THE UNIVERSITY OF MANITOBA

THE EFFECT OF ERGOT INGESTION ON THERMOREGULATION IN SHEEP

by

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A THESIS

SUBMITTED TO THE FACULTY OF GRADUATE STUDIES

IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE

OF MASTER OF SCIENCE

DEPARTMENT OF ANIMAL SCIENCE

WINNIPEG, MANITOBA

DECEMBER 1981

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ABSTRACT

Preliminary studies have suggested that long term, low level ingestion of ergot alkaloids may result in a generalized impairment of temperature regulation in ruminants. The present study was conducted to determine the extent of this impairment in ergot fed ewes.

Groups of four sheep each fed a pelleted ration containing 0%, 0.07%, 0.14% or 0.28% ground ergot sclerotia for a period of 19 weeks were then subjected to mild heat (27.7 °C - 31.5 °C), mild cold (0 °C- 4.5 °C) and thermoneutral conditions (16.0 °C - 23.6 °C).

Heat stress was demonstrated in all groups receiving ergot at temperatures which would normally be considered within the thermoneutral zone. In ewes fed ergot at a level of 0.07% this stress was evidenced by an increase in mean respiratory rate. In ewes receiving the two highest levels of dietary ergot, the rapid shallow panting typical of both the control group and those sheep receiving 0.07% ergot during exposure to mild heat, was replaced by a slower deeper panting similar to that described for sheep during severe heat stress. The respiratory response was sufficient to prevent a rise in body heat storage and rectal temperature.

Blood flow to the ear, as evidenced by changes in the thermal circulation index, was reduced at all ambient temperatures in ewes receiving 0.14% ergot or greater. Heat production was not affected by dietary ergot and it was concluded that an increase in peripheral vasomotor tone was responsible for the observed lowering of the upper critical

temperature by impairing heat flow from the body to the environment.

The findings of the present study are inconsistent with the effects predicted by assuming an action of ergot alkaloids on central monoamine receptor sites and appear to support the hypothesis that ergot alkaloids impair temperature regulation by directly stimulating vascular smooth muscle to increase PVMT.

In view of the above findings animal producers would be well advised to refrain from feeding grain containing even very low levels of ergot to their livestock at extremes of ambient temperature.

ACKNOWLEDGMENTS

Sincere thanks are extended to my supervisor, Dr. G.D. Phillips, Professor of Animal Physiology and present Head of the Department of Animal Science. I would also like to express gratitude to Dr. A.D. Graham for her assistance and advice during the course of this study, and to Dr. R.J. Parker, Dr. J.C. Rauch and Dr. R.R. Marquardt for their helpful suggestions.

Appreciation is also extended to Ms. D. Talbot for her technical assistance, to my parents and my aunt, S. Manson, for their indefatigable moral support, and to my wife, Angela Yount, for her support and typing of this thesis.

Financial support for this study was provided in part by a Natural Science and Engineering Research Council postgraduate scholarship and by an assistantship from the Department of Animal Science.

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LIST OF ABBREVIATIONS

A	area
AC	alternating current
ACh	acetylcholine
AVA	arteriovenous anastomoses
BW	body weight
C	Celsius
cAMP	cyclic adenosine monophosphate
CCh	carbachol
CE	controlled environment
CIVD	cold-induced vasodilation
cm	centimetre
CNS	central nervous system
CO	cardiac output
d	day
DC	direct current
g	gram
h	hour
HP	heat production ($kJ \cdot kgBW^{-0 \cdot 75} \cdot min^{-1}$)
H_p	heat production ($kJ \cdot m^{-2} \cdot min^{-1}$)
HR	heart rate
5-HT	5-hydroxytryptamine

LIST OF ABBREVIATIONS CONTINUED

ICV	intracerebroventricular
I_T	tissue insulation
kg	kilogram
kJ	kilojoule
km	kilometre
l	litre
LCT	lower critical temperature
LSD-25	lysergic acid diethylamide
m	metre
Mcal	megacalorie
min	minute
ml	millilitre
mm	millimetre
NA	noradrenalin
NF	norfenfluramine
PVMT	peripheral vasomotor tone
resp	respirations
RQ	respiratory quotient
RR	respiratory rate
T_a	ambient temperature
TCI	thermal circulation index
TNZ	thermoneutral zone
T_R	rectal temperature
T_{sk}	skin temperature
$\bar{T}_{sk}$	mean body skin temperature

UCT	upper critical temperature
V_{O_2}	oxygen consumption per minute
w/w	weight to weight
μm	micrometres

INTRODUCTION

The fungus ergot (Claviceps species) parasitizes many North American fodder grasses and cereal crops of economic importance. The sclerotia produced as a result of the infection contain a variety of pharmacologically active alkaloids which, if ingested, may result in serious illness or death. In livestock the symptoms of acute ergot toxicity include lameness, muscular incoordination, convulsions and gangrene of the extremities. Recovery, except for advanced gangrene, is usually prompt following a switch to clean feed.

In humans, sporadic outbreaks of ergot poisoning were reported throughout the middle ages and as recently as 1926 in Europe (Young, 1979). The symptoms are similar to those in livestock and both gangrenous and convulsive forms of the disease have been documented.

The grain grower may bear the brunt of the economic loss caused by ergot infection due to downgrading and reduced yields, but, the problem is of concern to other sectors of the food production industry as well. In 1978 about 1.1% of railcar loads of western red spring wheat inspected over a three month period in Canada were downgraded as a result of ergot contamination (Young, 1979). Strict government regulations prevent such grain from reaching commercial food channels. Contaminated feed grains and fodder grasses, if inadvertently used in the animal production industry, may result in reduced performance and/or quality of livestock. The animal producer who grows his own grain may be doubly burdened by heavy infections of ergot in his crops,

from both reduced yields and a reduction in livestock performance.

The level of ergot in feed grains generally considered to be safe is below 0.1% on a w/w basis. However, recent reports indicate that individual and total alkaloid contents vary considerably between sclerotia and that the level and kind of effect observed depends upon the spectrum of alkaloids present and the species to which they are fed (Young, 1979). Thus, of two rations each containing 0.1% ergot, one may be toxic, the other not.

The symptoms of acute ergot toxicity in livestock have been fairly well described, but the effects of long term, low level feeding of ergot (less than 0.15% w/w) are less well known. Preliminary studies in this and other laboratories have suggested that chronic ingestion of ergot alkaloids at low levels can cause generalized impairment of temperature regulation in ruminants. The fullest expression of ergot toxicity may therefore be influenced by ambient temperature.

LITERATURE REVIEW

Ergot

Life Cycle and Control

The occurrence of ergot throughout the world has been reviewed by Lorenz (1979) who identified thirty two Claviceps species capable of parasitising over six hundred host plants. All eight of the leading cereal grains produced in the world, wheat, rice, corn, sorghum, rye, barley, oats and millets are susceptible. A wide range of fodder grasses, including species of Lolium, Poa, Agrostis, Dactylis and Holcus will also support infections (Mantle, 1969).

The life cycle of ergot begins when a mature sclerotium falls from the head of an infected plant. Subsequent events have been summarized by Bové (1970) and Lorenz (1979). Unless buried deeply by fall tilling, winter temperatures activate the sclerotium which germinates in the spring. Stroma are raised above the soil surface within a week after the first signs of germination. Ascospores are then produced which, when released, may infect a floret during the flowering stage. Initial infection results in the production of a sticky substance, called honeydew, which collects on the floret. Honeydew contains millions of conidia, or secondary spores, which are capable of infecting other florets if spread by insects or by rain.

As the infection proceeds the developing mycelial mass destroys the embryo of the floret by crowding out all the tissues that would

normally constitute the grain. Gradually the mass changes into the dry hard sclerotial stage and upon maturity of the ergotized grain, the ergot bodies fall to the ground to complete the cycle.

The ergot bodies themselves tend to vary with the host and between species. They may be curved, straight or round, and white, yellow, brown, green or black to purplish brown. They are nearly always conspicous on the plant or in the seed bin, tending to be slightly larger than the seed they replaced. The length of the sclerotia varies from between 1 and 2 mm on some of the smallest grasses (Mantle, 1969) to over 8 cm for sclerotia of the species C. gigantea (Lorenz, 1979). Normally, only one or two sclerotia are produced per head but up to 41 have been observed in rye (Young, 1979).

The incidence and intensity of ergot infection is highly variable from year to year. A number of environmental factors and farming practices have been associated with outbreaks of the fungus (Lorenz, 1979; Young, 1979). Cool, damp springs favour the germination of sclerotia while dry and windy weather is required for dissemination of the ascospores. After infection has occurred, hot weather promotes sclerotial growth. When all these conditions are met relatively high concentrations of ergot are found in cereal grains.

Plant species themselves vary in susceptibility and a farmer's choice of crops and cultivars may influence the incidence of ergot infection. Cross pollinating species such as triticale and rye require a longer flowering period than do self pollinating plants such as wheat, barley or oats and as a result are prone to heavier ergot infections. Male sterile cereals are susceptible for the same reason.

There is some disagreement as to the degree of synchronization necessary between flowering and ascospore discharge for heavy initial infections to occur, but early planting dates have been shown to reduce ergot contamination. Presumably this results from minimizing the overlap of these two factors.

Other control measures available to the farmer include; (1) alternating fields between susceptible and non-susceptible crops to reduce the number of dormant sclerotia in the soil, (2) deep tilling to bury sclerotia beneath 3 - 5 cm of soil, preventing germination, and (3) cutting stands of wild grasses adjacent to cultivated fields where sclerotia or honeydew may be harboured.

Contaminated crops may be mechanically cleaned or blended with non-contaminated seed to reduce the concentration of ergot to below toxic levels.

Effects on Livestock

The symptoms of acute ergot toxicity in livestock have been fairly well described in the literature. Unfortunately, many of the early experiments used uncharacterized ergot, that is to say, the exact source of the ergot and its chemical composition were not documented. Recent reports indicate that individual and total alkaloid contents vary considerably between sclerotia, and that the level and kind of effect observed depends upon the spectrum of alkaloids present. LD_{50} values for individual alkaloids have been used to estimate toxicity of sclerotia. A single sclerotium may be 240 times more toxic than another sclerotium from a different field or 110 times more toxic than one from the same field (Young, personal communication). This variability may account for some of the apparent contradictions in the literature.

Although the exact physiological response to ergot depends upon its toxicity, the level of consumption, and on the species in question, a few generalizations are possible. Unpalatability and reduced appetite are common and often lead to reduced feed intake and an increase in feed to gain ratios. Classical symptoms of convulsive or gangrenous ergotism have been observed in almost all livestock species where the level of feed contamination is high. Recovery, except for advanced gangrene, is usually prompt following a switch to clean feed. Young animals are affected more than adults.

Species specific clinical symptoms have been reviewed by Lorenz (1979) and Young (1979) and are summarized in table 1.

In cattle, convulsive ergotism with nervousness, tremors and muscle incoordination has been observed. Gangrene, when it occurs, affects mainly the feet, ear tips and tail ends. Diarrhoea, salivation, increased water intake, heat stress and the failure to shed winter coats have also been associated with the disease while reproduction is minimally affected (Lorenz, 1979; Young, 1979).

In sheep, convulsive ergotism has been reported but difficulty in breathing, salivation, diarrhoea, heat stress and inflamation of the digestive tract are the more common symptoms. Necrosis of the tongue has also occasionally been noted. Pregnancy rate may be reduced, but, ergot induced abortions are rare (Lorenz, 1979; Young, 1979).

The effect of ergot on horses has not yet been investigated thoroughly but the convulsive syndrome has been documented in cases of ergot poisoning.

In pigs, convulsive ergotism is not usually observed and gangrenous ergotism, when it occurs, is confined to the tips of the ears and the tail.

TABLE 1. Effects of Ergot from Various Sources on Livestock (Young, 1979)

Effect	Species Affected by Various Ergot Sources				
	Poultry	Swine	Sheep	Cattle	Horses
Death					
Observed	GJRUVWX[1]	BNV[3]	BEGIR	KP	PU
Not observed	GJRVW[2]	-	G	G	-
Visible Symptoms					
Nervousness/hypersensitivity	nr	nr	P	PR	nr
Tremors observed	nr	nr	BEGP	CPRU	CP
—— not observed	-	-	G	-	-
Muscle incoordination	JRW	nr	GEIP	GPRU	CGP
Inability to stand	JRW	nr	nr	CP	nr
Paralysis	nr	nr	nr	P	PU
Tenderness/swelling of limbs	nr	V	nr	FGLKRSWY	nr
Lameness	nr	UV	B	BFGLKRSWY	nr
Limbs cold	nr	nr	ER	nr	nr
—— unaffected	nr	nr	GW	nr	nr
Gangrene of limbs observed	G	nr	nr	FGLPRUY	nr
—— not observed	-	B	-	G	-
—— of tails observed	-	O	nr	BFGMR	nr
—— not observed	-	-	-	S	-
—— of ears	-	O	nr	MPR	nr
—— not observed	-	-	-	S	-
—— of beak observed	U	-	-	-	-
—— of comb observed	U	-	-	-	-
—— of tongue observed	-	nr	ERU	nr	nr
Breathing difficulty	JRW	nr	EGR	BEFMPRW	U

/ continued

Effect	Poultry	Swine	Sheep	Cattle	Horses
Visible Symptoms					
Pulse faster	nr	nr	P	EFGPY	nr
—— slower	nr	nr	nr	MRW	U
—— weaker	nr	nr	nr	R	nr
Salivation	-	nr	EG	BFGPRW	nr
Diarrhoea	VW[1]	nr	EGR	PRX	nr
Temperature increased	-	nr	EGR	BFGLMPRWY	nr
—— decreased	-	nr	nr	R	nr
Water intake increased	nr	W	nr	RW	nr
Heat stress	-	nr	BMRW	BMRW	nr
No visible toxicity	-	U	-	-	nr
Dilation of pupils	-	-	E	-	nr
Heavy coat	-	-	-	BRW	nr
Internal Physiological Effects					
Not observed	G	RVW	I	-	nr
Ulcers in digestive tract	nr	W	PU	nr	nr
—— in liver	nr	W	-	nr	nr
—— in mouth	nr	nr	nr	R	nr
Inflamation of digestive tract	nr	nr	EPR	R	nr
Hemorrhages	nr	nr	ERZ	FGPX	nr
Brain blood vessels affected	nr	nr	nr	P	nr
Lungs affected	nr	nr	nr	X	nr
Blood cells affected	nr	nr	IZ	nr	nr
CNS affected	nr	P	nr	nr	nr
Reproduction					
Pregnancy rate unaffected	-	A	-	ABG	nr
—— reduced	-	B	B	GMRW	nr
Male fertility unaffected	-	nr	nr	MRW	nr

/continued

Effect	Poultry	Swine	Sheep	Cattle	Horses
Reproduction					
Abortions observed	-	-	E	APR	nr
—— not observed	-	BV	BR	BGRS	nr
Fetus/embryo death	-	V	ER	G	nr
—— toxicity	F	nr	-	nr	nr
—— weight increased	nr	B	nr	nr	nr
—— unaffected	nr	R	-	-	-
Offspring at birth normal	nr	B	nr	BG	nr
Birth weight reduced	-	B	nr	nr	nr
Lactation unaffected	-	nr	AB	nr	nr
—— reduced	-	BNOV	-	AGY	nr
—— delayed	-	nr	-	A	nr
Prolactin levels reduced	-	E	A	A	nr
Time to conception unaffected	-	A	nr	nr	nr
—— reduced	-	nr	nr	AE	nr
Estrous cycles unaffected	-	nr	nr	AB	nr
—— shortened	-	nr	nr	A	nr
Uterine muscle contraction	-	E	nr	R	nr
N retention/excretion affected	-	W	nr	nr	nr
No effect alkaloid free ergot	-	nr	R	nr	nr
Feeding					
Unpalatability	U	RW	nr	BG	nr
Appetite unaffected	R	-	-	GP	nr
—— reduced	G	W	BEGR	nr	nr
Preference for ergotized feed	-	-	-	P	nr
Reduced feed intake	nr	W	nr	BTRWX	nr
—— weight gain	UW	RUW	BIMRW	RW	nr
Feed/Gain ratio increased	W	W	BMRW	nr	nr
—— unaffected	R	-	-	MRW	nr

/continued

Effect	Poultry	Swine	Sheep	Cattle	Horses
Feeding					
Feed format important	W	R	-	nr	nr
Feed wastage	-	V	-	-	nr
Digestive problems	-	-	P	-	nr
Recovery from Symptoms	nr	OV	EGR	GKPSU	CP
Veterinary Applications					
Purpureal metritis	-	E	E	E	nr
Endometritis	-	-	-	E	nr
Other					
Alkaloid free tissues	nr	W	nr	nr	nr
—— excreta	nr	W	nr	nr	nr
—— milk	nr	nr	nr	S	nr
Less resistance to disease	nr	nr	nr	PRW	nr
Dampness and cold increase effects	nr	nr	R	nr	nr
Variable symptoms	nr	nr	G	nr	nr
Young affected more than adults	Yes	Yes	Yes	Yes	nr

Ergot Sources

A = Analog 2-bromo-alpha-ergocryptine
E = pure ergot alkaloid eg. Ergotamine
I = Ipomoea muelleri
L = clover
O = Claviceps purpurea in oats
S = Silage from undetermined source
V = Various sources
Y = rye not ergotized

B = Claviceps purpurea in barley
F = fescue
J = pearl millet (Pennisetum)
M = mixed grasses
P = Claviceps paspali in Paspalum
T = Claviceps purpurea in triticale
W = Claviceps purpurea in wheat
Z = Claviceps purpurea in undetermined cereal

C = Bremuda grass (Cynodon sp)
G = perennial rye grass (Lolium)
K = milk from ergotized cattle
N = bullrush millet (Pennisetum)
R = Claviceps purpurea in rye
U = Undetermined source
X = Aspergillus fumigatus

nr = not reported
[1] = chickens only
[2] = adults only
[3] = by malnutrition from agalactic mother

Agalactia is common in sows fed contaminated feed prior to farrowing. Most piglets are born live but eventually die due to malnutrition (Lorenz, 1979; Young, 1979).

Ducks and poultry exhibit necrosis of the comb, wattle and tongue when fed ergot. At levels greater than 1.6%, mortality among chicks is high, death being preceeded by an initial depression in growth, poor feathering, nervousness, incoordination and finally by the inability to stand (Lorenz, 1979; Young, 1979).

The effects of long term, low level (less than 0.15 percent) feeding of ergot, have not been as thoroughly studied as the effects of acute poisoning. Some of the above symptoms may still occur but the convulsive and gangrenous syndromes are usually absent. Preliminary studies in this and other laboratories have suggested that chronic ingestion of ergot alkaloids at low levels can cause generalized impairment of temperature regulation. Dinnusson et al. (1971) initiated a study to determine whether the results obtained from an evaluation of triticale as a feed grain were due to the grain itself or to the trace amounts of ergot the grain contained. Two experiments were reported in detail. In the first, beef heifers were fed a finishing ration containing 0.5% w/w of either rye or wheat ergot or 1.0% w/w of wheat ergot for 49 days. In the second, 0.5% w/w uncharacterized ergot was added to a barley ration being fed to beef steers and dairy-beef crossbred steers for 232 days. In all cases where animals received ergot, the authors reported an increase in water intake and urination, increased respiration and salivation on warmer days, and the inability to shed winter coats. A further, though perhaps somewhat more subjective observation, was that the animals fed ergot appeared to show more stress from warm weather than did

the controls. Considering that some of these same symptoms were noted during trials with triticale containing only 0.06% ergot, the authors concluded that any ration containing ergot at levels greater than this should be regarded as toxic.

In a study designed specifically to assess ergot induced thermoregulatory impairment, Cowan and Phillips (unpublished data) fed high grain diets containing ergot, at levels of 0.023, 0.10 and 0.123% w/w to Hereford heifers over a four month period. At the end of this time animals were subjected to a standard heat stress test. Cardiac and sweating rate, rectal and surface temperatures, and respiratory rate were measured during a three hour exposure, over which time the environment chamber was programmed to reach 33°C and 93% relative humidity.

A significant ergot effect was demonstrated with regard to both respiratory rate and rectal temperature, parameters which have been used as indicators of an animals ability to modulate heat stress (Findlay, 1963; Hales, 1969). Those animals receiving ergot exhibited respiratory rates of over 100 respirations/minute while control animals reached maximum values of 60-80 respirations/minute. Excess salivation and a notable exciteability were also associated with the ergot diets. Rectal temperatures of ergot treated animals rose by a rate approximately two fold that of the controls, 0.058°C/15 minute interval as compared with 0.021°C/15 minute interval.

