The effect of cyproterone acetate on the antler cycle in red deer /Cervus elaphus L./

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SUMMARY

The aim of the study was to test the effect of antiandrogen, cyproterone acetate (CA) on the antler cycle in the red deer (Cervus elaphus). CA was administered to three adult red deer stags (Edward, Fuks and Gacek) in weekly intervals. Edward and Fuks were given 600 mg + 600 mg of CA, whereas Gacek was given 600 mg + 300 mg. CA was injected during the hard antler phase: in mid-October (Edward), at the end of November (Fuks) and at the end of January (Gacek). CA caused the antler casting 17 to 22 days after the first injection. In all stags, the casting of antlers was followed by a period of intensive growth of new antlers. Edward was given CA at the end of October. This treatment was responsible for occurrence of the two antler cycles in the year of the experiment. When CA was administered during the middle of the hard antler phase an additional short antler cycle occurs followed by new antler growth. CA treatment in the later part of hard antler phase may cause a prolonged antler cycle. Reproductive Biology 2004 4(2): 165-176.
**Key words:** Red deer, *Cervus elaphus* L., antler cycle, cyproterone acetate, antler growth.

**INTRODUCTION**

Annual antler cycles in the *Cervidae* species of the temperate climate are closely associated with the length of day. The annual antler cycle consists of soft and hard phase. In red deer, the soft phase begins in February/March. It encompasses antler growth and mineralization and is ended by velvet shedding. Velvet shedding is followed by the hard phase of the antler cycle which in red deer starts around the end of July. At that time a period of increased reproductive activity begins. In this species, the peak of mating season takes place in September-October. The hard phase of the antler cycle lasts until March and is followed by antler casting. The antler casting occurs in precisely established periods, strictly specified for particular deer species [6, 7, 10]. In the middle of the antler soft phase, testes reach their minimal size and testosterone (T) production decreases significantly [7]. Antler mineralization and velvet shedding are parallel to an increasing testicular activity. The phase of hard antlers occurs when T increase is observed in blood, seminal plasma and testes [13-15]. Thus, there are close relationships among annual antler cyclicity, photoperiod and changes in androgen concentrations in red deer.

Anti-androgens are useful tools for studies of mechanisms of seasonal reproductive processes. Bubenik et al. [5] was the first who examined the effect of the synthetic antiandrogen cyproterone acetate (CA) on the antler cycle. The studies conducted on white-tailed deer (*Odocoileus virginianus*), fallow buck (*Dama dama*) and pudu (*Pudu pudu*) revealed that CA strongly affected the antler cycle [6, 11, 12]. However, no data on CA effects on red deer antler cycle are available.

The present preliminary experiment was aimed to test the effect of CA on the antler cycle in the red deer (*Cervus elaphus*). In addition, an attempt was made to increase the size and weight of antlers by inducing earlier casting and prolonging the period of antler growth.
MATERIALS AND METHODS

The study was conducted during the hard phase of the antler cycle on six adult red deer stags kept on a deer farm of the Polish Academy of Science’s Research Station in Popielno. All experimental stags (Edward, Gacek, Fuks) received CA produced by Schering AG (Berlin, Germany). Edward and Gacek were injected with commercial preparation, Androcur-Depot (100 mg CA/ml). CA preparation for Fuks (treatment concentration: 100 mg CA/ml) was made by dissolving 2.589 g of CA in 4.315 ml benzyl benzoate and combined with 21.535 ml of castor oil. Then, the mixture was heated for 10 minutes (150-180°C) and castor oil was added in drops.

Anesthesia was induced by 10% Xylazine (Biowet, Poland; 1.8 to 2.0 ml/stag) or 2.5% Chlorsuccillin (Jelfa, Poland; 0.37 to 0.43 ml/stag). CA was twice i.m. injected and the first injection contained 600 mg of CA. The second one, performed 8 days later, contained 600 mg for Edward and Fuks and 300 mg for Gacek. Data characterizing particular males before, during and after CA treatment as well as control stags during two subsequent seasons are presented in tab. 1. The physical condition of the stags during the experiment was very good.

RESULTS

Details concerning the timing of particular phases in control animals; Guzik, Ezop and Cesarz, are shown in tab. 1. In control stags, the full antler cycle lasted from 355 to 373 days. The soft and the hard antler phases lasted 142 - 161 and 205 - 223 days, respectively (tab. 2). The weight of antlers in control animals ranged from 4.04 to 5.17 kg. The antler length ranged from 88.5 to 97.0 cm (tab.3).

