discounted as it has been shown that infants above the age of 15 months show an endogenous morning eosinopenia similar to that of adults (Halberg & Ulstrom, 1952).

During the period of the investigation, the blind subjects were actively occupied in their daily activities in the institution and the nurses in their regular work. Although it is difficult to compare the emotional and bodily stresses of the two groups, it should be mentioned that a normal endogenous morning eosinopenia was reported in institutionalised patients with mental deficiency (Halberg et al., 1953) in hospitalized patients selected at random (Halberg, Cohen & Flink, 1951), as well as in normal subjects who were under controlled conditions and whose activities were sedentary and limited (Halberg et al., 1951). From the above, it is evident that an important difference between the blind subjects examined in this study and normal people, is the lack of perception of light. There was no question of any pituitary, adrenal or other disease in these subjects which could be responsible for the impaired endogenous eosinopenia.

Our results would indicate, therefore, that light, which is one of the most important factors connected with the initiation of daily activity in man, seems to affect the drop of the circulating eosinophils in the morning hours, probably as the result of its effect through the hypothalamus and the adenohypophysis on the adrenal cortex.

The mean absolute number of eosinophils in the morning hours was somewhat higher in the group of blind people as compared with the control group. This slight difference may possibly reflect the effect of light on adrenocortical function as well.

In fact, light has been shown to influence the activity of other endocrine glands through the anterior lobe of the pituitary gland. In amphibians, light increases the melanophore hormone content of the hypophysis (Selye, 1948). In certain species of birds, light may cause laying of eggs before puberty (Rowan, 1929); in males of these species, darkness inhibits the development of testes in the sexual period but illumination, on the other hand, causes a
growth of testes in non-reproductive periods (Benoit, 1937). It has been shown further, that bilateral optic enucleation delays the onset of sexual maturity of both male and female rats (Brownman, 1940) and that this delay in maturity was also obtained under conditions of constant darkness. Male rats kept under these conditions had lighter hypophyses and testicles than did males kept in continuous light (Fiske, 1939). On the other hand, light in rats prolonged the duration of oestrus, as the result of the stimulation of gonadotrophic activity of the anterior lobe of the pituitary gland (Fiske, 1941). These experiments would further confirm the assumption that there are special nervous pathways between the eye and the hypothalamo-pituitary system (Collin, 1938). Thus in addition to the influence of light on sexual functions, an effect of light on the diurnal activity of the adrenal cortex has been indicated in this study.

In man, observations have been made on the role played by the hypothalamus in visual perception. It has been shown that concentric depression of the visual field may be due to a lesion in the diencephalic region outside the optic pathways (Franceschetti, 1944). Hess (1943) believes that the hypothalamus has an indirect inductive influence on the power of the optic system by the hypothalamo-fugal fibres to the retina. On the other hand, Marburg (1942) has described fibres from the retina which detach themselves from the optic tract and terminate in the supra-optic and ventro-medial hypothalamic nuclei.

Examination of scotopic vision in various endocrine disorders has shown that dark adaptation is impaired in pathological conditions involving the diencephalic region. Constant impairment of dark adaptation was found in patients with adiposo-genital dystrophy, a syndrome conditioned by a hypothalamic disturbance, as well as in cases of brain tumour involving the hypothalamic region. These observations suggested the possible existence of a hypothalamic centre regulating dark adaptation (Landau & Bromberg).

The results of this investigation of endogenous eosinopenia in blind people, the experiments mentioned above and the clinical observations of impaired dark adaptation in hypothalamic disorders point to the intricate relations between light, visual perception and neuro-endocrine functions.

SUMMARY

Morning changes in the number of eosinophils were studied in 36 blind, but otherwise healthy subjects, and in 33 normal controls. They were not submitted to any other stimulation than daily routine. In the blind, a drop of 15% in the circulating eosinophils between 6.30 a.m. and 9.30 a.m. was observed, as compared with a drop of 38.3% in the control group. These results were analysed statistically and the difference was found to be signi-
ificant. Thus, diminished endogenous morning eosinopenia in a group of blind people was demonstrated.

The influence of light on the eosinophil count is discussed and it is concluded that light probably plays an important role in endogenous morning eosinopenia in normal subjects.

The effect of light on various endocrine glands is mentioned and the mutual relationship between light and neuro-endocrine functions is stressed.

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