An analysis of the rise in surface body temperature showed no significant differences among treatment groups, however, average surface temperatures for the entire three hour period were 0.75°C higher in groups receiving ergot. No treatment differences were found for cardiac and sweating rates.

Respiration rates taken in outdoor pens on four warm days (27°C) confirmed the findings of the heat stress test. Values were positively correlated with ergot content of the diet.

Moore (1975) reported much the same pattern as that found by Cowan and Phillips. Heat stress, increased rectal temperatures and increased respiration rates were observed in heifers, steers and sheep receiving 0.20%, 0.525% and 0.30% ergot respectively. The steers, however, exhibited a decrease in heart rate. A fourth group, composed of bulls, showed no significant differences between controls and animals receiving 0.30% ergot.

General observations of the pens by both Cowan and Phillips, and Moore were contrary to those of Dinnusson et al. (1971). The animals did not exhibit haircoat retention or an increase in water consumption and urination. These symptoms may only appear during long term feeding of ergot at levels greater than 0.5% and of similar toxicity to that used in the earlier experiment.

There are other reports of heat and humidity stress and hyperthermia in cattle and sheep fed low levels of ergot but in many cases these are associated with symptoms that have been reported for acute poisoning. Skarland and Thomas (1972), for example, found increased rectal temperatures and respiration rates, profuse salivation, and heat stress in heifers fed diets containing 0.8% or 1.6% ergot. At the higher level lameness and gangrene of the tail appeared in several of the animals. At the lower level two cows were reported as "walking stiffly". It is not clear to what extent these pathological conditions are involved in the observed impairment of temperature regulation. Certainly fever, and perhaps polypnoea, would be expected as a response to gangrene.

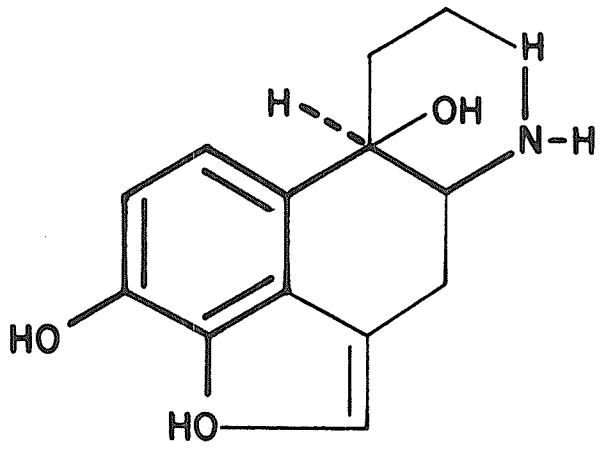
Enviromental conditions which allow the fullest expression of ergot toxicity may include cold temperatures as well as warm. In an experiment by Greatorex and Mantle (1973) ergot was well tolerated by sheep at pasture in mild weather or loosely housed, even at levels thought to be potentially lethal. Severe lameness and intestinal inflammation occurred in one animal exposed to cold, wet pasture conditions. The authors suggested that vasoconstriction due to ergot alkaloids were additive resulting in the progression of a lameness/gangrenous syndrome. This avenue of research has not been explored further.

Chemistry

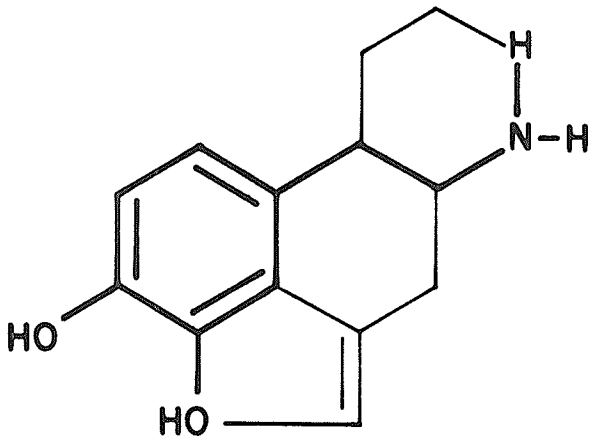
Ergot sclerotia are toxic because they contain pharmacologically active alkaloids. Individual and total content of these alkaloids varies, as indicated earlier, with location, climate, and with the host plant. Some species of Claviceps will produce a considerable number of alkaloids while others produce only one (see Lorenz, 1979). A few are totally incapable of alkaloid production. During the life cycle of ergot only the sclerotial stage produces alkaloids (Sim, 1965). Neither the "honeydew" nor conidia have been found to contain any of these compounds.

The alkaloids which have been isolated from ergot are all derivatives of the four ring structure of ergoline (figure 1). The two major groups are amines of lysergic acid. Within each of these groups, two series of optically active, isomeric alkaloids are found. The levorotatory or l-forms are pharamacologically active and believed to be naturally occurring alkaloids. The dextrorotatory or d-forms are completely inactive and are probably the result of chemical manipulations (Brazeau, 1970). The former are designated by the suffix "-ine" in their

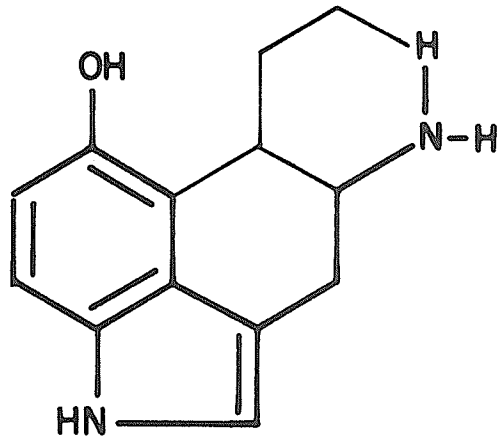
Figure 1. Structural relationship between ergoline and three biogenic amines: noradrenalin, dopamine, and serotonin (From Berde, 1980)



Ergoline
Noradrenalin



Ergoline
Dopamine



Ergoline
Serotonin

nomenclature, the latter by the suffix "-inine".

Hydrolysis of the first group yields lysergic acid and an amine, consequently they are designated as amine alkaloids (Brazeau, 1970). The second group contains alkaloids of higher molecular weight and hydrolysis yields lysergic acid, proline, another L-amino acid and an α-keto acid (Floss and Anderson, 1980). These alkaloids are known as amino acid alkaloids (Brazeau, 1970) or peptide alkaloids (Floss and Anderson, 1980). Individual structures of the six most common alkaloids are shown in figure 2 along with the structure of lysergic acid for comparison.

A third group of alkaloids, the clavine series, are water-soluble derivatives of ergoline which do not yield lysergic acid upon hydrolysis. One member of the series, Agroclavine has been shown to possess stimulating activity on the rabbit uterus (Sim, 1965) but for the most part other clavine alkaloids are not as active as the lysergic acid amines. Claviceps species which produce lysergic acid amines do not usually produce significant amounts of the clavine alkaloids.

The variety of ergot alkaloids has been extended by the production of several semi-synthetic compounds for medicinal uses. Saturation of the C9 - C10 double bond in lysergic acid has produced a series of stable dihydrogenated alkaloids which differ slightly from the parent compounds in terms of pharmacological action. Lysergic acid may also be combined with amines other than those found naturally. Lysergic acid diethylamide and methylergonovine are examples of this procedure. Methylation of the indole nitrogen of methylergonovine has produced one other widely used pharmacologically active alkaloid called methysergide. These compounds are shown in figure 2.

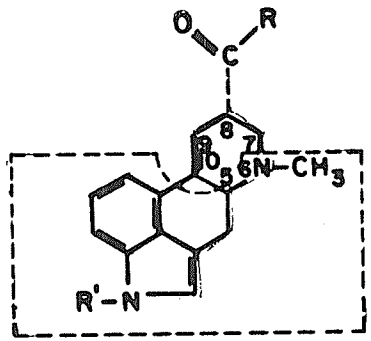
Figure 2. Ergot Alkaloids (Brazeau, 1970)

* The dotted enclosure indicates the tryptamine-like portion of the alkaloid

† The dihydrogenated derivatives differ only in being saturated at C 9 and C 10

Lysergic Acid and Amine Alkaloids *

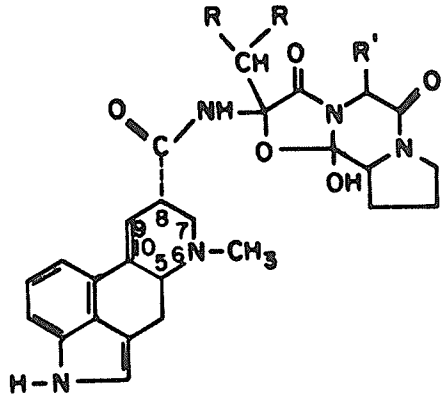
A.



Alkaloid	R	R'
Lysergic acid	$-OH$	H
Lysergic acid diethylamide	$-N(CH_2CH_3)_2$	H
Ergonovine (ergometrine)	$-NH-CH(CH_3)CH_2OH$	H
Methylergonovine	$-NH-CH(CH_2CH_3)CH_2OH$	H
Methysergide	$-NH-CH(CH_2CH_3)CH_2OH$	CH_3

Amino Acid Alkaloids †

B.



R=H	R=CH_3	R'
Ergotamine	Ergocristine	$-CH_2-C_6H_5$
Ergosine	Ergokryptine	$-CH_2CH(CH_3)_2$
	Ergocornine	$-CH(CH_3)_2$

Absorption, Breakdown and Excretion

Much of what is known about the metabolism of ergot alkaloids is a result of the medicinal use of these compounds. In general, alkaloids of higher molecular weight are poorly absorbed from the gastrointestinal tract. An effective oral dose requires 8 to 10 times as much alkaloid as an effective intramuscular dose and even then the resulting action is delayed and unpredictable (Brazeau, 1970; Nickerson, 1970). In the rat, 5 to 10% of a dose of radiolabelled ergotamine perfused, in situ, through the small intestine, is absorbed in the first 10 minutes (Franz et al., 1980). After 60 minutes the greater percentage still remains unabsorbed. Metabolic degradation of peptide ergot alkaloids apparently does not occur in the small intestine as degradation products are not detectable (Franz et al., 1980). Ergonovine, an amine alkaloid, is rapidly absorbed, however, and onset of action occurs within ten minutes (Brazeau, 1970).

The extraction and absorption of alkaloids from sclerotial tissue in the gastrointestinal tract has not yet been extensively studied. Balance experiments with pigs, fed freshly milled ergot at the 4% level w/w, have shown that 90% of the total alkaloid content may be absorbed; 70% from the stomach, the remainder from the small intestine (Whittemore et al., 1976). In ruminants such as sheep, ergotamine in solution and admininistered orally is far more toxic than an equivalent amount of the alkaloid administered in sclerotial tissue (Greatorex and Mantle, 1973). It has been suggested that rumen conditions during the active fermentation of pasture grass allow the most efficient extraction of alkaloids due to the rapid release of organic acids (Greatorex and Mantle, 1973). It should also be remembered that the possibility of microbial modification of the alkaloids

in the rumen exists, and that derivatives of either greater or lesser potency may be produced (Mantle, 1969).

Following absorption, ergot alkaloids are rapidly degraded in the liver (Brazeau, 1970; Nickerson, 1970). Clavines and amine alkaloids are metabolized mainly on the ergoline moiety while for peptide alkaloids the biotransformation occurs on the proline segment of the peptide moiety (Kiechel, 1979). The pathways of degradation may vary with species.

Ergot alkaloids have been isolated in most body tissues including the brain where until recently penetration of significant amounts had not been demonstrated.

Routes of excretion vary with the alkaloid and not apparently with the form of administration. Semisynthetic clavines are excreted mainly in urine while naturally occurring peptide alkaloids are excreted in bile. Lysergic acid and amine alkaloids are intermediate in character (Kiechel, 1979). Alkaloids present in fecal material may therefore be the result of a combination of incomplete absorption and biliary excretion of absorbed alkaloids, as suggested previously by Mantle (1968) and Whittemore et al. (1976).

Physiological Actions

The physiological activites of ergot alkaloids have traditionally been divided into three broad groupings based on the specific site of action (Brazeau, 1970; Nickerson, 1970; Van Rensburg and Altenkirk, 1974). These are outlined in table 3.

Peripheral effects are the result of direct stimulation of smooth muscle and include vasoconstriction, uterine contraction and an increase in peristaltic activity. All smooth muscle is affected (Van Rensburg

TABLE 2. Physiological Activities of Ergot Alkaloids (From Lorenz, 1979)

Central-nervous	Medulla oblongata	Lowered blood pressure, bradycardia
		Inhibition of vasomotor center and pressoreceptor reflexes
	Hypothalamus	Excitatory syndrome
		Mydriasis
		Hyperglycemia
		Hyperthermia
		Hyperreflexia
Neurohumoral	Myoneural junctions	Serotonin antagonism
		Adrenergic blockage
Peripheral-muscular	Blood vessels	Vasoconstriction
	Uterus	Uterine contraction

and Altenkirk, 1974).

Neurohumoral effects include 5-HT antagonism and adrenergic blockade and result from the interference, by ergot alkaloids with these amines at receptor sites of myoneural junctions.

At doses lower than those required to produce α-adrenergic blockade, ergot alkaloids may still have profound effects as a result of their actions on the CNS. Stimulation or inhibition of the medulla oblongata produces vomiting, bradycardia, lowered blood pressure and a decrease in the sensitivity of pressoreceptor reflexes while hyperglycemia, hyperrelexia, mydriasis and an impairment of temperature regulation result from some unspecified action on the hypothalamus.

More recently, the effects of ergot alkaloids have been examined with the emphasis on their actions at the level of specific receptor sites. Dopamine, noradrenalin and 5-HT are all structurally related to the ergoline ring (figure 1). In vitro binding studies suggest that ergot alkaloids have high affinities for receptors of these monoamines. Loew and Müller-Schweinitzer (1979) and Berde (1980) have reviewed the pharmacology of ergot. Amine alkaloids exhibit selective and high affinities for dopamine and 5-HT receptors at postjunctional receptor sites. At prejunctional sites they have a high affinity for α-adrenoceptors. Peptide alkaloids also display high affinity for α-adrenoceptors but only at postjunctional sites.

Affinity for a given receptor site and intrinsic activity varies with the alkaloid. Weber (1980) has hypothesized that a specific conformation of the alkaloid backbone is necessary for successful interaction with a receptor site. If this conformation is sterically hindered

in any way then the pharmacophore in the ergolene moiety is unavailable for any interaction to occur. Substituent side groups may enhance the interaction, sterically hinder it, or be redundant.

Originally it was believed that ergot alkaloids acted only as receptor antagonists. Stimulation of uterine and vascular smooth muscle was attributed to a direct action unrelated to either adrenoceptors or 5-HT receptors. Current evidence suggests that most ergot alkaloids are capable of acting as dualists (partial agonist/antagonist) at peripheral monoamine receptor sites. Specific behaviour depends on the concentration or dosage level, on the organ and on the species studied (Loew and Müller-Schweinitzer, 1979). Since the population of receptor sites to which they have access undoubtedly varies from organ to organ much of the wide range of biological activity of ergot alkaloids is now explainable.

Direct stimulation of vascular and uterine smooth muscle appears to be the result of an action on the same receptors involved in responses to catecholamines or 5-HT. Clark (1979) has reviewed cardiovascular responses to ergotamine, the most potent vasoconstrictor among the ergot alkaloids. Studies with isolated vessels have shown that ergotamine acts through α-adrenoceptors to stimulate constriction in veins. Constriction of arterial smooth muscle is due to the stimulation of 5-HT receptors.

Like ergotamine, ergonovine exerts its effect on coronary arteries primarily through 5-HT receptors (Müller-Schweinitzer, 1980; Sakanashi and Yonemura, 1980). It, however, is not nearly as potent a vasoconstrictor.

When ergotamine is administered there is an increase in vascular

resistance and systemic blood pressure. The increase in resistance is not uniform in all vascular beds and, within a single bed, veins may be constricted more than arteries (Clark, 1979). Lesions of the tunica intima can develop resulting in thrombi that may occlude smaller arteries (Brazeau, 1970). In humans, a decrease in muscle blood flow to the legs has been demonstrated following chronic overdoses of ergotamine tartrate (Leinonen, 1980). The effect is reversible if thrombosis has not yet occurred.

Under some conditions ergotamine may actually lower blood pressure. Two mechanisms have been implicated (see Clark, 1979). At low doses ergotamine may inhibit the release of transmitter substance from noradrenergic nerves. At higher doses preganglionic sympathetic nerve activity is diminished.

The uterine stimulating activity of ergot alkaloids is perhaps the oldest, medicinally exploited property of these compounds. All naturally occurring amine and amino acid alkaloids enhance basal tone and both frequency and amplitude of contractions (Berde, 1980). However, only at term is uterine muscle more sensitive than other smooth muscle. During the third trimester in humans relatively small amounts of alkaloid are capable of producing sustained contractions of the uterine wall. In early pregnancy dangerously large doses are required to elicit a similar response. Even then the effect is greater on the cervix than on the uterus (Van Rensburg and Altenkirk, 1974).

The mechanism of action seems to be one of direct stimulation via α-adrenoceptors. In vitro experiments with intact organs have demonstrated that the stimulating effect of ergot alkaloids can be

blocked with α-adrenergic blocking agents such as phenoxybenzamine. There is no relationship between the receptors involved in the uterotonic effect of oxytocin and receptors which mediate the response to ergot alkaloids (see Berde, 1980).

In the central nervous system ergot alkaloids exert many of their effects by receptor-mediated interactions affecting the synthesis of cAMP (Berde, 1980). Here, as in the periphery, most are capable of acting as dualists. U'Prichard (1980) has recently reviewed ergot-CNS receptor interactions. Experimentally, ergot alkaloids exhibit equal potencies in displacing ^{3}H-agonist or ^{3}H-antagonist ligand binding at α-adrenergic and 5-HT receptor sites. At dopamine sites they are slightly weaker inhibitors of agonist binding. Most block striatal, dopamine stimulated, adenylate cyclase activity while many also block cAMP production induced by noradrenalin or 5-HT. Some, however, appear to have a partial action in stimulating adenylate cyclase activity in the brain and retina.

Metabolic functions other than cAMP production are also disturbed. The stimulation of dopamine receptors on prolactin producing cells results in the suppression of hormone secretion. The mechanism of this suppression has been reviewed by Flückiger (1980). Secretion is reduced by a reduction in hormone granule extrusion and not by an immediate reduction of hormone synthesis. There is no evidence that an increase in cAMP is involved. Whether or not the hypophyseal action of the alkaloids is augmented by suppression of the prolactin releasing factor at the level of the hypothalamus has not been answered.

Alternatively, the stimulation or inhibition of pre- and post-junctional monoamine receptor sites may lead to a reduction of nervous

impulse flow. This explanation has been given by Corrodi et al. (1975) to account for the observed decrease in 5-HT release and turnover in 5-HT neurons following the in vitro administration of ergocornine. It is readily apparent that an action of this nature in either the medulla oblongata or hypothalamus could produce the effects listed earlier. For example, considering the role of hypothalamic monoamines in the integration of sensory input and mediation of temperature response (to be discussed later), it is not surprising that ergot alkaloids can cause a generalized impairment of temperature regulation.