The experimental stags were given CA at different times of the hard antler phase. Edward was given CA at the end of October (tab.1) and casting of antlers was induced 17 days after first injection of CA (first antler casting). This was followed by a period of intensive growth of new antlers and subsequent velvet shedding. The new antlers were cast at the beginning of March, the typical time for red deer (see: control animals, tab. 1).
Table 1. Characteristics of antler cycles in control and experimental and stags.

<table>
<thead>
<tr>
<th>Item</th>
<th>Edward</th>
<th>Fuks</th>
<th>Gacek</th>
<th>Guzik</th>
<th>Ezop</th>
<th>Cesarz</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age /years/</td>
<td>10</td>
<td>9</td>
<td>8</td>
<td>8</td>
<td>10</td>
<td>12</td>
</tr>
<tr>
<td>Body weight /kg/</td>
<td>186.4</td>
<td>159.4</td>
<td>165.4</td>
<td>166.3</td>
<td>178.0</td>
<td>n.e.</td>
</tr>
<tr>
<td>Casting before CA</td>
<td>L</td>
<td>R</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Date and dose of CA</td>
<td>I</td>
<td>II</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Velvet shedding before CA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antler casting</td>
<td>R</td>
<td>L</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Velvet shedding after CA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antler casting</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

I, II - first and second injection of CA; L - left beam; R - right beam

The first antler cycle induced by CA lasted only 121 days; the soft and hard antler phase lasted 74 and 47 days, respectively (tab. 2). During this antler growth period, the stag produced antlers weighing 1.32 kg with beam length of 27.5 and 33.0 cm (tab. 4). During the next cycle antlers were produced at the normal time. The antlers weighed 4.15 kg and their length was 81.0 and 89.5 cm. The results of the experiment showed that it was possible to induce antler casting with CA in red deer.
The other experimental stags were treated with the antiandrogen later in the hard antler phase. Fuks was given CA one month later than Edward. This caused the casting of antlers 17-22 days after the first injection of CA. Gacek was given CA at the end of January, and his antlers were cast 16-17 days after the first CA injection (tab. 1). In contrast to Edward, only one antler cycle was observed in these stags. The antlers were cast approximately 80 (Fuks, December) and 40 (Gacek, February) days earlier than during the natural antler cycle (March). In consequence, the phase of soft antlers was extended to 216 days in Fuks, with the total length of the cycle of 443 days (tab. 2). The respective antler phases of Gacek were accordingly shorter than those of Fuks.

**DISCUSSION**

In the current study, all experimental stags were injected with CA during different months of the hard phase of the antler cycle i.e. during time of high T plasma level. Cyproterone acetate is an anti-androgen which was previously found to decrease volume of testes and neck circumference in

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**Table 2.** Length of the soft and hard antler phases in experimental and control red deer stags.

<table>
<thead>
<tr>
<th>Antler cycles and phases</th>
<th>Length of the antler phase (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Experimental stags</td>
</tr>
<tr>
<td></td>
<td>Edward&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td>Soft</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>74</td>
</tr>
<tr>
<td>II</td>
<td>133</td>
</tr>
<tr>
<td>Hard</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>47</td>
</tr>
<tr>
<td>II</td>
<td>219</td>
</tr>
<tr>
<td>Total</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>121</td>
</tr>
<tr>
<td>II</td>
<td>352</td>
</tr>
</tbody>
</table>

<sup>1</sup>I, II – designate two subsequent seasons in control stags (1996/97, 1997/98);  
<sup>2</sup>I, II – designate two antler cycles observed in Edward (1996/1997)
Table 3. Characteristics of antler casting in control red deer stags.

<table>
<thead>
<tr>
<th>Date of antler casting</th>
<th>Antler weight /kg/</th>
<th>Antler length /cm/</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Left or right</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td></td>
</tr>
<tr>
<td><strong>Guzik</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>02.03.96</td>
<td>L</td>
<td>2.07</td>
</tr>
<tr>
<td>04.03.96</td>
<td>R</td>
<td>2.20</td>
</tr>
<tr>
<td>10.03.97</td>
<td>L</td>
<td>2.40</td>
</tr>
<tr>
<td>10.03.97</td>
<td>R</td>
<td>2.77</td>
</tr>
<tr>
<td>05.03.98</td>
<td>L</td>
<td>2.13</td>
</tr>
<tr>
<td>04.03.98</td>
<td>R</td>
<td>2.40</td>
</tr>
<tr>
<td><strong>Ezop</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>26.02.96*</td>
<td>L</td>
<td>0.064</td>
</tr>
<tr>
<td>28.02.96*</td>
<td>R</td>
<td>0.082</td>
</tr>
<tr>
<td>28.02.97</td>
<td>L</td>
<td>2.19</td>
</tr>
<tr>
<td>28.02.97</td>
<td>R</td>
<td>1.85</td>
</tr>
<tr>
<td>18.02.98</td>
<td>L</td>
<td>2.59</td>
</tr>
<tr>
<td>18.02.98</td>
<td>R</td>
<td>1.89</td>
</tr>
<tr>
<td><strong>Cesarz</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>02.03.96</td>
<td>L</td>
<td>2.57</td>
</tr>
<tr>
<td>02.03.96</td>
<td>R</td>
<td>2.55</td>
</tr>
<tr>
<td>10.03.97</td>
<td>L</td>
<td>2.05</td>
</tr>
<tr>
<td>10.03.97</td>
<td>R</td>
<td>2.24</td>
</tr>
</tbody>
</table>

