ERGOT ON CEREAL GRAINS

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INTRODUCTION

Ergot is probably best known as a disease of rye, but it also affects wheat, barley, triticale, corn, rice, and other small grains. Actually, no known commercially grown varieties of cereal grains are completely resistant to ergot.[13]

Consumption of cereal grains containing ergot can result in very serious illness or even death. The literature contains very detailed descriptions of ergot epidemics which crippled or killed hundreds of thousands of people in Europe. References to epidemics of this dreadful affliction are found in the literature as far back as the time of Caesar. Outbreaks ravaged Europe frequently in the Middle Ages.

An outbreak of ergot poisoning in the ancient French town of Pont St. Esprit in 1951 has drawn attention again to ergot of rye. It emphasizes the fact that what happened in the past can happen again in modern times.

THE FUNGI AND THEIR HOST

Ergot is caused by fungi (*Claviceps* species) which attack cereals. Among these parasitic fungi, *Claviceps purpurea* is the outstanding species, forming its conspicuous sclerotial stage in the heads of cereal grains. Long before its developmental history was known, it was looked upon with suspicion, and later was shown to be the cause of the disastrous epidemics reported throughout history.

The search for the different species of *Claviceps* and the plants they parasitize began in the 1850s. Today, a complete list of all the hosts shows about 600 plants. New species and also new hosts are still being discovered today.[13]

A list of *Claviceps* species is given in Table 1. The exact number of species is not known because some are challenged as being misnamed and thus duplicates of an already discovered species.[13]

All known species of *Claviceps* on Gramineae, the grass family to which the true cereals belong, show some degree of host restriction. With the exception of *C. purpu-*

TABLE 1

Claviceps Species

C. annulata Langdon	*C. nigricans* Tul.
C. cinerea Griff	*C.iorthocladae* (P. Henn.) Diehl
C. cynodontis Langdon	*C. paspali* Stev. & Hall
C. cyperi	*C. phalaridis* Walker
C. diadema (Möller) Diehl	*C. platytricha* Langdon
C. digitariae Hansford	*C. purpurea* (Fr.) Tul.
C. flavella (Berk. & Curt.) Petch	*C. pusilla Ces.*
C. gigantea	*C. queenslandica* Langdon
C. glabra Langdon	*C. ranunculoides* Möller
C. grohii Groves	*C. rigidifolius*
C. hirtella Langdon	*C. sulcata* Langdon
C. inconspicua Langdon	*C. tripsaci* Stev. & Hall
C. litoralis Kawatani	*C. uleana* P. Henn.
C. lutea Möller	*C. viridis* Padwick & Azmat.
C. maximensis Theis	*C. yanagawaensis* Togashi
C. microcephala (Wallr.) Tul.	*C. zizaniae* Fyles

Adapted from Langdon,[80] Brady,[14] and Loveless.[83]

rea, the host range of any one species is confined to grasses of a single tribe. Most *Claviceps* species have a monogeneric host range, while others are found on several genera restricted to a single tribe. *C. purpurea* is unique because it has a very wide host range from members of several tribes.[83]

It is truly remarkable that so many hundreds of plants found in almost every country of the world can be hosts to a parasitic fungus and that the fungus can adopt itself to form so many varieties.

The eight leading cereals produced in the world are wheat, rice, corn, sorghum, rye, barley, oats, and millets and they all can be hosts to ergot.

C. purpurea (Fr.) Tul. attacks primarily cross-pollinated species in which florets tend to remain open for a relatively long time and in which sterility occurs. Rye is notorious for harboring ergot. It is cross-pollinated, has large florets, and a high degree of sterility.[20,75,76,124] The infection of wheat with ergot is relatively common, but seldom severe.[29,46,102,136] An ergot sclerotium on a head of wheat is shown in Figure 1.

Because of its potential for increased yield, interest in hybrid wheat (*Triticum aestivum* L. em. Thell.) has continued. Ergot caused by *C. purpurea* (Fr.) Tul. may be the primary problem in the northern Great Plains in the production of hybrid spring wheat seed.[108] Ergot is quite severe in male sterile spring wheat,[105,127] because the florets of the cytoplasmic male sterile plants used in hybrid wheat production generally remain open until pollinated, which greatly enhances the opportunity for infection by ergot.[104] Winter wheat, male sterile or fertile, usually escapes ergot infection because it flowers when ergot inoculum levels are extremely low.