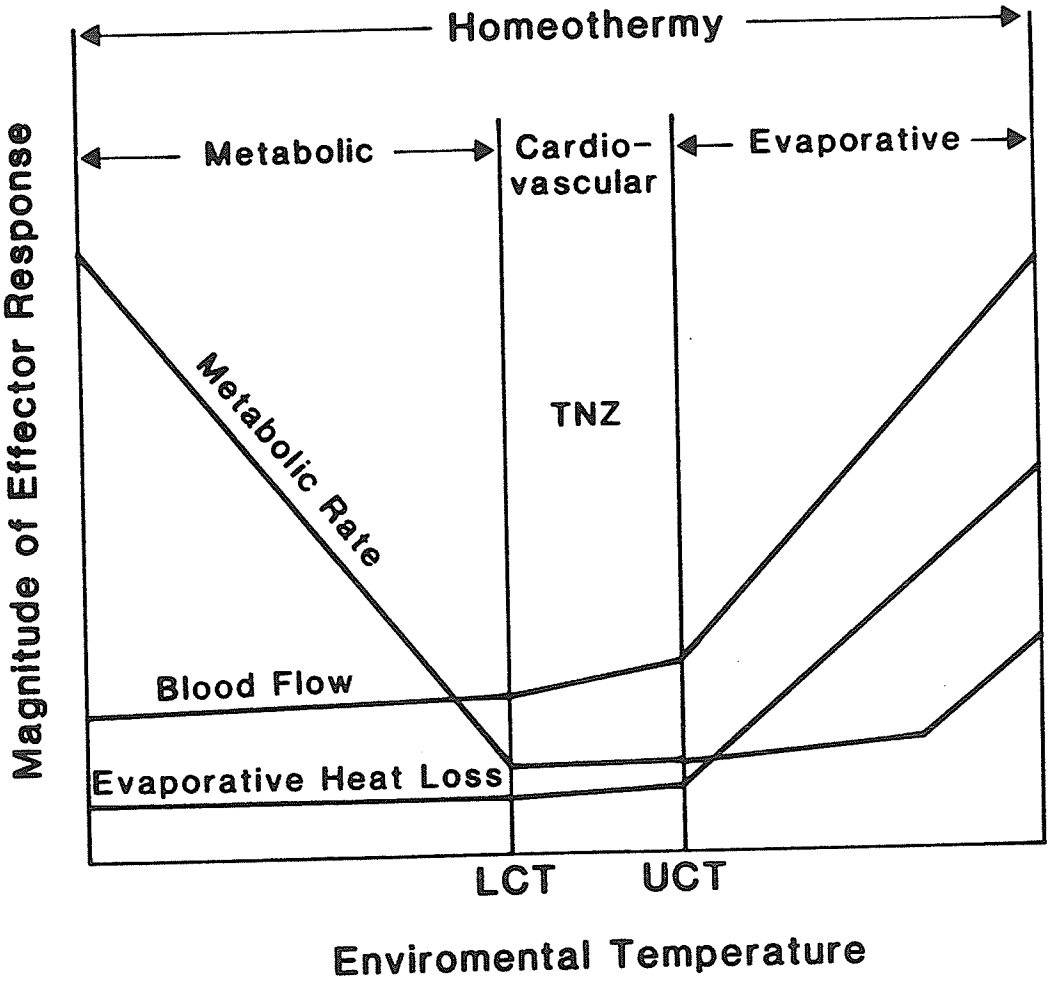
Vasomotor Function and Thermoregulation

In endothermic animals a relatively constant body temperature is maintained by balancing the rate at which heat is lost to the environment with the rate at which heat is gained through metabolic processes. A rise in body temperature can indicate either a rise in heat production or a decrease in heat loss. The converse is true of a decline in body temperature.

The thermoregulatory profile for a hypothetical endotherm is illustrated in figure 3. The thermoneutral zone (TNZ) represents the ambient temperature range of minimal energy expenditure for thermal regulation. It is within this range that vasomotor adjustments are made to regulate heat exchange between the body core and periphery and between the body surface and the environment.

The maintenance of heat flow away from the body is dependent upon the existence of an adequate thermal gradient. Under most conditions the gradient between the body surface and the environment is sufficient

Figure 3. General thermoregulatory profile for a hypothetical endotherm indicating primary effector reponses (Elizondo, 1977)


Homeothermy
Metabolic
Cardio-
vascular
Evaporative
Magnitude of Effector Response
Metabolic Rate
TNZ
Blood Flow
Evaporative Heat Loss
LCT
UCT
Enviromental Temperature

to ensure a continual net loss of heat from the body surface. The rate of this loss is dependent upon physical factors affecting conduction, convection and radiation. These include environmental "coldness" and the degree of thermal insulation provided by the body covering. Environmental "coldness" in turn is influenced by air temperature, wind velocity, precipitation and radiation exchange.

The deeper tissues of the body are unable to lose heat directly to the environment. Instead they rely on the continuous removal of endogenous heat by the circulating blood. The rate of heat flow from these tissues is dependent upon the extent and tone of the capillary bed, the rate of flow of the blood and on the temperature of the arterial supply (Bligh, 1973).

At the lower end of the thermoneutral zone the rate of heat loss from the body surface increases in accordance with physical principles as the ambient temperature declines. An animal's first response is to resist this increase in heat flow away from the body by increasing its thermal insulation. In terms of vasomotor adjustment, this may be accomplished by the constriction of blood vessels supplying the skin and extremities. Webster (1974) has defined the extremities as "those parts of the head and limbs which have little muscle or visceral tissue capable of producing heat <u>in situ</u>". Thus the anatomy of these regions dictates that they rely on their blood supply to provide heat. Constriction of the appropriate vessels results in a lowered surface and tissue temperature and a reduction in the gradient between the surface and the environment. Considering the high surface-to-volume ratio and the metabolic expense that would be involved in maintaining elevated limb temperatures in the cold, it is not surprising that

regional heterothermy is utilized as a major heat conserving mechanism.

If whole body conductance is measured as an index of vasomotor variability, it becomes apparent that a temperature exists below which conductance is minimal and constant, indicating a state of maximal peripheral vasoconstriction (Elizondo, 1977). This point corresponds to the point at which an increase in heat production is necessary to compensate for the increase in heat loss, and is termed the lower critical temperature (LCT).

At the upper end of the TNZ peripheral vasodilation occurs and thinly furred appendages and other body surfaces act as ports through which body heat can be lost. Blood flow is reduced to regions other than those directly concerned with the production of heat or its dissipation. As with vasoconstriction, a temperature exists above which the response is maximal and no longer effective in maintaining thermal balance. This is the upper critical temperature (UCT). At higher ambient temperatures evaporative cooling is generally utilized to increase heat loss.

Low Temperature

Peripheral Vasomotor Response. Skin temperatures of sheared sheep exposed to cool or cold environments have been measured in a number of studies. Joyce and Blaxter (1964) demonstrated that when sheep were exposed to air temperatures just above freezing, ear and leg temperatures fell to within 2 or 3°C of ambient. At air temperatures below 0°C no further cooling occurred. Sykes and Slee (1968, 1969) recorded an 8 - 10°C, 20°C and 20 - 25°C drop respectively in midside, ear and foot skin

temperature when sheep were exposed to 8°C. They attributed the fall in midside temperature to the direct effect of greater heat loss rather than to vasoconstriction (Sykes and Slee, 1968).

Webster (1966) exposed sheep to a sudden drop in ambient temperature and measured the time elapsed before re-establishment of thermal equilibrium. When the exposure temperature was 0°C or above, the skin temperature of the shanks cooled slowly to reach a steady state 3°C above ambient after about 120 minutes. The rate of cooling was independent of fleece length and the shape of the cooling curve depended upon the initial vasomotor tone of the limb. The fall in skin temperature of the shank following exposure was roughly exponential if the leg was initially vasoconstricted. If the leg was vasodilated, exposure resulted in a fairly rapid fall in skin temperature as vasoconstriction occurred, followed by a slower approach to equilibrium. When sheep were exposed to air temperatures below 0°C, approximately 90 minutes were required to attain the limit in shank cooling. In contrast to the pattern observed for skin temperature of the shank, the time taken for mean skin temperature of the trunk to equilibrate was dependent on the fleece length. When exposed to temperatures of 2°C, shorn sheep exhibited a rapid fall in skin temperature of the trunk, 90% of the total fall taking place within 10 minutes. When fleece depth was between 25 and 40 mm, 40 minutes were required to attain an equivalent proportion of the total response. As in the study by Sykes and Slee (1968) the implication is that the fall in mean trunk skin temperature is more a result of heat loss than decreased blood flow.

Three other areas that have been investigated as potential sites for regulating heat loss are the scrotum, the udder and the horns, when

present. The scrotum contains the pampiniform plexus which functions as a heat exchanger to keep the testes cooler than body temperature (Smith et al., 1978). This in itself leads to a reduction in heat loss from the scrotum. The additional saving to be had by employing extensive vasoconstriction in the scrotum during cold exposure might well be negligible and its seems likely that the specific temperature requirements of sperm production preclude its use.

The observation in the sheep that udder surface temperature does not change much with changing environmental temperature has led Smith et al. (1978) to suggest that, like the skin of the trunk, the skin of the udder is not under vasomotor control. Thompson (1980), however, was able to show that cold exposure significantly reduced blood flow to the skin of the udder, and to the teat, by approximately the same amount as it reduced flow to the skin of the leg. This reduction in flow was balanced by an increase in blood flow to adipose tissue such that total blood flow to the udder was unaffected. The author concluded that vasoconstriction in udder skin of the sheep is a mechanism for reducing heat loss in much the same way as it is in the skin of the leg. In goats, Thompson and Thomson (1977) have demonstrated that during lactation cold exposure may cause a significant decrease in total udder blood flow.

In the horns of the goat, it has been shown that vessels constrict in response to cold (Taylor, 1966), however, this constriction can be overridden by exercise. Four percent of the running heat production of the goat may be lost through the horns at 0°C. Cessation of exercise results in a transitory increase in flow before vasoconstriction once again sets in.

Counter Current Heat Exchange. A mechanism that has been postulated as an important factor in decreasing heat transfer from the extremities to the environment in conjunction with vasoconstriction is that of counter-current heat exchange. The operation of the heat exchange system has been summarized by Richards (1973) and Schmidt-Nielsen (1975). When the conservation of body heat is important, superficial veins in the limbs constrict and force blood to flow through deeper vessels lying adjacent to the arteries that supply the appendages. A large proportion of the heat contained in the blood is thus able to be transferred to the cooled blood returning from the periphery. Since the flows of warm and cool blood are in opposite directions, this type of heat exchanger is called a counter-current heat exchanger (Scholander and Schevill, 1955).

A steady state longitudinal temperature gradient may be reached after some time, depending on the conditions for heat exchange between the two vessels and on their length. The final result is that blood returning to the core has suffered less of a drop in temperature than would be the case in the absence of the heat exchange system. Since heat loss from the limbs is proportional to the difference in temperature betweeen the blood entering and leaving the limb, the counter-current effect represents a significant saving in heat loss not only from the limb but from the animal as a whole.

There are many reports in the literature of specific examples of this, and similar mechanisms. In the flippers of whales each artery is completely surrounded by veins in such a fashion that in a cold environment heat can only be transferred to the venous blood and not to the environment. Under warm conditions blood is shunted to superficial veins to facilitate heat dissipation (Scholander and Schevill, 1955).

In the sloth the artery to the foreleg splits into numerous small parallel vessels which intermingle with an equal number of veins. Scholander and Krog (1957) have demonstrated the effectiveness of this arrangement by immersing the foot of a sloth in ice water and measuring blood temperatures. Above the heat exchanger venous temperature is almost equal to core temperature. Below the heat exchanger blood temperatures drop off sharply.

The most effective heat exchange systems incorporate complex networks of small arteries and veins in place of parallel axial vessels. Such a system, called a rete mirabile provides a greatly enhanced area of contact across which heat transfer can occur. They are most notably found in the legs of aquatic and wading birds. Kahl (1963) was able to demonstrate a marked drop in leg surface temperature of the stork in the vicinity of the rete while Scholander (1955) showed that a gull placed with its feet in ice water for 2 hours lost only 1.5% of its metabolic heat production from the feet, an amount he considered insignificant.

Counter-current heat exchangers have also been attributed to most arctic mammals and birds (Scholander and Scheville, 1955), ungulates such as sheep (Webster and Blaxter, 1966) and even man (Thauer, 1963). However, it now seems likely that in many cases the observed longitudinal temperature gradients may have been the result of physical parameters affecting heat flow away from the limbs rather than the result of counter-current heat exchange. In a biophysical analysis of potential biological heat exchangers, Mitchell and Myers (1968) concluded that the usual anatomical arrangement of arteries and veins was not conducive to heat

transfer. They went on to add that only in specialized anatomical structures, such as the rete, where conductance between arteries and veins is high, could significant counter-current heat exchange occur. They dismissed entirely the existence of a heat exchanger in the forearm of a man or in the fluke of a porpoise but confirmed the significance of the system in the sloth.

This analysis has been largely ignored. In the opinion of Mitchell (1977), until such time as its shortcomings are made public, "one must conclude that countercurrent heat exchange cannot occur in animals, no matter how attractive the anatomy might appear".

Cold Induced Vasodilation. The temperature of the extremities in cold exposed endotherms is often very near freezing as a result of peripheral vasoconstriction and, in some cases, counter-current heat exchange. Protection of the tissues from damage by freezing is dependent upon very precise regulation of the blood supply to a degree that keeps their temperature above 0°C. Should the degree of chilling become sufficiently intense then the cold-induced vasoconstriction is released and replaced by cold-induced vasodilation (CIVD).

This phenomenon was first observed in 1930 by Lewis who described fluctuations in skin temperature of a human finger immersed in ice water. The initial response of rapid cooling to about 1°C was followed by a spontaneous rewarming after 10 to 15 minutes of exposure. Skin temperatures rose to 8 to 10°C and then began an exponential descent. The pattern repeated itself in a rhythmic fashion which Lewis termed the "hunting phenomenon".

Cold induced vasodilation has also been observed in the ox (Ingram and

Whittow, 1963), the cat (Schwinghamer and Adams, 1969), the rat (Brown and Baust, 1980) and in many other species, but not always in the form described by Lewis. Webster and Blaxter (1966) found that in sheep exposed to subzero temperatures, the temperature of the extremities was maintained above freezing by several mechanisms. In the ear classical "hunting" reactions were observed. Also in the ear, and occasionally in the limbs, single sharp increases in surface temperature were noted. These could take either of two forms; a sudden rise in temperature of about 15°C followed by an exponential decline over a period of 50 minutes, or a small, slower rise of less than 5°C which lasted under 20 minutes. Finally, at temperatures below -5°C, blood flow in the limbs increased continuously in proportion to heat loss and surface temperatures were maintained above freezing without marked variation. Similar observations have been made by Sykes and Slee (1968), Slee (1968), and Myer and Webster (1971), the latter reporting that these different patterns of CIVD were characteristic of individual sheep and were not attributable to breed differences or previous thermal history.

Cold induced vasodilation may occur synchronously in contralateral extremities as has been found in oxen (Ingram and Whittow, 1963) and rats (Brown and Baust, 1980), or asynchronously as has been observed in sheep (Myer and Webster, 1971).

High Temperature

Peripheral Vasomotor Response. In mammals the epidermal vasculature consists of a rich system of capillary loops supplied by arteries and arterioles lying deeper in the dermis. In some cutaneous regions, most

notably on the extremities, there are anastomoses connecting the arterial and venous supplies, bypassing the capillary loop. These arteriovenous anastomoses (AVAs) are muscular and well innervated and are capable of rapidly altering the amount of blood flowing through the extremities. The importance of thinly furred appendages as ports through which heat may be lost has already been noted and it seems likely that AVAs function in regulating heat exchange with the environment.

Whittow (1962) observed large differences in the surface temperatures of the extremities of the ox between environments that differed only 5° within the range of -5° to 25°C. He concluded that these differences were due to variation in the amount of blood flow to the extremities. In contrast, surface temperature of the trunk changed by relatively small amounts. Above an ambient temperature of 25°C changes in the skin temperature of the extremities were relatively small and parallelled changes on the trunk, indicating that a maximal response had been obtained.

Hales (1973a, b) has used radioactive microspheres to demonstrate the relationship between AVA blood flow and similar temperature patterns of the extremities in the conscious sheep. The fraction of the total cardiac output passing through AVAs greater than 15 μm in diameter ranges from 0.6% to 4.0% in a thermoneutral environment. This value rises maximally to 14.5% and 22.2% in mild and severe heat respectively. Heat exchange may occur within the open AVAs or, more likely, within the veins after the blood has passed through these low resistance pathways (Hales, 1974).

Paradoxically, the openings of AVAs during heat stress, may in

some instances be induced by local cold stimuli. In animals that pant, protrusion of the tongue during open mouth breathing causes a marked reduction in surface temperature. Kronert et al. (1980) have shown that a stepwise reduction in the tongue surface temperature of the dog, from 40°C to 28°C, results in an increase in total lingual blood flow that is entirely due to an increase in flow through mucosal AVAs. This increase in flow aids in the dissipation of heat via evaporative cooling.

The relatively small drop in temperature required to produce dilation of AVAs in the tongue contrasts with the reported effects of local cold stimuli on AVAs of the extremities. Only during a very strong local cold stimulus do these dilate. Replacement of cold induced vasoconstriction by cold induced vasodilation has already been discussed.

At ambient temperatures greater than body temperature normal heat flow patterns are reversed and the body gains heat from the environment. Hales (1973a, b) noted a decline in the percentage of cardiac output passing through AVAs in the sheep during the advanced stages of severe heat stress. Concomitantly, a decline in blood flow to the skin of the extemities was observed. Hammel (1968), in his review of temperature regulation, noted that species as divergent as the jackrabbit and the ostrich were capable of reducing blood flow to the extremities at high ambient temperatures. This apparent heat induced vasoconstriction may represent an attempt to minimize the uptake of heat from the environment under these conditions or may be the result of changes in the concentrations of circulating metabolites and hormones (Hales, 1974).

Carotid Rete. Many animals that rely on panting to cool themselves exhibit an unusually high tolerance to heat stress. Sheep, for example,

maintain a lower core temperature in response to a standard heat exposure than most other mammals and do not exhibit neurological signs of hyperthermia until rectal temperature is quite high. Lee (1950) reported that sheep were able to tolerate rectal temperatures of up to 43.3°C before signs of muscular weakness and incoordination were evident. Mice and rats exhibit similar symptoms at a rectal temperature of 41.7°C (Baker and Hayward, 1968b).

It has generally been assumed that the temperature of central arterial blood is the same as that of the blood perfusing the brain. Hemingway et al. (1966) were able to show that brain temperatures in sheep were 0.2 - 0.5°C less than rectal temperatures. In the African ungulate, Thomson's gazelle, central arterial blood temperatures have been observed to rise from a normal 39°C to 44°C following 5 minutes of running at a speed of 40 km/h (Taylor and Lyman, 1972). In the same experiment, brain temperature did not rise above 41°C, a level considered safe.

This dissociation of brain temperature and deep body temperature is a result of the presence of an arterial plexus called the carotid rete, interposed between extracranial and intracranial arteries. In the cat, this rete lies extracranially in a venous lake associated with the pterygoid plexus of veins. In the sheep, goat, ox and pig, the carotid rete lies intracranially in the cavernous sinus (Baker and Hayward, 1968a). The blood flowing through the rete is cooled by the venous blood returning from the nasal mucosa and the skin of the head (Baker and Hayward, 1968a, b) or by blood draining from the horns when present (Taylor, 1966). Vasoconstriction of the nasal mucosa and of the skin of the head results in an increase in cerebral arterial blood temperature

and in the temperature of the brain (Baker and Hayward, 1968a, b). Air blown artificially across the nasal mucosa of anaesthetized sheep produces the opposite effect, a drop in brain and cerebral blood temperatures. This selective cooling via counter-current heat exchange blood perfusing the brain is a major factor in the regulation of hypothalamic temperature. As such it should be considered in any discussion of thermoregulation in animals possessing a carotid rete.

Distribution of Cardiac Output

Changes in peripheral vascular resistance in response to changing ambient temperature must be compensated for by reciprocal alterations in resistance of deep vasculature. Thompson (1977) has reviewed the effects of cold exposure on the relative distribution of cardiac output. In a cool neutral environment, when vasoconstriction occurs but shivering does not occur, total peripheral resistance increases, cardiac output falls and blood pressure remains constant. Hepatic portal blood flow probably increases. At temperatures low enough to elicit shivering, resistance to flow through muscles and some other tissues falls to the extent that total peripheral resistance falls. Concomitantly, an increase in cardiac output (CO) and blood pressure occurs. In man the increase in CO is due to an increase in stroke volume with little increase in rate. In many animals, such as cattle and sheep, the opposite is true. Heart rate increases and stroke volume may even decrease slightly.

Regions that receive an increase in blood flow during cold exposure include skeletal muscle, heart, diaphragm, white and brown adipose tissue, kidneys, adrenal glands, viscera and liver. Expressed as a percentage of cardiac output, the muscular organs receive a greater

fraction, the internal organs and skin a smaller fraction.

The changes in distribution of cardiac output during mild heat stress are the exact opposite to those described above with respect to some regions. Hales (1973b, c) found a decline in the percentage of CO perfusing non-respiratory muscle from 14% to 7% when conscious sheep were exposed to an environmental temperature of 40°C. Blood flow to skin of the extremities, to respiratory muscle, to the naso-buccal region and through AVAs all increased. The fraction of CO distributed to the heart, brain and spinal cord fell slightly. Absolute values of cardiac output did not change significantly between a thermoneutral environment and conditions of mild heat stress.