*Antlers cut in season 1995/96; L - left beam; R - right beam; n.e. - not estimated

fallow deer [15, 16, 17]. Herein, we demonstrated that the CA-treated animals cast antlers from 17 to 22 days after the first injection of CA. Kierdorf et al. [11] performing an experiment on fallow deer (*Dama dama*), had also administered CA during the hard antler phase. The authors had treated two groups of bucks at weekly intervals with increasing doses of CA (400
Table 4. Characteristics of antler casting before and after cyproterone acetate (CA) treatment in experimental red deer stags.

<table>
<thead>
<tr>
<th>Date of antler casting</th>
<th>Antler weight /kg/</th>
<th>Antler length /cm/</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Left or right</td>
<td>Total</td>
</tr>
<tr>
<td>Edward</td>
<td></td>
<td></td>
</tr>
<tr>
<td>07.03.96*</td>
<td>L 2.64</td>
<td>6.3 94.0</td>
</tr>
<tr>
<td>07.03.96*</td>
<td>R 3.66</td>
<td>83.0</td>
</tr>
<tr>
<td>08.11.96</td>
<td>L 2.85</td>
<td>6.5 98.5</td>
</tr>
<tr>
<td>08.11.96</td>
<td>R 3.65</td>
<td>102.7</td>
</tr>
<tr>
<td>09.03.97</td>
<td>L 0.46</td>
<td>1.32 27.5</td>
</tr>
<tr>
<td>06.03.97</td>
<td>R 0.86</td>
<td>33.0</td>
</tr>
<tr>
<td>24.02.98</td>
<td>L 1.51</td>
<td>4.15 81.0</td>
</tr>
<tr>
<td>24.02.98</td>
<td>R 2.64</td>
<td>89.5</td>
</tr>
<tr>
<td>Fuks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>04.03.96*</td>
<td>L 1.51</td>
<td>3.09 76.0</td>
</tr>
<tr>
<td>06.03.96*</td>
<td>R 1.58</td>
<td>78.0</td>
</tr>
<tr>
<td>18.12.96</td>
<td>L 1.82</td>
<td>3.89 82.8</td>
</tr>
<tr>
<td>13.12.96</td>
<td>R 2.07</td>
<td>96.6</td>
</tr>
<tr>
<td>07.03.98</td>
<td>L 1.26</td>
<td>3.28 97.0</td>
</tr>
<tr>
<td>07.03.98</td>
<td>R 2.02</td>
<td>102.9</td>
</tr>
<tr>
<td>Gacek</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18.03.96*</td>
<td>L 1.73</td>
<td>3.57 80.5</td>
</tr>
<tr>
<td>17.03.96*</td>
<td>R 1.84</td>
<td>82.3</td>
</tr>
<tr>
<td>06.02.97</td>
<td>L 2.05</td>
<td>4.32 82.5</td>
</tr>
<tr>
<td>06.02.97</td>
<td>R 2.27</td>
<td>85.5</td>
</tr>
<tr>
<td>05.03.98</td>
<td>L 2.45</td>
<td>5.12 103.8</td>
</tr>
<tr>
<td>05.03.98</td>
<td>R 2.67</td>
<td>109.8</td>
</tr>
</tbody>
</table>

*Before administration of CA; L - left beam; R - right beam
to 800 mg/week). The first group was given CA from 29 September to 28 November (time of maximum levels of T in blood). CA caused the casting of antlers nine weeks later. In the second group, CA was given from 16 to 30 November, which caused the casting of antlers 16-17 days following CA administration. The casting was immediately followed by the growth of new antlers; the velvet shedding of those antlers took place in February and March of the next year. It appears that similar to fallow deer, CA treatment of red deer stags during the hard antler phase induced casting and onset of the growth of new ones. In red deer, only two injections were sufficient to induce antler casting. This may indicate that red deer are more sensitive to CA than fallow deer.