During the advanced stages of severe heat stress, Hales (1973b) observed a decline in the percentage of CO passing through the skin and through AVAs greater than 15 μm in diameter. Blood flow to the naso-buccal region which had increased only slightly during mild heat stress increased greatly during severe heat stress to allow for heat loss via panting.

Nervous Control

Vasomotor adjustments to regulate heat flow between the body core and periphery and between the body surface and the environment occur over the relatively narrow range of environmental temperatures that delineate the thermoneutral zone. The mechanisms which mediate changes in peripheral vasomotor tone (PVMT) must therefore be sensitive to small changes in either peripheral temperature, core temperature, or both.

Thauer (1963) has reviewed temperature induced circulatory adjustments in man. Blood flow through the extremities increases with increasing

local temperature and conversely, decreases with decreasing local temperature. Numerous investigations have revealed that, apart from an initial period of maximal vasodilation, the above response can be demonstrated following sympathectomy. A possible explanation for these local effects has been described by Richards (1973). The activation of temperature sensitive nerve endings results in an impulse passing towards the spinal cord but, instead of completing a normal reflex arc through the CNS, the impulse travels anti-dromically down other branches of the same fibre to receptors on or near cutaneous arterioles. The arterioles then respond as if normal sympathetic innervation were intact. This phenomenon is termed an axon reflex.

Alternatively, a myogenic mechanism, whereby intrinsic tone is sensitive to small changes in temperature, may function in mediating local temperature effects. In the rabbit, a segment of the facial vein has been identified which apparently acts as a temperature sensitive sphincter controlling the distribution of blood between superficial and deep venous drainage systems in the head and neck (Winquist and Bevan, 1980). Although richly endowed with sympathetic nerve endings, myogenic tone of the segment responds to very small changes in temperature, independent of sympathetic innervation. Clearly, further experimentation is needed to elucidate the interaction of these mechanisms and to investigate the possibility of a contribution of vasodilator metabolites and reduced blood viscosity (Elizondo, 1977).

Local effects of temperature on peripheral blood flow may be modified by the general thermal state of the body. As environmental temperature increases, blood flow through the human hand increases regardless of local temperature (see Thauer, 1963). When vasoconstrictor

tone is diminished by whole body heating, local heating effects are potentiated. Similarly, local cooling effects are potentiated if the body is cooled.

The response of cutaneous blood vessels to local temperature change is not restricted to the area of the skin heated or cooled. This interaction of local and whole body temperature effects is mediated by sympathetic nerve fibres to the skin and possibly to sweat glands. An area of controversy exists regarding the mode of action and relative role of vasoconstrictor and vasodilator nerves in the control of peripheral vasomotion. Experiments designed to determine whether vasodilation occurs actively or passively as the result of an interruption of sympathetic vasoconstrictor tone have indicated that the mechanism differs from site to site and perhaps between species.

In man, sympathetic blockade produces a rise in skin temperature of the hand equivalent to that induced by indirect whole body heating. In contrast, the skin of the forearm exhibits a secondary rise in temperature in response to whole body heating that is abolished by sympathetic blockade. These results indicate that in the hand cutaneous vasodilation occurs due to a decrease in vasomotor tone while in the forearm it involves both passive and active processes (Thauer, 1963).

The release of bradykinin by sweat glands has been suggested by some authors as the mechanism responsible for forearm cutaneous vasodilation. According to this theory only the glands themselves are directly innervated and controlled by sympathetic cholinergic nerve fibres. Elizondo (1977) has reviewed a number of experimental observations which contradict this hypothesis and has discounted it entirely.

Stimulation of specific sites in the hypothalamus of the dog evokes

cutaneous and muscular vasodilation of the hindlimb (Lang et al., 1976). The existence of vasodilator fibres in the sympathetics of skeletal muscle has also been demonstrated in the cat, fox, jackal and mongoose but not in the rabbit, hare, badger, skunk, lemur or monkey (Uvnäs, 1966). These tracts are cholinergic in some instances (Uvnäs, 1966) but evidence is accumulating to suggest that other neurotransmitters may be involved. Treatment with atropine eliminates the vasodilatory response to stimulation of some hypothalamic sites in the dog but not all (Lang et al., 1976). Other dilator responses are abolished by intra-arterial administration of dopamine and antihistamine antagonists (Lang et al., 1976). Brody (1966) concluded, as a result of his experiments on neurohumoral mediation of active reflex vasodilation, that the evidence strongly implicates histamine as the neurotransmitter released from sympathetic nerves during vasodilation.

It has already been noted that exposure of any part of the body to a change in temperature results in changes in circulation, not only locally, but to other regions as well. This observation implicates the involvement of neural reflexes, initiated from both peripheral and central thermal receptors, in the mediation of changes in PVMT. The role of hypothalamic thermal receptors in vasomotor adjustment to temperature change has been investigated in several species including the ox (Ingram and Whittow, 1962) and the pig (Baldwin and Ingram, 1968). In general, a change in hypothalamic temperature results in blood flow changes proportional to the ambient temperature. At a given ambient temperature, graded changes in hypothalamic temperature produce graded changes in peripheral blood flow. In the squirrel monkey, skin of both the foot and the tail vasodilates at discrete ambient temperature thresholds

(Lynch et al., 1980). Raising the preoptic/anterior hypothalamic temperature lowers these thresholds which are approximately linear functions of central and mean skin temperatures.

Cutaneous blood flow may also be influenced by central temperature receptors outside the hypothalamus. Ingram and Legge (1971) measured blood flow to the tail of conscious pigs while subjecting the hypothalamus, the spinal cord and the skin to graded changes in temperature. They concluded from their observations that peripheral blood flow is influenced by ambient temperature, mean trunk skin temperature, hypothalamic temperatue and spinal cord temperature in addition to local temperature of the site under consideration. Furthermore, it appeared as if each temperature exerted its effect independent of the others. In a warm environment where skin temperatures were elevated, cooling of the spinal cord or hypothalamus did not result in complete peripheral vasoconstriction. Similarly, heating of the spinal cord or hypothalamus did not result in vasodilation if the environment was cool and skin temperature low. The simplest explanation of these results seems to be that input from a variety of peripheral and central temperature receptors is fed into an integrating centre where the appropriate vasomotor response is determined.

Hypothalamic Monoamines and Thermoregulation

The initial discovery in 1954 that the hypothalamus contains relatively large amounts of the monamines adrenalin, noradrenalin (Vogt, 1954) and 5-HT (Amin et al., 1954) has since led to a number of studies designed to elucidate their role in thermoregulatory processes. Feldberg and Myers (1963, 1964a, b) began this line of investigation by injecting

microgram doses of the catecholamines and 5-HT into the lateral cerebral ventricles of the cat. Each of these substances caused regular and predictable changes in body temperature indicating a specific action rather than the non specific disturbance of brain function that might be expected. Administration of adrenalin or noradrenalin resulted in a fall of rectal temperature brought about by peripheral vasodilation and a reduction in heat production. The opposite effect was observed with 5-HT. Shivering, vasoconstriction and piloerection led to a rise in rectal temperature.

In a later experiment (Feldberg and Myers, 1965), similar results were achieved by injecting the monamines directly into the anterior hypothalamus whereas injections into other regions of the cat brain had no temperature effects. Evidence of this nature prompted the authors to suggest that temperature regulation is achieved by a balance in the relative rates of release of catecholamines and 5-HT in the anterior hypothalamus. The implication was that these substances were acting as neurotransmitters.

Additional evidence in support of this hypothesis has been reviewed by Feldberg (1970), Hellon (1972), and Bligh (1973). In the hypothalamus these monoamines are found localized in terminal nerve endings and enzymes for their synthesis and destruction have been identified. Experimentally, drugs which interfere with synthesis, storage, release and inactivation of the catecholamines or 5-HT have effects on the control of body temperature. Finally, it has been observed that perfusate from the anterior hypothalamus of a cold or heat stressed animal contains monoamines and, when infused into the anterior hypothalamus of another animal at a thermoneutral temperature, is capable of eliciting

a thermoregulatory response.

Although the exact pathways of temperature regulating neurons in the hypothalamus have not yet been anatomically defined experimental evidence suggest that responses to heat and responses to cold are controlled by two distinct sets of neurons with a reciprocal inhibitory link (see Bligh, 1973). The specific role of the putative transmitter adrenalin, noradrenalin and 5-HT, in these pathways, appears to differ between species and has been the subject of much debate. Feldberg (1970) in his review of the literature identified four broad groupings of response to monoamines administered centrally at a neutral ambient temperature (figure 4). Catecholamines were hypothermic in the cat, dog and monkey but hyperthermic in rabbits and sheep. In the rat and mouse both an increase and a decrease in body temperature had been observed following administration. In oxen and goats catecholamines had no effect.

All groups except the first responded to 5-HT with a fall in temperature although in rabbits and sheep the fall was slight and somewhat inconsistent. In the cat, dog and monkey 5-HT was hyperthermic.

In some instances supposed species differences may be attributable to differences in dose level or the prevailing ambient temperature during testing. A large, single dose of a monoamine might cause synaptic blockade rather than excitation while a response observed at room temperature need not necessarily be the response observed above or below the thermoneutral zone. If, for example, a monoamine induced hypothermia at a neutral temperature by activating heat loss pathways, the response would be attenuated or abolished at temperatures where these pathways were already active.

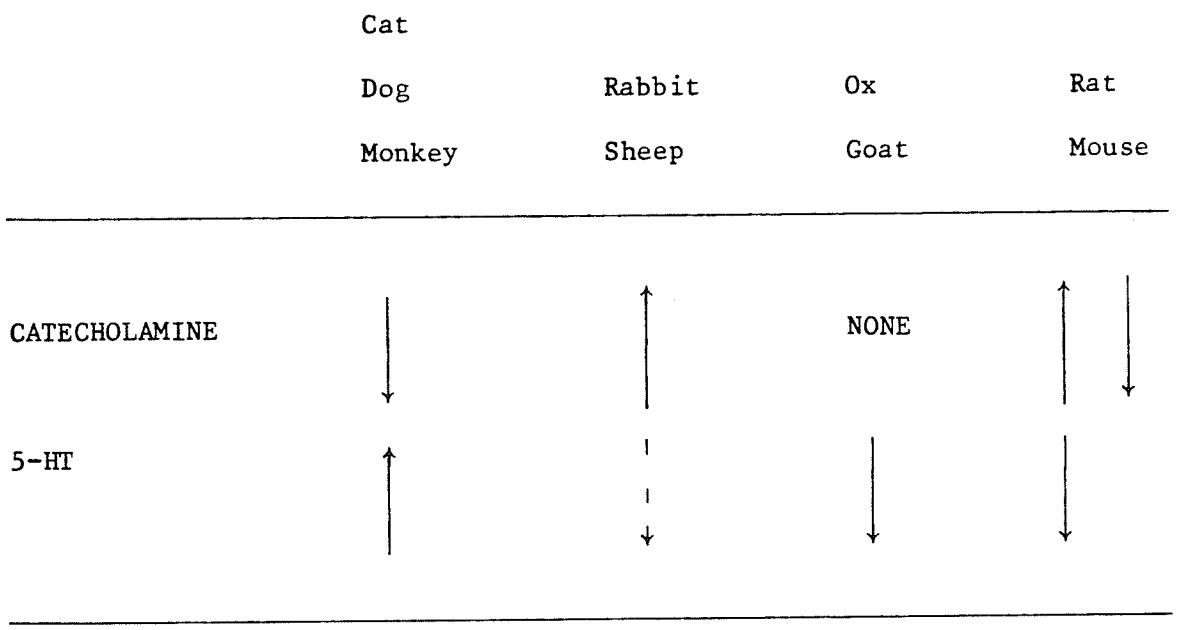


Figure 4. Effect of catecholamines and 5-hydroxytryptamine (5-HT), injected into the cerebral ventricles or directly into the anterior hypothalamus, on body temperature, in different species. (From Feldberg, 1970)

The relationship between ambient temperature and central transmitter substances, in sheep, has been thoroughly investigated and expressed in terms of a simple neuronal model (figure 5). Bligh et al. (1971) showed that an intracerebroventricular (ICV) injection of 5-HT at low ambient temperatures caused an increase in heat loss by panting and a decrease in heat production from shivering. At high ambient temperatures the animals were already panting and 5-HT was without effect. Blood vessels in the ear became dilated if they had been constricted at the time of the injection and if the test temperature was within or slightly below the thermoneutral zone.

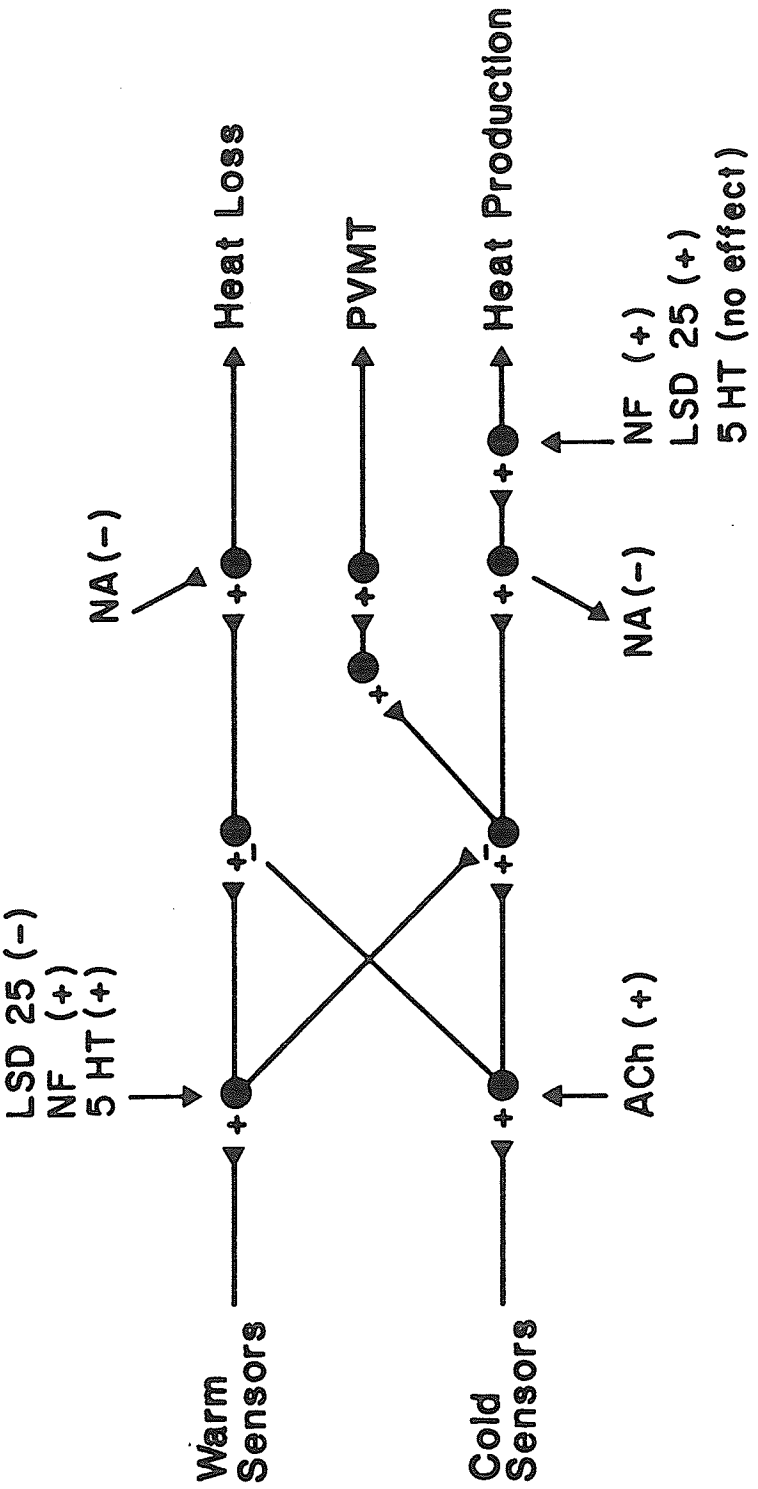
In contrast, ICV carbachol (CCh), a cholinomimetic substance, resulted in decreased respiratory evaporative heat loss at high temperatures and increased heat production via shivering at low ambient temperatures.

Blood vessels in the ear constricted if they had been dilated and if temperature was within or slightly above the thermoneutral zone.

Noradrenalin exhibited a general inhibitory action on the prevalent thermoregulatory activity at any given temperature and had no effect on PVMT. In a later study, Tollerton et al. (1978) confirmed most of these findings but demonstrated that, like carbachol, ICV NA caused constriction of dilated ear vessels within the thermoneutral zone.

The above findings have been interpreted as being indicative of the role of 5-HT as the on-line neurotransmitter between warm sensors and heat loss effectors, and the role of acetylcholine (ACh) as the excitatory neurotransmitter on the heat production pathway. Their dual actions strongly suggest a crossed inhibitory link, perhaps utilizing γ-amino-butyric acid as the transmitter substance (Bligh et al., 1979b).

Figure 5. A neuronal format to illustrate apparent sites of exitatory (+) or inhibitory (-) actions of 5-hydroxytryptamine (5-HT), norferfluramine (NF), lysergic acid diethylamide (LSD-25), acetylcholine (ACh) and noradrenalin (NA) on the heat loss and heat production pathways in the hypthalamus of the sheep (From Bligh et al., 1979b)


Warm Sensors
Cold Sensors
LSD 25 (-)
NF (+)
5 HT (+)
NA (-)
ACh (+)
Heat Loss
PVMT
Heat Production
NA (-)
NF (+)
LSD 25 (+)
5 HT (no effect)

Originally, NA was thought to act at these synapses but results obtained by Bligh et al. (1977) support the alternative hypothesis that noradrenergic inhibitory pathways originate outside the hypothalamus and do not form part of the direct link between thermosensors and thermoregulatory effectors. The excitatory action of ICV NA on PVMT represents a specific action on a separate pathway that may be due to the stimulation of the excitatory function of another monoamine. It has not been demonstrated that PVMT is under the control of centrally released endogenous noradrenalin (Tollerton et al., 1978).

The concept that a serotonergic synapse exists only on the heat loss pathway has been compromised by the observation that centrally administered lysergic acid diethylamide (LSD-25), a partial agonist/antagonist of central 5-HT receptors, and norfenfluramine (NF), a drug believed to release endogenous 5-HT, stimulates heat production (Bligh et al., 1979a). This effect persists following ICV NA suggesting that if a serotonergic synapse exists on thp heat production pathway it is beyond the point at which NA exerts its inhibitory action. Since ICV 5-HT does not produce an increase in heat production, the action of LSD-25 and NF may reflect the involvement of another indoleaminergic system or differential accessibility of synaptic sites.

EXPERIMENTAL OBJECTIVES

Peripherally, ergot alkaloids are known to stimulate vascular smooth muscle via an action on the same receptors involved in responses to catecholamines or 5-hydroxytryptamine (5-HT). Constriction of the vessels in the extremities results in a lowered surface temperature and a reduction in the gradient between the surface and the environment. This action of ergot alkaloids could lead to a reduction in the rate at which heat is lost to the environment and present a challenge to strict homeothermy at temperatures which would otherwise be considered within the thermoneutral zone. It has also been suggested (Greatorex and Mantle, 1973) that vasoconstriction due to cold exposure and the disturbance of peripheral circulation due to ergot alkaloids are additive and could lead to the progression of a lameness/gangrenous syndrome or frostbite.

Centrally, ergot alkaloids may still produce profound effects at doses lower than those required to produce significant peripheral effects. The stimulation or inhibition of pre- or post-junctional monoamine receptor sites may lead to a reduction of nervous impulse flow. Corrodi *et al*. (1975) have observed a decrease in 5-HT release and turnover in 5-HT neurons following the *in vitro* administration of ergocornine. In sheep and cattle it has been postulated that 5-HT is the principle on line neurotransmitter between warm sensors and heat loss effectors. Interference with the release of 5-HT in this pathway could result in decreased heat tolerance but would probably not affect thermoregulation in the cold.

The objective of the present study was to assess the extent of any impairment in temperature regulation in ewes resulting from long term, low level ingestion of ergot sclerotia. The relationship between thermoregulatory response to a range of environmental temperatures and three levels of dietary ergot was also examined in an attempt to determine the relative significance of central and peripheral effects of ergot alkaloids on temperature regulation.

MATERIALS AND METHODS

Animals

Sixteen yearling ewes comprising 4 Finnish Landrace, 4 Suffolk and 8 crossbreds were allocated to four treatment groups of equal size. Each group was balanced to contain 2 crossbred animals and one each of Finnish Landrace and Suffolk. All animals weighed between 28 and 38 kg at the beginning of the experiment. During the course of the experiment one crossbred ewe died and was not replaced. A post mortem examination was performed by the Manitoba Department of Agriculture.

Diet

A complete pelleted ration containing 36.8% barley, 36.7% wheat, 20% chopped hay (50:50 brome:alfalfa), 5% molasses and 0.5% each of rock phosphate, trace mineral mix and vitamin premix (A, D and E) formed the basis of the diet of each treatment group. Ground ergot sclerotia were added to the diets of groups I, II and III to constitute 0.07%, 0.14% and 0.28% by weight respectively. Group 0 was designated as the control group.

An analysis of the ergot by high pressure liquid chromatography was conducted by J.C. Young (Agriculture Canada, Ottawa, Ontario). The alkaloid spectrum determined by this analysis is presented in table 3 along with data from the analysis of heat treated ergot included for comparative purposes.

TABLE 3. Comparison of alkaloid content of ground, and heated and ground wheat ergot.[1]

ALKALOID	Sample A[2]	Sample B[3]
Number of Estimations[4]	2	2
Total (%)	0.191	0.188
	% of Total Alkaloids[5]	
Ergocristine	24.07	18.59
Ergocristinine	21.84	20.79
Ergocornine	7.74	5.37
Ergocorninine	5.98	5.77
Ergocryptine	7.11	4.90
Ergocryptinine	6.30	6.16
Ergotamine	6.32	7.98
Ergotaminine	8.16	8.56
Ergometrine	4.24	7.62
Ergometrinine	1.62	2.38
Ergosine	3.14	3.64
Ergosinine	4.63	3.01

[1]Wheat ergot was purchased from Northern Sales, Ltd., Winnipeg. (Original source North Dakota)
[2]Ground wheat ergot.
[3]Wheat ergot heated for 18 hours at 60°C and then ground.
[4]Twenty sclerotia were ground for each estimation.
[5]Analysis conducted by J.C. Young (Agriculture Canada, Ottawa, Ontario)

Management and Housing

The sheep were maintained in individual adjoining pens under continuous lighting of medium intensity. Water and cobalt-iodized salt block were offered ad libitum. Animals were fed 1200 grams of the pelleted ration once daily between 8:30 and 9:30 a.m. Feed not consumed the previous day was removed and weighed. Feeding began in May and continued for 28 weeks following a two week adjustment period to the pelleted ration. On occasion it became necessary to offer small amounts of alfalfa hay to animals with digestive disturbances.

During weeks 4 through 10 inclusive, respiratory rates of resting animals were recorded once weekly, between 1:30 and 3:30 p.m., by observation of flank movements with the aid of a stopwatch. Rectal temperatures were measured during the same time period with a glass-mercury thermometer inserted a distance of 12 cm.

Temperature Tolerance Tests

Experimental Procedure

Temperature tolerance tests were carried out in a controlled environment (CE) chamber at 3 different environmental temperature ranges between the 19th and 26th weeks of feeding. Mean fleece length of each treatment group during this period is indicated in table 4. All sheep were subjected to mild heat (27.7°C - 31.5°C, mild cold (0°C - 4.5°C), and thermoneutral conditions (16.0°C - 23.6°C) in random order. Due to malfunction of the environmental chamber cooling system, dry bulb air temperature cycled about the set point within the range specified above. Humidity was not controlled.

Each test was conducted in the following manner. Two sheep

TABLE 4. Means and standard errors for fleece length.[1]

Treatment Group	Number of Sheep	Fleece Length (cm)
0	4	2.27 ± 0.14
I	4	2.17 ± 0.14
II	4	1.95 ± 0.14
III	3	2.08 ± 0.16

[1]Fleece length was measured at 18 sites on the trunk of each animal.

were weighed and loosely chained in stalls within the CE chamber at approximately 6:00 p.m. the evening before the test. Any unconsumed feed from the day's ration was transferred to the chamber and water was offered ad libitum. Lighting in the chamber was continuous and of medium intensity. Ambient temperature was maintained overnight within the thermoneutral range.

At 8:30 a.m. feed and water were removed, the ventilated face mask and all thermocouples and electrodes were attached and the chamber was set for the desired temperature range. Upon reaching this range, the animals were allowed one hour to attain thermal equilibrium. Measurements were then taken on a one hour alternating basis over a period of 4 hours with each hour being divided into 10 minute intervals. Thus each animal was continuously monitored for a total of 2 hours per test. All recording equipment was located outside the chamber.

Following completion of the test the CE chamber was reset for thermoneutral conditions and the animals were returned to their regular stalls to be fed. Two more animals were then weighed and transferred to the chamber.

On two occasions equipment failure necessitated leaving sheep a second night in the chamber before repairs were made and the test conducted. On two other occasions thermoneutral tests were conducted in an adjacent animal holding room (4.5 m x 2.85 m) under conditions similar to those within the CE chamber.

Temperature Measurements

Temperatures were recorded with 24 s.w.g. copper-constantan thermocouples cemented to depilated skin under small pieces of adhesive

tape. All thermocouples were connected to a 6 channel Speedomax potentiometric chart recorder (Leeds and Northrup, North Wales, Pa.) with a temperature range of -10°C to 45°C. Surface temperatures were measured on the ear, shoulder, midside, rump and shank. Rectal temperatures were determined by means of a thermocouple inserted to a depth of 12 cm.

All skin temperatures were measured on the side of the animal toward the centre of the chamber where air flow was most uniform. It was assumed that under identical air flow conditions temperatures on the opposite side of the animal would not be significantly different.

Mean trunk skin temperatures were calculated as the arithmetic mean of the 3 trunk measurements. Mean body skin temperatures were obtained by multiplying the mean trunk skin temperature by 0.9 and the leg skin temperature by 0.1. These coefficients represent the proportions of fleece covered and hair covered areas respectively (Blaxter et al., 1959).

Regional and mean body skin thermal circulation indices (TCIs) were calculated using the formula of Burton and Edholm (1955):

$$TCI = \frac{T_{sk} - T_a}{T_R - T_{sk}}$$

where; T_{sk} = skin temperature

T_a = ambient temperature

T_R = rectal temperature

All measurements are in degrees Celsius.

Heart Rate and Respiratory Rate Measurements

Heart rates were measured for 2 minutes at the beginning of each 10 minute interval by means of 3 surface electrodes pinned to

skin of the chest and back connected to a physiograph (Narco Bio-Systems, Inc., Houston, Texas) for electrocardiogram recordings.

Respiratory rates were measured at the same time by observation of flank movements with the aid of a stopwatch. Each animal was recorded as lying or standing for covariate analysis.

Heat Production Measurements

Heat production was estimated by measuring oxygen consumption using an open circuit ventilated mask technique similar to that described by Young et al. (1975). Masks consisted of a cylindrical plastic frame 12 cm in diameter fitted with an adjustable neoprene rubber cuff to provide an air seal and comfortable fit for the animal. Inlet and outlet tubes 2.5 cm in diameter protruded from the bottom of the mask in a downward direction. Canvas harness straps riveted to the frame served to hold the mask in place. Animals had been previously accustomed to wearing the mask.

Air was drawn through the face mask by a vacuum pump at an average rate of 33 l/min. On the inspiratory side of the mask tygon tubing was attached to a 22.5 l reservoir to ensure that expired air driven against the direction of flow was not lost. Tubing from the outlet side led through a port in the CE chamber to a cold moisture trap and a large gas rotometer. Pressure in the system was monitored with a mercury filled manometer. Thermistor probes were used to record the temperature inside the cold trap and in the line adjacent to the rotometer. Air flow through the system was held constant during a measurement period.

A subsample of 200 ml/min was drawn from the main line through a column containing anhydrous $CaSO_4$ and glass wool by a small diaphragm

vacuum pump. Oxygen concentration was determined by passing this sample through a Beckman OM-14, polarographic oxygen analyser (Beckman Instruments, Inc., Schiller Park, Illinois) connected to a single pen, Heathkit model EUW-20A servo recorder, (Heath Company, Benton Habour, Michigan) fitted with an AC/DC offset circuit. The analyzer was calibrated at the beginning and end of each measurement period against room air (20.94% O_2) and a prepared mixture of compressed cylinder gas containing 16.4% O_2 and 83.6% N_2.

The volume of O_2 consumed was calculated using the formula of Depocas and Hart (1957). Heat production was estimated by using a value of 20.44 kJ per litre as the energy equivalent of oxygen (McLean, 1970). Final values are expressed as $kJ \cdot kgBW^{-0.75} \cdot min^{-1}$.

Withers (1977) has examined the error inherent in calculating V_{O_2} if CO_2 is not absorbed from the air prior to both the flowmeter and oxygen analyser. In an open mask system the rate of air flow from the mask is constant and determined by the downstream vacuum pump. The respiratory quotient (RQ) of the animal within the mask and evaporative water loss alter the inlet flow rate. If water vapour is removed from the air and CO_2 is not, as in the present experiment, an error of ± 3% is introduced. Withers (1977) has provided a means of correcting for this error by incorporating RQ into the calculation. Respiratory quotient may be determined by periodically employing a CO_2 absorbent in the system. However, in ruminants a tremendous amount of CO_2 is produced in the digestive tract by anaerobic bacterial fermentation. This extra-metabolic CO_2 is indistinguishable from the CO_2 produced via respiratory metabolism and RQ, therefore, has no metabolic significance (Brody, 1945). For this reason the heat

production values calculated during the present study are not intended to be taken as absolute values but rather, only as comparative values within the conditions of this experiment.

Tissue Insulation

Tissue insulation was calculated using the formula of Joyce and Blaxter (1964):

$$I_T = \frac{(T_R - T_{sk})}{H_p}$$

where; T_R = rectal temperature in degrees Celsius

T_{sk} = skin temperature in degrees Celsius

H_p = heat production in Mcal $m^{-2} \cdot d^{-1}$

Units have been converted such that final values are expressed as $°C \cdot m^2 \cdot min \cdot kJ^{-1}$.

Surface area was estimated according to the formula of Brody (1945):

$$A = 0.12 \times BW^{0.57}$$

where; A = area in m^2

BW = body weight in kg.

Cutaneous Moisture Loss

An attempt was made to measure cutaneous moisture loss gravimetrically by means of an unventilated capsule containing anhydrous $CaSO_4$ in fine mesh bags. The capsule was secured to the skin of the back with rubber cement. The technique was found to be unsatisfactory and was abandoned.

Ancillary Heat Tolerance Tests

Experimental Procedure

Observations made during the first series of temperature tests seemed to indicate that, in some cases, respiratory rates, heart rates and rectal temperatures were unduly elevated during exposure to mild heat. Sheep rely largely on panting to cool themselves at ambient temperatures above their UCT. For this reason ancillary heat tolerance tests were conducted without the face masks to determine if high humidity within the masks was interfering with evaporative cooling and creating an environment more stressful than that anticipated on the basis of ambient temperature. These tests were carried out immediately following completion of the first series in an animal holding room measuring 4.25 m x 2.85 m.

Four sheep, one chosen randomly from each treatment group, were loosely chained in stalls within the holding room at approximately 6:00 p.m. the evening before the test. Unconsumed feed from the day's ration was transferred to the holding room and water was offered ad libitum. Lighting and temperature in the room were similar to that in the CE chamber.

At 8:30 a.m. feed and water were removed, all thermocouples and electrodes were attached and space heaters were set to bring ambient temperature (measured 1 m above floor level) to 30°C ± 2°C. Animals were allowed 1 hour to attain thermal equilibrium after this set point had been reached. Measurements were then taken over a two hour period, each hour being divided into 15 minute intervals. All recording equipment was located in an adjacent recording room.

Following completion of the test, the animals were returned to their regular stalls, the room was allowed to cool and 4 more animals were transferred.

Temperature, Heart Rate, and Respiratory Rate Measurements

Rectal temperature, heart rate, and respiratory rate were measured in the same manner as described for the temperature tolerance tests with the exception that heart rate of every animal was monitored continuously over one 15 minute interval during each hour.

Respiratory rates were recorded for all animals at the beginning of each 15 minute interval and activity (lying or standing) was noted for covariate analysis.

Statistical Analysis

Analysis of variance and covariance were conducted for all data using the General Linear Models (GLM) procedure of the Statistical Analysis System (SAS Institute, Inc., Cary, N.C.). The GLM procedure utilizes the least squares principle to fit linear models.

Data from the temperature tolerance tests were analysed as a split-plot design with complete block changeover. The level of ergot in the feed was blocked by breed and each feed X breed cell was subdivided into 3 temperature treatments. Temperature treatments were administered in random order and repeated measurements were taken within each treatment. Mean values of each parameter from the first and second hour were used in this analysis. Breed and feed mean squares were tested against the breed X feed interaction mean square while temperature, breed X temperature, and feed X temperature mean squares were tested against the three way interaction mean square. The mean square for hour was tested against the combined

mean squares of all the remaining interactions. A sample anova table is included in Appendix A.

Similarly, feed intake and pre-test respiratory rate and rectal temperature data were blocked by breed. Within each feed X breed cell measurements were repeated on a weekly basis. Breed and feed mean squares were tested against the two way interaction mean square while the mean squares for week, breed X week and feed X week were tested against the 3 way interaction mean square. A sample anova table is included in Appendix A.

Data from the ancillary heat test was analysed in exactly the same manner as that described for feed intake with hourly means replacing weekly measurements.

Tests of the significance of the difference between means were made using a Student-Neuman Keul test (Snedecor and Cochran, 1967).

The level of probability accepted as being significant for all analyses was $P<0.05$.

RESULTS

General

Ergot sclerotia were well tolerated at all dietary levels apart from recurring bouts of diarrhoea which lasted up to 4 weeks in some sheep. Symptoms of muscular incoordination, lameness and general malaise were never observed. Post mortem examination of the crossbred ewe from group III (0.28% ergot), which died during the eleventh week of feeding, failed to reveal any indication of ergotism. Veins, arterioles and lymphatics in the gut wall appeared morphologically normal. Capillaries in tissues from the lower limbs contained blood and seemed to be patent. Overall body condition was good. A few disseminated abscesses throughout the body with a particularly large one in the pharyngeal region implicated a generalized bacterial infection as the most likely cause of death.

Feed intake and pre-test respiratory rate and rectal temperature data are summarized in table 5. The level of dietary ergot had no significant effect on feed intake ($P>0.05$) although the group receiving the highest level of ergot consumed an average of 95.2 $g \cdot d^{-1}$ less than the control group. This observation is contrary to reports by Dinnusson et al. (1971) and Greatorex and Mantle (1973). Inclusion of molasses in the diet may have reduced the effect of ergot on palatability.

Respiratory rate was unaffected by ergot in the diet under the temperature conditions prevalent in the animal holding area. During

TABLE 5. Effect of dietary ergot on feed intake and pre-test respiratory rate and rectal temperature (T_R). (Mean ± standard error of the mean)

Group	Ergot Level (%)	Feed Intake ($g \cdot d^{-1}$)	Respiratory Rate ($resp \cdot min^{-1}$)	T_R (°C)
0	0.00	1,114 ± 38	147.7 ± 4.9	39.8 ± 0.1
I	0.07	1,089 ± 37	150.8 ± 4.9	40.0 ± 0.1
II	0.14	1,077 ± 37	144.6 ± 4.9	40.0 ± 0.1
III	0.28	1,019 ± 43	149.9 ± 5.7	40.2 ± 0.2

the time period in which respiratory rate and rectal temperature were measured, ambient temperature fluctuated between 28.8°C and 26.4°C, a range probably toward the upper end of the thermoneutral zone for these animals considering their relatively high respiratory rates. A slight but not significant ($P>0.05$) trend in rectal temperature was observed, T_R increasing with increased dietary ergot. Both respiratory rate and T_R varied from week to week as ambient temperature increased or decreased.

When the data were grouped by breed across all treatments, significant differences were noted with regard to T_R. For this analysis the crossbred ewes were divided into two groups based on the percentage of Finnish Landrace in their ancestry. Group CBF contained 4 animals with a minimum of 25% Finnish Landrace in their ancestry. Group XB contained 3 animals without any Finnish Landrace in their ancestry. These two groups had the highest mean rectal temperatures at 40.4 ± 0.1°C and 40.1 ± 0.2°C respectively, but, were not significantly different. Rectal temperature was significantly lower ($P<0.05$) at 39.5 ± 0.1°C in the purebred Finnish Landrace ewes. Suffolks were intermediate with a T_R of 39.9 ± 0.1°C.

Temperature Tolerance Tests

Temperature Measurements

Table 6 presents regional and mean body skin temperatures, and rectal temperature during exposure to mild cold, mild heat and thermoneutral conditions. Individual hourly means for ear, trunk, shank and rectal temperature are included in Appendix B. In general responses were similar at all dietary levels of ergot. Thermal

TABLE 6. Effect of dietary ergot on regional and mean body skin temperatures ($T_{\overline{sk}}$) and rectal temperature (T_R) during exposure to mild cold (MC), thermoneutral conditions (N) and mild heat (MH). (Mean ± standard error of the mean)

	Ergot Level in Feed (%)											
	0.00			0.07			0.14			0.28		
	Exposure Range			Exposure Range			Exposure Range			Exposure Range		
	MC	N	MH	MC	N	MH	MC	N	MH	MC	N	MH
Ear	7.9 ±2.2	26.4 ±2.4	38.6 ±2.4	9.7 ±2.4	35.0 ±2.2	37.4 ±3.6	5.6 ±2.6	32.5 ±3.1	36.0 ±2.4	5.0 ±2.6	29.7 ±2.8	36.4 ±2.8
Trunk	27.0 ±1.1	31.7 ±1.1	37.1 ±1.1	25.0 ±1.1	32.4 ±1.1	36.5 ±1.1	25.6 ±1.1	32.9 ±1.1	37.1 ±1.1	24.5 ±1.2	32.9 ±1.2	37.0 ±1.4
Shank	29.4 ±1.6	33.2 ±1.6	36.4 ±1.7	22.0 ±1.8	33.2 ±1.7	37.0 ±2.0	21.5 ±1.7	33.4 ±1.6	36.2 ±1.6	19.4 ±1.8	30.5 ±2.3	36.7 ±2.0
$T_{\overline{sk}}$	26.3 ±0.8	31.8 ±0.8	37.0 ±0.9	26.3 ±0.9	32.8 ±0.9	36.5 ±1.1	24.9 ±0.9	32.9 ±0.8	36.9 ±0.8	24.0 ±1.0	34.0 ±1.2	36.9 ±1.1
T_R	39.1 ±0.2	39.2 ±0.3	40.0 ±0.3	39.7 ±0.3	39.4 ±0.3	39.8 ±0.3	39.5 ±0.3	39.2 ±0.3	40.3 ±0.3	39.3 ±0.3	39.6 ±0.3	39.9 ±0.4

Source of Variation	Ear	Trunk	Shank	$T_{\overline{sk}}$	T_R
Breed (B)	N.S.*	N.S.	N.S.	N.S.	N.S.
Feed (F)	N.S.	N.S.	N.S.	N.S.	N.S.
Temperature (T)	0.0001**	0.0001	0.0001	0.0001	0.01
B X T	N.S.	N.S.	N.S.	N.S.	N.S.
F X T	N.S.	N.S.	N.S.	N.S.	N.S.
Hour	N.S.	N.S.	N.S.	N.S.	N.S.
Covariate	N.S.	N.S.	N.S.	N.S.	N.S.

* Nonsignificant ($P>0.05$)
** Level of significance

equilibrium was established with regard to all sites prior to commencement of recording and differences between first and second hour were not significant ($P>0.05$). The covariate coefficient for time spent standing was also not significant ($P>0.05$) and the means in table 6 are therefore unadjusted. While under thermoneutral conditions, it was not uncommon for individual sheep to alter the vasomotor state of the ear or limb being monitored and a wide range of skin temperatures were recorded from these sites. The number of animals exhibiting a change in the degree of vasoconstriction seemed to be consistent from group to group.