Earlier administration of CA was studied in white-tailed deer (*Odocoileus virginianus*) and fallow deer. Cyproterone acetate administered (150 mg/week) white-tailed deer stags [5] immediately after velvet shedding i.e. at the beginning of the hard phase caused antler casting 24-96 days later. When the beginning of CA administration (600-1000 mg/week) to fallow bucks [12] started during the middle soft phase (mid-April) and was continued until the middle hard phase (end of November) antlers were cast and new ones grew undisturbed. In these animals velvet shedding was delayed until January of the next year and the subsequent antler casting took place in typical time i.e. April. In contrast, administration of CA (3.5 mg/kg/week) during the soft phase of antler growth (time of low T plasma level) delayed or prevented velvet shedding in white-tailed deer [3]. It appears that the effect of CA on the antler cycle clearly depends on the timing of its administration. However, detailed conclusions require further examination.

In our experiment, cyproterone acetate given to Edward resulted in two antler cycles being completed in one year. The soft phase of the first antler cycle began, as usual in this species, in March and was completed in July. The followed hard phase was interrupted by the October injections of CA. The second soft phase started immediately after casting i.e. nine days after the last CA injection and was completed in January. The new antlers were cast at the beginning of March. During the short period of the second soft phase antlers weighing 1.32 kg were produced. It is of interest that during the subsequent, undisturbed antler cycle Edward produced antlers weighing
4.15 kg. The total weight of both antlers, 5.47 kg, was still lower than that of the antlers from the cycle preceding the experiment (tab. 4; 6.5 kg). It seems that the weight of the second antlers was reduced due to the shortening of the soft antler phase. Such effect might be caused by disturbance of plasma spring T level [1, 2, 4, 18].

After CA-induced antler casting, antlers of Fuks and Gacek started to grow much earlier (December, February) compared to their previous cycles or cycles of control animals (March). This resulted in the longer soft phase ended at typical period of year (end of July). The soft antler phase of Fuks was extended to 216 days. This means that in Fuks and Gacek, new antlers started to grow during the period of increasing day length accompanied by decreasing plasma androgen level [12-14]. It is possible that the lack of the March velvet shedding was caused by the action of CA and gradually decreasing T level. Bubenik et al. [3] observed a similar CA-induced delay in antler shedding in white-tailed deer.

It was anticipated that prolongation of the period of antler growth would cause an increase in size and weight of antlers. However, though the antler growth period in Fuks was extended by appr. 80 days, the weight of both beams (3.28 kg) was lower in comparison to previous natural cycle (3.89 kg). This decrease in antler weight might result from either the age of the stag or antiandrogen action during the initial stage of antler growth. It is of interest that the changes in weight of Fuks’ antlers were not synchronized with the changes in the length of his beams. In contrast to the observed decrease in antler weight of Fuks, the length of beams in the year following the CA treatment was higher compared to the year of the experiment.

Such tendency in decrease of antler weight in year following the CA treatment was not observed in Gacek. This could be associated with the fact that Gacek is one year younger than Fuks. Further studies on more animals are necessary to substantiate such hypothesis.

In all three stags, in which CA administration caused premature antler casting in late autumn or in winter, new antlers began to grow soon after casting. These antlers grew and developed normally (fig. 1), despite the low temperature (-11.9°C to -25°C). In the initial stages of growth, the antlers were covered with hairless velvet, which seemed to be deprived of
any insulation from cold. It should be noted that frost-bitten antlers were grown in none of the stags in this experiment. This may be explained by intensive blood circulation in the growing antlers. Thus, for the first time in red deer, growing antlers were shown to be extremely resistant to low temperatures.

Bubenik et al. [5] found that in white tailed deer the antlers cast as a result of CA action had a concave or flat surface of antler seals. Such feature is also characteristic for castrated stags and progesterone-treated deer [8, 9]. In contrast to these results, we did not observe the CA-induced concave shape of the seal in red deer. It has to be determined whether these differences resulted from species-specific mechanisms of CA action, timing of CA administration or used CA doses.

In summary, CA treatment of red deer stags during the hard antler phase induced casting. When CA was administered during the middle of the hard antler phase an additional short antler cycle occurred followed

*Fig. 1. Intensive growth of velvet antlers in experimental stag Edward (December 1996; photo Z. Giżejewski).*
by new antler growth. The effect of CA treatment in the later part of hard antler phase caused a prolonged next antler cycle. The question whether it is possible to increase the antler weight and size by elongation requires further examination.

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Antiandrogen and antlers in red deer

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