A slight though not significant ($P>0.05$) trend was observed in ear surface temperature during exposure to both mild cold and mild heat. In the cold, values for sheep receiving the two highest levels of ergot were 2.5°C to 2.9°C lower than the values for sheep receiving the control ration. In mild heat, temperatures were 2.2°C to 2.6°C lower.

Similarly, mean body skin and trunk skin temperatures in group III (0.28% ergot) were 2.3°C and 2.5°C lower, during cold exposure, than mean body skin and trunk skin temperatures in group 0. The differences were not significant ($P>0.05$).

Shank skin temperature and rectal temperature were unaffected by the level of ergot in the feed. During cold exposure, ear, trunk and shank skin temperatures were 28 - 31°C, 10 - 13°C and 15 - 17°C lower, respectively, than during exposure to mild heat. Mean body skin temperatures were depressed by 10 - 13°C. The relatively small drop in mean trunk temperature was probably a result of increased heat loss rather than vasoconstriction (Sykes and Slee, 1968).

At no time during cold exposure was there any evidence of classical CIVD in either the ear or the shank. In the ear, however, surface temperature often exhibited a slow rise of less than 5°C which lasted for 20 to 30 minutes. This occurred in all groups but only as ambient temperature closely approached 0°C.

When the data were grouped by breed, rectal temperature was the only parameter in which breed differences approached significance ($P<0.07$). Surprisingly, the Suffolks, who had been intermediate during the pretest feeding period, exhibited the highest rectal temperature at 40.0 ± 0.1°C averaged across all ambient temperature exposures. This was largely due to an apparent intolerance to mild heat exposure. Mean rectal temperature in all other groups was 39.4 ± 0.1°C.

Thermal Circulation Indices and Tissue Insulation

Regional and mean trunk skin thermal circulation indices (TCIs) were calculated and are presented in table 7. These values represent the ratio of external to the internal component of specific insulation expressed as temperature gradients. Externally, insulation is afforded by the fleece and the air/fleece interface. Internally, insulation is provided by the tissues of the body. As long as thermal equilibrium exists between the subject and the environment and there are no changes in external insulation, any change in the value of the index reflects a change in internal insulation. This would imply a change in blood flow to the superficial tissue. A change in skin temperature resulting from the direct physical effect of ambient temperature does not change the ratio of external to internal insulation and therefore does not alter the index.

During the present experiment, thermal equilibrium was established,

TABLE 7. Effect of dietary ergot on regional thermal circulation indices (TCIs) and tissue insulation (I_T) during exposure to mild cold (MC), thermoneutral conditions (N) and mild heat (MH). (Mean ± standard error of the mean)

	Ergot Level in Feed (%)											
	0.00			0.07			0.14			0.28		
	Exposure Range			Exposure Range			Exposure Range			Exposure Range		
	MC	N	MH	MC	N	MH	MC	N	MH	MC	N	MH
TCI_{ear}	0.18 ±1.37	1.73 ±1.58	7.09 ±1.46	0.54 ±1.58	5.54 ±1.46	10.45 ±2.23	0.07 ±1.58	2.44 ±1.94	2.04 ±1.46	0.06 ±1.58	2.47 ±1.73	3.21 ±1.73
TCI_{trunk}	2.08 ±0.57	2.18 ±0.66	2.65 ±0.61	1.90 ±0.66	2.10 ±0.61	1.78 ±0.66	1.75 ±0.57	2.43 ±0.57	2.74 ±0.57	1.46 ±0.77	2.21 ±0.66	2.79 ±0.72
TCI_{shank}	0.90 ±0.50	4.08 ±0.58	3.16 ±0.54	1.10 ±0.58	2.66 ±0.54	2.57 ±0.64	1.40 ±0.54	2.92 ±0.50	2.10 ±0.50	1.02 ±0.58	1.39 ±0.71	2.53 ±0.64
I_T ($°C \cdot m^2 \cdot min \cdot kJ^{-1}$)	2.564 ±0.164	1.819 ±0.189	0.790 ±0.175	2.575 ±0.189	1.383 ±0.175	0.783 ±0.207	2.953 ±0.175	1.480 ±0.164	0.844 ±0.164	2.956 ±0.189	1.188 ±0.231	0.749 ±0.207

Source of Variation	TCI_{ear}	TCI_{trunk}	TCI_{shank}	I_T
Breed (B)	N.S.*	N.S.	N.S.	N.S.
Feed (F)	0.01**	N.S.	N.S.	N.S.
Temperature (T)	0.01	N.S.	0.01	0.0001
B X T	N.S.	N.S.	0.05	N.S.
F X T	N.S.	N.S.	N.S.	N.S.
Hour	N.S.	N.S.	N.S.	N.S.
Covariate	N.S.	N.S.	N.S.	0.03

* Nonsignificant ($P>0.05$)
** Level of significance

with regard to all sites, prior to commencement of recording (see previous section). The covariate coefficient for time spent standing was not significant ($P>0.05$) and it was assumed that external insulation on the ear, trunk and shank was unaffected by the limited postural changes which occurred during each test period.

Exposure to mild heat resulted in thermal circulation indices for the ear (TCI_{ear}) that were 20 - 50 times greater than during exposure to mild cold. Thermal circulation indices for the shank were typically 1.5 to 3.5 times greater while TCIs for the trunk remained relatively unchanged.

A significant (P 0.01) ergot effect on TCI_{ear} was observed (Figure 6) that appeared to be due to a large reduction of the index in those groups receiving 0.14% and 0.28% ergot, during exposure to mild heat. The feed X temperature interaction, however, was not significant ($P>0.05$).

The level of dietary ergot had no effect ($P>0.05$) on TCIs for the trunk or the shank although TCI_{shank} did exhibit a slight decrease with increased ergot during exposure to both mild heat and thermoneutral conditions.

Breed differences were not evident but a significant (P 0.05) breed X temperature interaction, with regard to TCI_{shank}, was noted (Figure 7). Exposure of the Finnish Landrace ewes to mild heat resulted in an increase of the index over the values observed during exposure to thermoneutral conditions. In the Suffolks and both groups of crossbred sheep the index declined.

While thermal circulation indices provide a useful measure of changes in regional skin blood flow, tissue insulation (I_T) was determined to provide a more accurate measure of change in the overall ability to resist heat loss (Table 7). Individual hourly means of H_p are included in Appendix B. In general, responses to the three

Figure 6. The effect of dietary ergot on ear thermal circulation indices (TCIs) averaged across all ambient temperature exposures

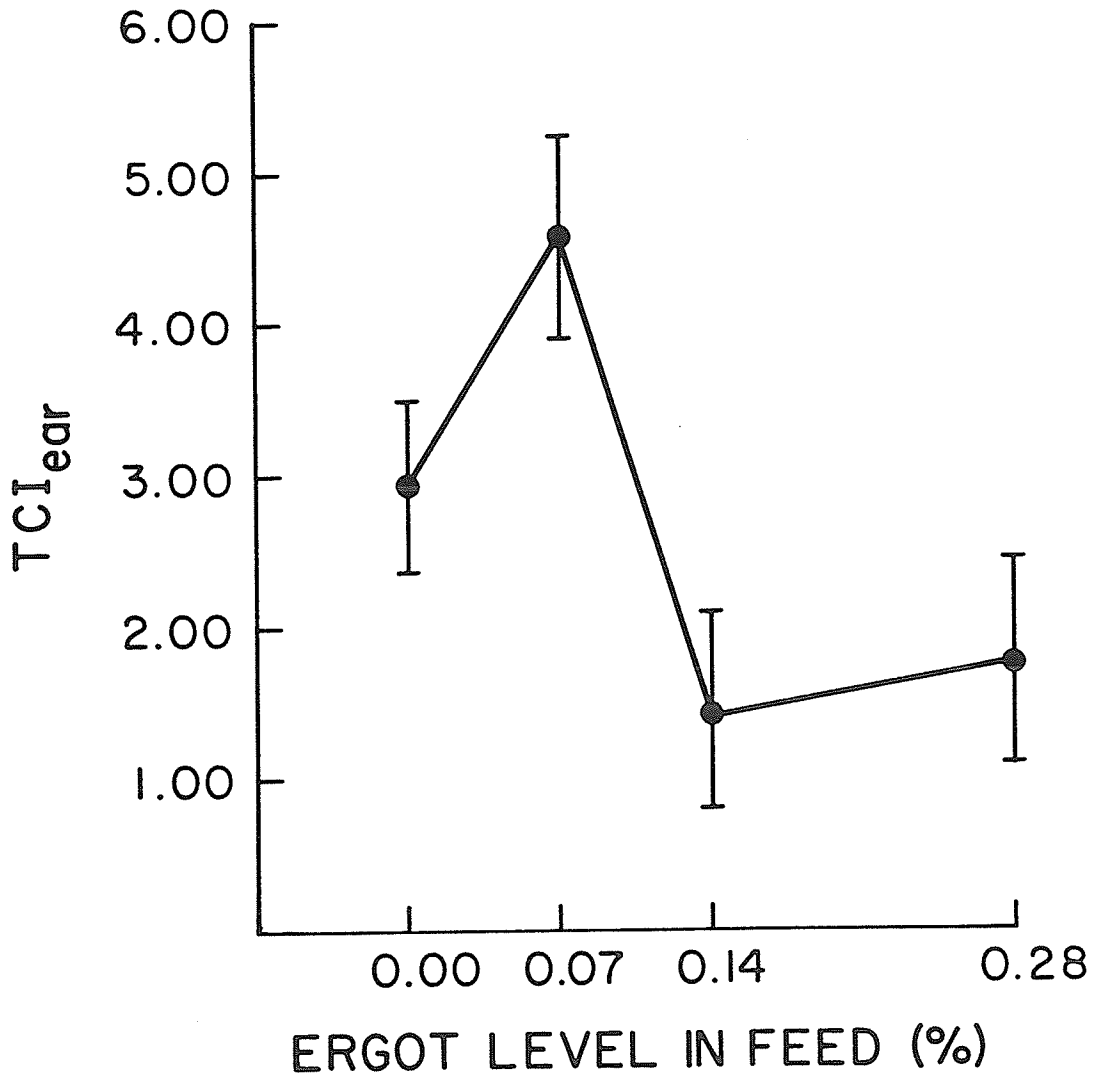
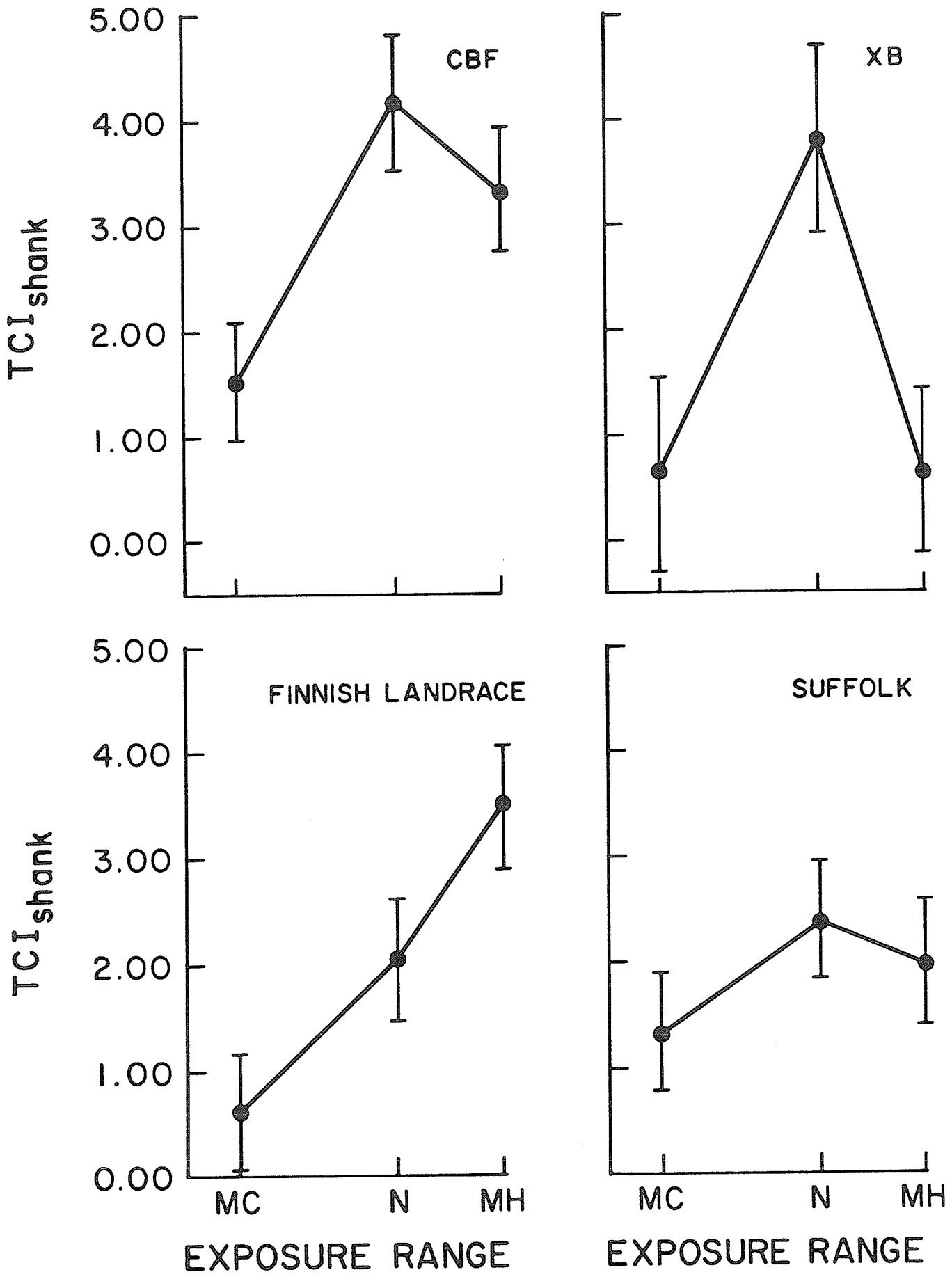

6.00
5.00
4.00
3.00
2.00
1.00
TCI ear
0.00
0.07
0.14
0.28
ERGOT LEVEL IN FEED (%)

Figure 7. The Effect of Breed on TCI_{shank} during exposure to mild cold (MC), thermoneutral conditions (N), and mild heat (MH)


5.00
4.00
3.00
2.00
1.00
0.00
TCI shank
CBF
XB
FINNISH LANDRACE
SUFFOLK
MC
N
MH
EXPOSURE RANGE

temperature ranges were similar at all dietary levels of ergot. Insulation values were highest in mild cold and lowest during exposure to mild heat, reflecting changes in blood flow to superficial tissue. A slight trend was observed during exposure to mild cold. Mean insulation increased with each successive increase in the level of ergot to a value of 15% higher than that for the controls, but, the difference was not significant ($P>0.05$).

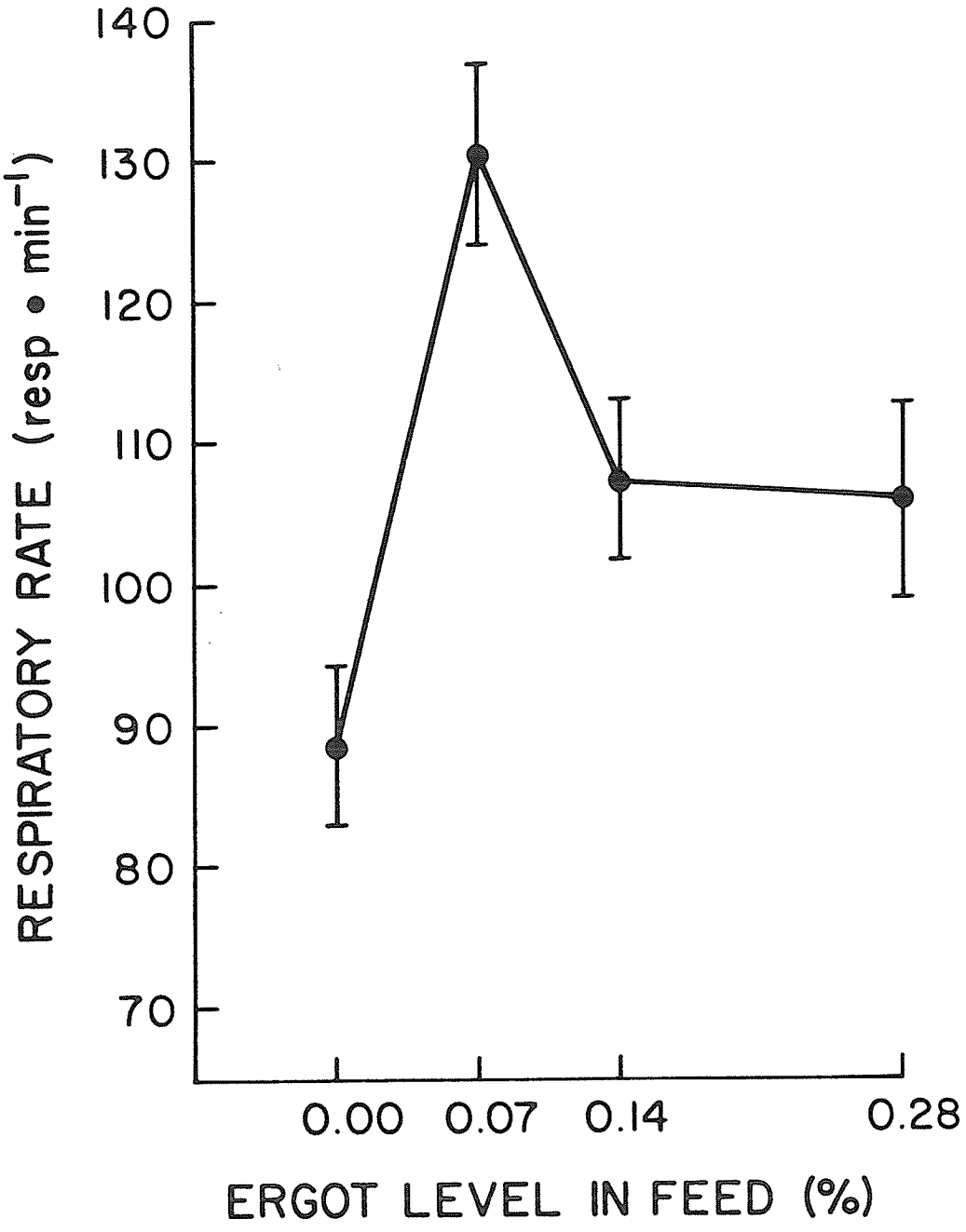
The covariate coefficient for time spent standing was significant ($P<0.03$) for tissue insulation. Standing resulted in a slight decrease in I_T values, but, since no main effect or interaction differences were revealed by covariate analysis, the means presented in table 7 are unadjusted.

Respiratory Rate, Heart Rate and Heat Production

The effect of ergot on respiratory rate when averaged across all ambient temperature exposures is illustrated in figure 8. Inclusion of 0.07% ergot in the diet resulted in an increase ($P<0.05$) in mean respiratory rate of 42 respirations$\cdot$min^{-1} over that of the control group. At higher levels of ergot mean respiratory rates were intermediate and not significantly different ($P>0.05$) from either the control sheep or those in group I.

During exposure to mild heat the rapid shallow panting observed in the first two groups was replaced by slower deeper panting in the groups receiving 0.14% or 0.28% ergot (Table 8). Under thermoneutral conditions a pattern similar to that of the pooled data was observed while, during cold exposure, respiratory rates were virtually identical.

Figure 8. The effect of dietary ergot on respiratory rate (RR) averaged across all ambient temperature exposures


140
130
120
110
100
90
80
70
RESPIRATORY RATE (resp • min⁻¹)
0.00
0.07
0.14
0.28
ERGOT LEVEL IN FEED (%)

A highly significant ($P<0.0002$) reduction in respiratory rate occurred during the second hour of all ambient temperature exposures (Table 8). This may reflect a progressive calming of each animal following the initial trauma of having the face mask and electrodes attached, although metabolic rates were not lowered during the second hour as might be expected if such were the case.

Heart rate and heat production were unaffected by ergot in the diet (Table 8). The covariate coefficient for time spent standing was significant ($P<0.01$) with regard to heat production, but, as the analysis of covariance did not alter the level of significance of either main effect or interaction differences, the means presented in table 8 are unadjusted.

Breed differences were noted with respect to heat production and respiratory rate but not heart rate. Figure 9 illustrates the magnitude of the differences between breeds for both parameters. As with rectal temperature, the Suffolks exhibited the highest values attaining a mean respiratory rate of 133 respirations$\cdot min^{-1}$ and a mean heat production of $0.308 \cdot kJ \cdot kgBW^{-0.75} \cdot min^{-1}$. The two groups of crossbred ewes had the lowest values while the group of Finnish Landrace ewes were intermediate.

A significant ($P<0.02$), but, highly suspect, breed X temperature interaction was observed with regard to heat production. The XB group of crossbred ewes displayed unusually low values during exposure to mild heat. It should be remembered that this group contained only 3 animals and as such would be more susceptible to bias resulting from a failure, during one test, in the respiratory gas collecting and analysis system.

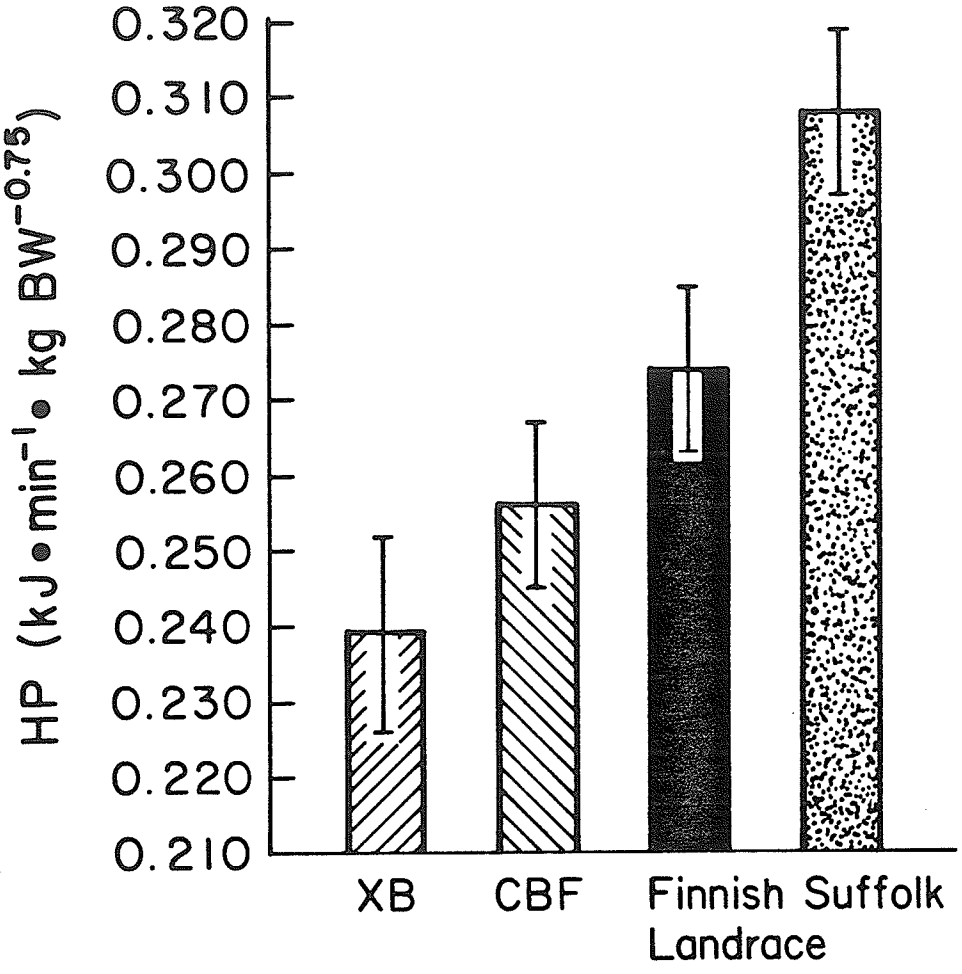
TABLE 8. Effect of dietary ergot on respiratory rate (RR), heart rate (HR) and heat production (HP) during exposure to mild cold (MC), thermoneutral conditions (N) and mild heat (MH). (Mean ± standard error of the mean)

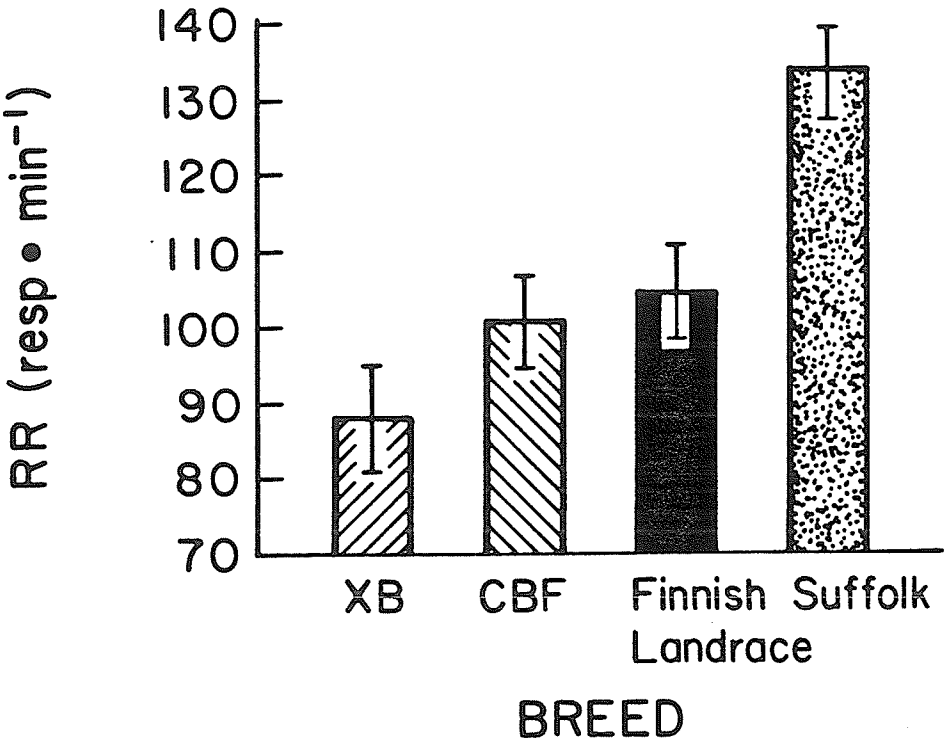
	Ergot Level in Feed (%)											
	0.00			0.07			0.14			0.28		
	Exposure Range			Exposure Range			Exposure Range			Exposure Range		
	MC	N	MH	MC	N	MH	MC	N	MH	MC	N	MH
RR (resp • min^{-1})	32.4 ±15.0	53.9 ±15.0	192.3 ±16.0	37.7 ±15.0	154.9 ±16.0	212.1 ±16.0	33.9 ±15.0	97.6 ±15.0	109.5 ±15.0	24.2 ±17.0	126.9 ±17.0	179.2 ±19.0
HR (beats • min^{-1})	71 ±6	61 ±5	74 ±6	66 ±5	72 ±5	74 ±6	68 ±5	63 ±6	78 ±6	63 ±6	67 ±7	70 ±8
HP ($kJ \cdot min^{-1} \cdot kgBW^{-0.75}$)	0.297 ±0.013	0.212 ±0.013	0.247 ±0.014	0.297 ±0.013	0.285 ±0.013	0.278 ±0.014	0.292 ±0.013	0.253 ±0.013	0.257 ±0.013	0.313 ±0.015	0.278 ±0.015	0.246 ±0.017

Source of Variation	RR	HR	HP
Breed (B)	0.01*	N.S.**	0.05
Feed (F)	0.05	N.S.	N.S.
Temperature (T)	0.0001	0.05	0.05
B X T	N.S.	N.S.	0.02
F X T	N.S.	N.S.	N.S.
Hour	0.0002	N.S.	N.S.
Covariate	N.S.	N.S.	0.01

* Level of significance
** Nonsignificant ($P>0.05$)

Figure 9. The effect of breed on heat production (HP) and respiratory rate (RR) averaged across all ambient temperature exposures


HP (kJ • min⁻¹ • kg BW⁻⁰·⁷⁵)
0.320
0.310
0.300
0.290
0.280
0.270
0.260
0.250
0.240
0.230
0.220
0.210
XB
CBF
Finnish Suffolk Landrace


RR (resp • min⁻¹)
140
130
120
110
100
90
80
70
XB
CBF
Finnish Suffolk Landrace
BREED

Individual hourly means for respiratory rate, heart rate and O_2 consumption are included in Appendix B.

Ancillary Heat Tolerance Test

Rectal Temperature, Heart Rate and Respiratory Rate

Ancillary heat tolerance tests were conducted without the face masks to determine if high humidity within the masks was interfering with evaporative cooling and creating an environment more stressful than that anticipated on the basis of ambient temperature. In the absence of the mask, rectal temperature, heart rate and respiratory rate values were considerably lower than those recorded in the first series of tests, during exposure to mild heat (Table 9). As in the first series of tests, rectal temperature and heart rate were unaffected by the level of ergot in the feed. Thermal equilibrium apparently took longer to achieve and rectal temperatures were slightly although significantly ($P<0.004$), higher during the second hour.

The ergot effect on respiratory rate that had been demonstrated earlier, disappeared in the absence of the mask. Although all groups receiving ergot in the diet had higher mean respiratory rates than the control group, the differences were not significant ($P>0.05$). The slower deeper panting observed, during mild heat exposure, in the groups receiving 0.14% or 0.28% ergot, also disappeared and was replaced by the typical rapid shallow panting observed in the other groups. The covariate coefficient for time spent standing was significant for respiratory rate ($P<0.05$) but since no main effect or interaction differences were noted the means presented in table 9 are unadjusted.

The sheep in all groups spent less time standing during the

TABLE 9. Rectal temperature (T_R), respiratory rate (RR) and heart rate (HR) response to ancillary heat exposure. (Means ± standard error of the mean)

Ergot Level (%)	T_R (°C)	RR (resp.·min^{-1})	HR (beats·min^{-1})
0.00	39.3 ± 0.1	75.8 ± 14.1	62.1 ± 3.1
0.07	39.5 ± 0.1	105.1 ± 14.1	62.8 ± 2.9
0.14	39.2 ± 0.1	87.8 ± 14.1	60.4 ± 2.9
0.28	39.2 ± 0.1	108.2 ± 16.3	59.1 ± 3.4

Source of Variation	T_R	RR	HR
Breed	N.S.*	N.S.	N.S.
Feed	N.S.	N.S.	N.S.
Hour	0.004**	N.S.	N.S.
Covariate	N.S.	0.005	N.S.

* Nonsignificant (P>0.05)
**Level of significance

ancillary heat exposure than they had during heat exposure in the first series of tests. The face mask, while not restricting movement per se, apparently caused some discomfort while lying.

When the data were grouped by breed the differences that had been noted previously with regard to respiratory rate and rectal temperature were no longer evident. The Suffolk ewes, who had consistently demonstrated an intolerance to mild heat exposure while wearing the face mask, responded in a manner indistinguishable for the other sheep.

Individual hourly means for T_R, RR and HR are included in Appendix B.

DISCUSSION

Almost all of the reports in the literature which examine the effect of dietary ergot on animal performance have alluded to the inability of ergot fed animals to modulate heat stress. Thermal polypnoea has been observed in cattle maintained outdoors at ambient temperatures above 27°C when ergot has been included in the diet at levels as low as 0.06% (Dinnusson et al., 1971). In more controlled experiments increased rectal temperatures as well as increased respiratory rates have been noted in heifers, steers and sheep receiving 0.20%, 0.525% and 0.30% ergot respectively (Moore, 1975).

A rise in body temperature is indicative of an increase in heat storage due to an increase in heat production and/or PVMT and a reduction in evaporative heat loss. The simplest way in which ergot alkaloids could cause these effects would be to exert some unspecified action at the level of the hypothalamus. Alternatively, a rise in PVMT with its concomitant rise in rectal temperature could be produced as a result of direct stimulation of peripheral vascular smooth muscle. Greatorex and Mantle (1973) have suggested that the disturbance of peripheral circulation due to ergot alkaloids and vasoconstriction due to cold exposure may be additive leading to a lameness/gangrenous syndrome.

During the present experiment inclusion of ergot in the diet resulted in an increase in respiratory rate under thermoneutral conditions but not during exposure to mild heat. Instead, the rapid shallow

panting typical of both the control group and those sheep receiving 0.07% ergot was replaced by a slower deeper panting in those groups receiving 0.14% or 0.28% ergot. Contrary to reports by Moore (1975), rectal temperature was unaffected by ergot in the feed.

Hales (1969) described similar changes in the respiratory pattern of heat stressed oxen and sheep. During severe heat stress, rapid shallow panting was superceded by slower deeper panting coincidental with the attainment of a temperature of 40.4°C - 40.8°C in the hypothalamus. In an earlier study (Hales and Webster, 1967), the change in panting pattern of heat stressed sheep had been found to occur at rectal temperatures of as low as 39.7°C.

The failure to demonstrate a significant effect of ergot on rectal temperature in the present experiment need not imply that animals receiving ergot were free from climatic stress. Rather, it appears as though respiratory mechanisms responded to heat stress to prevent a rise in heat storage and body temperature. If this is the case ergot fed animals were clearly stressed at temperatures within what had been considered the thermoneutral zone.

Heat production responses during exposure to mild cold, mild heat and thermoneutral conditions were similar at all dietary levels of ergot leaving an increase in PVMT as the most likely cause of this downward shift in the upper critical temperature. Constriction of the vessels in the extremities could lead to a lowered surface temperature and a reduction in the rate at which heat is lost to the environment. A slight though not significant trend was observed in ear surface temperatures during exposure to both mild cold and mild heat. Considering

that a similar trend was observed for mean trunk skin temperature, an area not considered to be under vasomotor control (Webster, 1966; Sykes and Slee, 1968), the trend in ear surface temperature should probably be ignored. However, a significant ergot effect with regard to the thermal circulation index for the ear was observed that appeared to be due to a large reduction of the index in those groups receiving 0.14% or 0.28% ergot during exposure to mild heat. As has been previously noted, any change in the value of the index reflects a change in internal insulation due to a change in blood flow.

The remaining area which might be expected to exhibit a reduced surface temperature and/or thermal circulation index is the shank. While ergot had no effect on skin temperature of the shank, TCI_{shank} did exhibit a slight decrease with increased ergot during exposure to both mild heat and thermoneutral conditions.

In contrast to the above findings, Cowan and Phillips (unpublished data) observed an increase in mean body surface temperature in Hereford heifers fed ergot at levels of 0.023% to 0.123% and exposed to 33°C and 93% relative humidity. A significant ergot effect was also demonstrated with regard to rectal temperature and it seems likely that high surface temperatures were a function of high rectal temperatures and not of increased blood flow.

Tissue insulation was determined during the present experiment to provide a measure of ergot induced changes in the overall ability of the sheep to resist heat loss. A slight, though not significant, trend was observed during exposure to mild cold, mean insulation increasing with each successive increase in the level of ergot to

a level of 15% higher than that for the controls. Tissue insulation is dependent on the convective transfer of heat via the bloodstream and changes in blood flow to the periphery represent a major means of altering insulation (Richards, 1973). In conjuction with the TCI data, an increase in mean tissue insulation does suggest an alteration in peripheral blood flow patterns.

To summarize, it would appear that ergot in the diet results in an increase in PVMT and a reduction in the rate at which heat is lost to the environment. This in turn lowers the upper critical temperature and presents a challenge to strict homeothermy at temperatures which would otherwise be considered within the thermoneutral zone. The major response of an ergot fed sheep is to increase its rate of panting in an effort to prevent a rise in heat storage. At ergot levels above 0.14%, panting patterns during mild heat exposure are similar to those described for sheep during severe heat stress.

The relative significance of central and peripheral effects of ergot alkaloids on temperature regulation have not yet been examined. Corrodi et al. (1975) observed a decrease in 5-HT release and turnover in 5-HT neurons from the rat following the in vitro administration of ergocornine. In sheep and cattle it has been postulated that 5-HT is the principle on line neurotransmitter between warm sensors and heat loss effectors (Bligh et al., 1971). Intracerebroventricular injections of 5-HT receptor blockers at thermoneutral temperatures in sheep cause a reduction in heat loss by panting and an increase in PVMT (Bligh et al., 1979a). At high ambient temperatures the reduction in respiratory heat loss is especially pronounced.

If, during the present experiment, ergot alkaloids had been acting at the level of the hypothalamus to block 5-HT release on the heat loss pathway, a decrease in heat loss by panting and an increase in rectal temperature should have been noted in addition to the increase in PVMT. Instead, respiratory heat loss apparently increased to balance the reduction in nonevaporative heat loss, and rectal temperatures were maintained at a constant level.

Ergot alkaloids have also been shown to exhibit equal potencies in displacing ^{3}H-agonist or ^{3}H-antagonist ligand binding at central α-adrenergic receptor sites while at dopamine sites they are slightly weaker inhibitors of agonist binding (U'Prichard, 1980). Both noradrenaline and dopamine have been implicated as neurotransmitters in the central control of body temperature, but, it has not yet been demonstrated that centrally released, endogenous noradrenaline is involved in thermoregulatory adjustment of PVMT (Tollerton et al., 1978). Dopamine may be the on line neurotransmitter of the influence of cold sensors on PVMT (Tollerton et al., 1978), but, as indicated above, ergot alkaloids are stronger antagonists than agonists of dopamine receptors and would probably cause a reduction in PVMT during exposure to cold rather than an increase in PVMT during exposure to mild heat.

It isn't possible to entirely rule out central involvement of ergot alkaloids in the impairment of temperature regulation during the present experiment, but, one more argument against such an hypothesis can be raised. All of the effects predicted by assuming an action of ergot alkaloids on central monoamine receptor sites are temperature dependent. During the course of this experiment not one parameter measured exhibited a significant feed X temperature interaction. The

results seem to be consistent with the alternative hypothesis, that ergot alkaloids impair temperature regulation by directly stimulating peripheral vascular smooth muscle and concomitantly lowering the upper critical temperature.

Only one report in the literature has previously examined the possibility of ergot induced thermoregulatory impairment at temperatures below the thermoneutral zone. As noted previously Greatorex and Mantle (1973) observed severe lameness and intestinal inflamation in one ergot fed sheep exposed to cold, wet pasture conditions. Other sheep, at pasture in mild weather, tolerated ergot at levels thought to be potentially lethal. The authors suggested that cold induced vasoconstriction was additive to the disturbance of peripheral circulation caused by ergot alkaloids.

Originally it had been thought that ergot alkaloids exerted their effect on vascular smooth muscle directly and did not involve either adrenoceptors or 5-HT receptors. More recently it has been demonstrated that the response to ergot alkaloids appears to be the result of an action on the same receptors involved in the response to catecholamines or 5-HT (see Clark, 1979).

There was no evidence in the present experiment to suggest that ergot induced and cold induced vasoconstriction were additive. The one parameter which demonstrated a strong effect of ergot on peripheral blood flow, TCI_{ear}, showed the smallest differences between treatment groups during cold exposure.

At temperatures below freezing, ergot may have a profound effect on thermoregulation. Protection of the tissues from damage by freezing is dependent upon very precise regulation of the blood supply. Webster

and Blaxter (1966) reported 3 forms of CIVD in sheep exposed to subzero temperatures. In the ear, classical "hunting" reactions were observed. Also in the ear, and occasionally in the limbs, single sharp increases in surface temperature were noted that could last up to 50 minutes. Below a temperature of -5°C, continuous proportional control ensured that surface temperatures remained above freezing and without marked variation.

The effect of ergot on this precise control of blood flow to the extremities is unknown. In the present study ear surface temperatures often exhibited a slow rise of less than 5°C which lasted for 20 to 30 minutes. This occurred in all groups but only as ambient temperature closely approached 0°C. The sheep were not exposed to subzero temperatures and it is possible that tissue damage by freezing could result if the increase in PVMT prevented an adequate blood flow to the extremities during exposure to severe cold. Until this avenue of research has been explored further, animal producers should refrain from utilizing ergoty grain in ration formulations during severe winter weather.

The downward shift of upper critical temperature resulting from long term, low level ingestion of ergot sclerotia has its own implication to the producer. Sheep fed ergot at a level of 0.14% and 0.28% in the present study were severely stressed at ambient temperatures of as low as 27.7°C, a daytime temperature commonly reached on the Canadian prairies during the summer months. Fuquay (1981) has reviewed the effects of heat stress on animal production. A reduction in feed conversion efficiency commonly occurs when beef heifers and lactating dairy cows are subjected to heat stress. This reduced efficiency has been attributed to an increase in the energy required for thermoregulation.

There is some indication that heat stress also results in an increase in maintenance protein requirements in both cattle and sheep.

The respiratory response observed in the groups of sheep receiving the two highest levels of ergot in this experiment was due, in part, to high humidity within the face mask. In the absence of the mask the slower deeper panting, previously observed, disappeared to be replaced by the typical rapid shallow panting noted in the other groups. Superimposition of high ambient humidity upon high ambient temperature, such as might be found in a poorly ventilated barn, would present the most stressful set of circumstances to ergot fed animals. Bligh (1963) has noted that even in the absence of an increase in rectal temperature, respiratory frequency increases in response to increasing humdity.

In addition to the inability of ergot fed animals to modulate heat stress, the symptoms ascribed to long term, low level feeding of ergot to ruminants include reduced feed intake and gain, an increase in feed to gain ratios and an increase in both water intake and urine output. While the development of tolerance or hypersensitivity to ergot alkaloids might be expected to occur, an examination of ergotamine abusing human migraine patients failed to reveal any indication of either (Tfelt-Hansen and Olesen, 1981).

Dinnusson et al. (1971) in the experiment previously described, reported all of the above symptoms in cattle receiving 0.06% ergot. Moore (1975) noted a slight reduction in weight gain of sheep fed 0.15% or 0.30% ergot but was unable to demonstrate a significant reduction in feed intake or the efficiency of feed conversion in either sheep or cattle receiving up to 0.525% ergot.

During the present experiment the effect of ergot on weight gain and feed conversion was not examined but the level of ergot in the diet had no effect on feed intake. General observations of the animal holding area were contrary to those of Dinnusson et al. (1971) and in accordance with observations by Moore (1975) and Cowan and Phillips (unpublished data). Ergot fed animals did not exhibit any indication of an increase in drinking frequency or urination. Apparent contradictions of this nature in the literature may be due to the considerable variation in individual and total alkaloid contents between sclerotia. The symptoms observed by Dinnusson et al. (1971) may only be valid for ergot of similar toxicity.

With regard to feed intake, the inclusion of molasses in the diet during the present study may have reduced the effect of ergot on palatability. Ground ergot was fed to the sheep in a complete pelleted ration to prevent sorting and rejection of sclerotia. Molasses were added as a binding agent to aid in pellet formation. The process of pelleting involves steam heating and may have slightly reduced the toxicity of the ergot used in this study. Heat treated ergot typically shows a reduction in total alkaloid content (see table 3).

Species differences in the response to acute ergot poisoning have been noted in the literature (see Lorenz, 1979; Young, 1979) and it seems likely that they exist with regard to chronic poisoning as well. The question of whether or not breed differences influence the response to ergot has never been examined. During the present experiment Suffulk ewes consistently demonstrated an intolerance to mild heat exposure. Slee (1968, 1974) has reported differences in the ability to thermoregulate in the cold between Scottish Blackface and Merino

sheep although Armstrong et al.(1960) were unable to discern any difference in response between Scottish Blackface, Down Cross and North Country Cheviot breeds. As the fullest expression of ergot toxicity is influenced by ambient temperature and breed differences in the ability to thermo-regulate have been noted, some breeds may be more tolerant of ergot than others.

SUMMARY AND CONCLUSIONS

1. Long term, low level feeding of ergot to ewes resulted in demonstrable heat stress at temperatures which would normally be considered within the thermoneutral zone.
2. In ewes fed ergot at a level of 0.07%, this stress was evidenced by an increase in mean respiratory rate at all ambient temperature exposures.
3. During mild heat exposure, the rapid shallow panting typical of both the control group and those sheep receiving 0.07% ergot was replaced by a slower deeper panting in those groups receiving 0.14% or 0.28% ergot, similar to that described for sheep during severe heat stress. This was due in part to high humidity within the face mask. Superimposition of high ambient humidity upon high ambient temperature, such as might be found in a poorly ventilated barn, would represent the most stressful set of circumstances to ergot fed animals.
4. Blood flow to the ear, as evidenced by changes in the thermal circulation index, was reduced at all ambient temperatures in ewes receiving 0.14% ergot or greater. Trends in both TCI_{shank} and I_T support the contention that peripheral blood flow was reduced as a result of ergot ingestion.
5. The increase in PVMT appeared to reduce heat flow from the body to the environment and effectively lowered the upper critical temperature.

6. Heat production was unaffected by ergot in the feed.
7. Respiratory mechanisms responded to heat stress sufficiently to prevent a rise in heat storage and rectal temperature.
8. The findings of the present study are inconsistent with the effects predicted by assuming an action of ergot alkaloids on central monoamine receptor sites and appear to support the hypothesis that ergot alkaloids impair temperature regulation by directly stimulating vascular smooth muscle to increase PVMT and lower the upper critical temperature.
9. Reduced feed intake and an increase in water intake and urine output, symptoms generally ascribed to long term, low level feeding of ergot to ruminants, in addition to heat stress, were not evident during the present experiment.
10. In view of the above findings animal producers would be well advised to refrain from feeding ergotized grain to their livestock at extremes of ambient temperature.
11. Further studies are necessary to evaluate the influence of breed differences on response to ergot. Breeds that are better able to modulate temperature stress may be more tolerant of ergot than others.

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APPENDIX A

TABLE A1. Analysis of variance of rectal temperatures of 15 sheep fed ergot at levels of 0.00%, 0.07%, 0.14% and 0.28% ergot w/w and exposed to 3 environmental temperature ranges.

Source of Variation	df[1]	Type IV Sum of Squares	Mean Square	F-value	Significance
Breed (B)	3	3.2100	1.0700	2.39	N.S.[2]
Feed (F)	3	0.6895	0.2298	0.51	N.S.
B X F	8	3.5883	0.4485		
Temperature (T)	2	8.9160	4.4580	6.75	0.01
B X T	6	4.2623	0.7104	1.07	N.S.
F X T	6	3.6435	0.6073	0.92	N.S.
B X F X T	13	8.5921	0.6609		
Hour	1	0.0001	0.0001	0.00	N.S.
Error	38	2.9727	0.0782		
Total	80	36.7651			

[1] degrees of freedom for each source of variation are consistent with respect to the presence or absence of missing values

[2] Not Significant

TABLE A2. Analysis of variance of rectal temperatures of 15 sheep fed ergot at levels of 0.00%, 0.07%, 0.14% and 0.28% w/w measured once weekly for 7 weeks.

Source of Variation	df	Type IV Sum of Squares	Mean Square	F-value	Significance
Breed (B)	3	7.5063	2.5021	5.44	0.02
Feed (F)	3	2.6241	0.8747	1.90	N.S.*
B X F	8	3.6795	0.4599		
Week (Wk)	6	4.0759	0.6793	16.87	0.0001
B X Wk	18	4.0199	0.2233	5.55	0.0001
F X Wk	18	0.6374	0.0354	0.88	N.S.
Error	48	1.9330	0.0403		
Total	104	27.8339			

* Not Significant

APPENDIX B

TABLE B1. Mean hourly ear temperature (^{o}C) during exposure to mild cold, thermoneutral conditions, and mild heat.

Sheep	Ergot Level in Feed (%)	Exposure Range: Mild Cold, Hour 1	Mild Cold, Hour 2	Thermoneutral, Hour 1	Thermoneutral, Hour 2	Mild Heat, Hour 1	Mild Heat, Hour 2
Finnish Landrace	0.00	8.8	6.8	20.6	20.8	39.1	-
CBF		11.8	7.8	18.0	18.6	38.6	38.9
Suffolk		8.5	8.2	36.2	36.0	38.4	38.3
XB		5.9	5.5	34.7	-	38.5	38.3
Finnish Landrace	0.07	6.1	5.8	36.1	35.4	-	-
CBF		27.2	18.9	38.1	38.1	37.4	-
Suffolk		4.5	4.3	34.0	33.5	37.0	37.8
XB		1.0	-	32.0	33.1	-	-
Finnish Landrace	0.14	5.3	5.2	-	-	37.1	37.3
CBF		-	-	29.0	30.4	36.4	37.6
Suffolk		4.4	4.5	35.2	35.2	-	36.9
XB		7.4	7.0	-	-	33.6	33.5
Finnish Landrace	0.28	7.2	5.2	21.3	21.2	38.4	38.3
CBF		4.7	4.5	35.0	34.8	36.6	37.2
Suffolk		4.7	3.8	36.4	-	31.5	-

TABLE B2. Mean hourly trunk temperature (^{o}C) during exposure to mild cold, thermoneutral conditions, and mild heat.

Sheep	Ergot Level in Feed (%)	Exposure Range: Mild Cold, Hour 1	Mild Cold, Hour 2	Thermoneutral, Hour 1	Thermoneutral, Hour 2	Mild Heat, Hour 1	Mild Heat, Hour 2
Finnish Landrace	0.00	26.0	25.5	31.3	31.9	38.7	-
CBF		28.2	28.8	32.5	33.2	36.9	37.0
Suffolk		29.1	27.6	33.9	33.6	37.0	37.3
XB		24.9	26.2	28.6	28.3	36.2	36.4
Finnish Landrace	0.07	28.2	27.8	35.0	34.7	36.5	36.6
CBF		28.7	27.7	33.7	33.0	35.2	35.0
Suffolk		24.3	23.8	31.8	32.0	36.7	37.2
XB		19.5	20.1	29.0	29.8	38.6	-
Finnish Landrace	0.14	30.2	29.6	34.7	35.3	37.1	37.6
CBF		22.0	21.5	30.3	30.5	37.7	38.5
Suffolk		24.6	23.7	32.2	32.7	37.0	38.0
XB		25.1	28.3	33.4	33.8	35.1	35.4
Finnish Landrace	0.28	26.0	25.5	33.2	33.0	37.7	37.9
CBF		24.3	24.3	30.2	29.9	36.5	36.6
Suffolk		23.6	23.1	35.4	35.9	36.1	-

TABLE B3. Mean hourly shank temperature (^{o}C) during exposure to mild cold, thermoneutral conditions, and mild heat.

Sheep	Ergot Level in Feed (%)	Exposure Range: Mild Cold, Hour 1	Mild Cold, Hour 2	Thermoneutral, Hour 1	Thermoneutral, Hour 2	Mild Heat, Hour 1	Mild Heat, Hour 2
Finnish Landrace	0.00	21.0	17.2	30.5	33.0	39.3	-
CBF		17.0	18.7	35.4	36.4	37.6	38.0
Suffolk		24.0	24.1	35.4	36.0	37.8	37.6
XB		17.2	16.1	28.2	31.4	33.9	30.8
Finnish Landrace	0.07	21.9	17.9	35.0	34.1	37.5	37.7
CBF		25.7	23.8	36.2	36.2	-	35.2
Suffolk		20.9	21.7	31.2	31.2	37.2	37.6
XB		-	-	28.3	-	-	-
Finnish Landrace	0.14	13.8	10.8	34.8	34.5	37.0	37.5
CBF		30.5	29.6	31.7	32.0	37.0	38.1
Suffolk		23.9	23.4	32.0	32.0	34.7	37.2
XB		18.5	-	34.7	36.0	34.0	33.9
Finnish Landrace	0.28	12.4	9.6	27.6	26.0	37.2	37.6
CBF		24.6	18.6	-	-	36.9	36.5
Suffolk		24.9	26.1	33.4	35.2	35.4	-

TABLE B4. Mean hourly rectal temperature (^{o}C) during exposure to mild cold, thermoneutral conditions, and mild heat.

Sheep	Ergot Level in Feed (%)	Exposure Range: Mild Cold, Hour 1	Mild Cold, Hour 2	Thermoneutral, Hour 1	Thermoneutral, Hour 2	Mild Heat, Hour 1	Mild Heat, Hour 2
Finnish Landrace	0.00	38.8	39.0	39.2	39.2	41.1	-
CBF		39.0	39.2	39.1	39.0	39.6	39.7
Suffolk		39.4	39.2	39.3	39.2	40.1	40.2
XB		39.3	39.1	-	-	39.8	39.8
Finnish Landrace	0.07	39.5	39.1	39.0	38.7	39.9	40.1
CBF		39.8	39.8	39.9	39.4	38.9	38.7
Suffolk		39.8	40.0	40.0	39.4	40.3	41.0
XB		-	-	39.8	-	-	-
Finnish Landrace	0.14	39.8	40.0	38.4	38.8	39.0	39.4
CBF		39.5	39.4	39.4	39.5	40.3	40.4
Suffolk		39.4	39.3	39.7	39.4	41.7	43.0
XB		39.5	39.2	38.9	39.1	39.3	39.2
Finnish Landrace	0.28	39.7	39.6	39.4	39.4	39.5	40.2
CBF		38.7	38.8	40.0	38.8	39.7	39.8
Suffolk		39.6	39.2	39.9	40.0	40.2	-

TABLE B5. Mean hourly respiratory rate during exposure to mild cold, thermoneutral conditions, and mild heat.

Sheep	Ergot Level in Feed (%)	Exposure Range					
		Mild Cold		Thermoneutral		Mild Heat	
		Hour		Hour		Hour	
		1	2	1	2	1	2
Finnish Landrace	0.00	30.8	13.7	61.2	28.5	81.7	-
CBF		13.3	15.0	20.0	11.7	74.5	78.3
Suffolk		19.0	11.3	26.6	22.8	123.7	121.0
XB		14.0	12.3	22.2	22.7	99.7	94.3
Finnish Landrace	0.07	12.0	10.2	62.2	61.0	113.0	113.3
CBF		32.3	23.0	83.5	74.2	100.3	90.7
Suffolk		37.4	16.5	106.0	84.8	103.7	108.3
XB		10.0	9.5	-	70.5	113.2	-
Finnish Landrace	0.14	12.5	9.6	55.3	52.0	87.3	107.5
CBF		9.8	8.5	49.8	36.5	108.7	95.0
Suffolk		34.0	26.3	87.8	78.5	100.2	95.0
XB		22.3	12.7	17.7	13.0	89.5	79.0
Finnish Landrace	0.28	10.5	8.5	36.2	34.7	112.3	87.5
CBF		17.8	12.3	55.0	47.6	74.7	72.5
Suffolk		13.0	10.3	109.3	98.2	101.0	-

TABLE B6. Mean hourly heart rate during exposure to mild cold, thermoneutral conditions, and mild heat.

Sheep	Ergot Level in Feed (%)	Exposure Range					
		Mild Cold		Thermoneutral		Mild Heat	
		Hour		Hour		Hour	
		1	2	1	2	1	2
Finnish Landrace	0.00	72	71	67	63	122	-
CBF		79	83	67	63	70	71
Suffolk		60	58	56	53	61	66
XB		-	-	59	60	68	63
Finnish Landrace	0.07	76	74	70	66	73	81
CBF		70	67	72	76	74	74
Suffolk		64	56	73	68	71	-
XB		63	59	74	74	74	-
Finnish Landrace	0.14	79	72	-	65	69	69
CBF		66	65	67	60	81	105
Suffolk		64	63	-	66	107	-
XB		68	69	60	59	58	57
Finnish Landrace	0.28	72	67	64	60	73	-
CBF		64	64	82	70	62	63
Suffolk		56	54	-	58	80	-

TABLE B7. Mean hourly heat production as a function of body surface area ($kJ \cdot m^{-2} \cdot min^{-1}$) during exposure to mild cold, thermoneutral conditions and mild heat.

Sheep	Ergot Level in Feed (%)	Exposure Range: Mild Cold, Hour 1	Mild Cold, Hour 2	Thermoneutral, Hour 1	Thermoneutral, Hour 2	Mild Heat, Hour 1	Mild Heat, Hour 2
Finnish Landrace	0.00	4.970	5.093	3.231	3.092	6.218	5.363
CBF		5.227	6.005	3.538	2.810	3.552	3.546
Suffolk		7.166	4.578	4.482	4.343	4.754	4.961
XB		4.108	4.559	3.444	3.591	3.537	2.704
Finnish Landrace	0.07	4.686	5.275	3.421	3.667	3.901	4.546
CBF		4.911	4.743	5.094	4.598	3.346	3.480
Suffolk		6.064	5.470	5.712	5.618	5.568	5.748
XB		3.557	5.497	5.140	5.428	3.829	-
Finnish Landrace	0.14	4.132	4.408	3.852	4.473	4.722	5.037
CBF		5.838	4.671	3.807	4.142	4.399	4.734
Suffolk		5.392	5.296	5.431	4.572	5.034	5.168
XB		5.137	4.309	4.043	3.699	3.017	2.603
Finnish Landrace	0.28	5.326	5.072	5.123	5.003	4.805	4.158
CBF		4.794	4.921	3.998	4.298	3.464	3.169
Suffolk		5.369	5.583	5.870	3.489	4.878	6.360

TABLE B8. Mean hourly oxygen consumption ($ml \cdot min^{-1}$) during exposure to mild cold, thermoneutral conditions, and mild heat.

Sheep	Ergot Level in Feed (%)	Exposure Range: Mild Cold, Hour 1	Mild Cold, Hour 2	Thermoneutral, Hour 1	Thermoneutral, Hour 2	Mild Heat, Hour 1	Mild Heat, Hour 2
Finnish Landrace	0.00	260.18	266.63	175.44	167.91	337.67	291.24
CBF		288.99	331.99	192.12	152.59	196.38	195.89
Suffolk		406.65	259.83	247.80	240.12	262.82	274.27
XB		221.09	245.35	188.70	196.77	195.55	149.51
Finnish Landrace	0.07	256.75	289.04	187.43	200.93	213.75	249.07
CBF		281.12	271.48	294.08	265.46	193.15	200.88
Suffolk		361.94	326.47	338.11	332.58	329.60	340.26
XB		182.73	282.39	264.04	278.82	209.79	-
Finnish Landrace	0.14	202.15	215.66	188.45	218.84	231.02	246.43
CBF		331.31	265.07	217.91	237.08	249.66	268.69
Suffolk		295.45	290.22	292.27	246.04	273.39	280.63
XB		291.54	244.52	221.53	202.69	171.23	147.70
Finnish Landrace	0.28	255.33	243.20	253.13	247.21	237.43	205.48
CBF		250.98	257.63	211.25	227.10	184.74	168.98
Suffolk		294.18	305.92	327.40	194.62	279.21	364.04

TABLE B9. Individual animal weights (kg) during exposure to mild cold, thermoneutral conditions, and mild heat.

Sheep	Ergot Level in Feed (%)	Exposure Range		
		Mild Cold	Thermoneutral	Mild Heat
Finnish Landrace	0.00	46.36	49.55	49.32
CBF		51.36	49.32	51.36
Suffolk		53.86	51.36	51.36
XB		48.41	50.00	51.14
Finnish Landrace	0.07	50.00	50.23	50.46
CBF		54.09	55.46	54.77
Suffolk		58.18	57.27	57.27
XB		45.23	45.23	50.68
Finnish Landrace	0.14	41.36	41.36	41.36
CBF		53.41	54.55	53.64
Suffolk		50.00	49.09	49.55
XB		53.18	50.00	53.41
Finnish Landrace	0.28	40.00	41.82	42.05
CBF		46.14	47.50	48.18
Suffolk		50.00	51.82	54.09

TABLE B10. Mean hourly respiratory rate (RR), heart rate (HR) and rectal temperature (T_R) during ancillary heat exposure.

Sheep	Ergot Level in Feed (%)	RR Hour		HR Hour		T_R Hour	
		1	2	1	2	1	2
Finnish Landrace	0.00	61.0	70.0	59	61	39.4	39.7
CBF		69.0	92.5	61	-	39.2	39.4
Suffolk		72.0	64.0	70.0	58	39.1	39.2
XB		113.5	64.5	63	63	39.0	39.3
Finnish Landrace	0.07	92.0	105.0	69	62	39.2	39.2
CBF		100.5	117.5	61	67	39.6	39.7
Suffolk		55.5	110.0	52	65	-	-
XB		122.0	138.0	63	65	39.3	39.7
Finnish Landrace	0.14	52.5	48.5	60	57	39.2	39.4
CBF		77.0	89.0	73	66	39.1	39.2
Suffolk		127.0	127.0	58	61	39.0	39.2
XB		75.0	106.0	56	53	39.2	39.4
Finnish Landrace	0.28	60.5	92.0	68	60	39.4	39.5
CBF		160.0	177.0	73	64	39.0	39.2
Suffolk		93.0	66.5	47	44	39.2	39.1