Ergot, along with rusts, remains the most important disease of triticale, the cross-breed between wheat and rye.[18,47] Ergot sclerotia harvested from triticale are shown in Figure 2. The outer edge (A) and the center (B) of cut surfaces of ergot sclerotia, viewed with the scanning electron microscope, are shown in Figure 3. A highly irregular and porous structure of intertwined hyphae of the mycelium is apparent.

Ergot occurs on sorghum in Asia and Africa.[37] The use of male sterile barley (*Hordeum vulgare* L.) and sorghum (*Sorghum bicolor* [L.)] Moench) in the production of hybrid seeds in the developed countries has increased the seriousness of ergot in these hosts.[26,105] The increased susceptibility of these male-sterile cereals is believed to be due to their open florets which allows the inoculum greater access to the unpollinated ovary.[128]

FIGURE 1. Ergot sclerotium on wheat. (From Field Manual of Common Wheat Diseases and Pests, Inf. Bull. 29, International Maize and Wheat Improvement Center, Mexico. With permission.)

Ergot has been observed on oats.[90] On pearl millets (*Pennisetum typhoideum*), it has been recorded from several parts of the world.[84]

That rice can be attacked by fungi, which develop sclerotia, is certain.[13,118,100] *C. zizaniae* parasitizes wild rice, which served as food for the Indians of the U.S. and Canada, and is now available on supermarket shelves everywhere.

Ergot on corn has been observed in Mexico, Peru, India, and in the U.S.[14,46,98] The prevalence of this plant disease is dependent upon a number of environmental factors such as moisture, air movement, availability and quantity of spores, and availability of a suitable host. Consequently, outbreaks of the disease may be severe in certain local areas.

THE LIFE CYCLE OF ERGOT

The life cycle of ergot begins when sclerotia, having fallen to the ground in the fall, become wholly or partially buried during the winter. They are stimulated to germinate by low winter soil temperatures and subsequently germinate when soil temperatures become warmer in the spring. Stroma are raised above the soil surface producing ascospores which are ejected into the atmosphere to infect the host.[23] Generally, a period of about a week elapses from the first sign of germination to maturity of the stromata. Sclerotia from rye stimulated by a period of chilling have been observed to germinate over a period of 14 days.[72] Spore discharge from stromata may occur for the relatively short period of 14 days after this.[23]

For heavy initial infection, discharge of the ascospores should synchronize with early anthesis of the particular host attacked and primary infections are said to be more

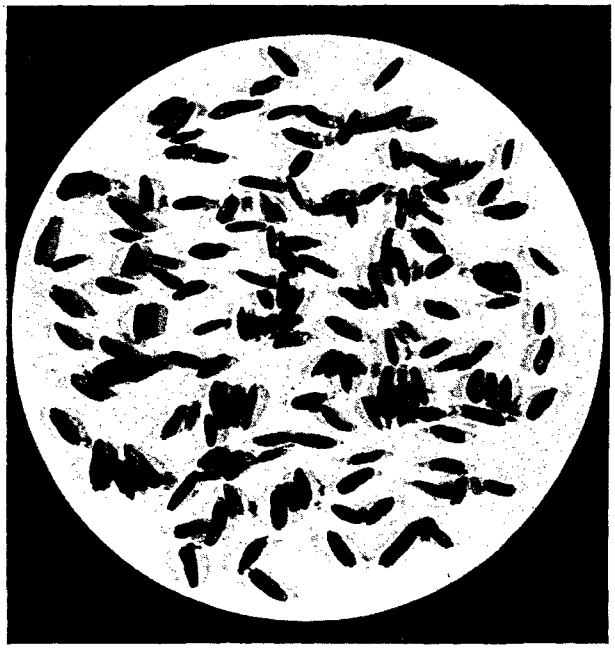


FIGURE 2. Ergot sclerotia from triticale.

successful when the flowers have just opened, presumably because germ tubes grow better in the absence of interference from a deposit of pollen.[23]

Fresh infections may take place for about 15 days after flowering has begun, the infections being heavier the longer the flowers are open.[23]

Synchronization of sclerotium germination and ascospore discharge with host flowering does not inevitably take place, however. If ascospores are released before the flowering of the host, they must remain in the atmosphere long enough to allow infection when flowering subsequently occurs.

Cooke and Mitchell[23] reported that a population of sclerotia, which reached maximum germination, may continue to form new stromata up to 56 days from the onset of germination, and that ascospores may be released for over 50 days reducing the need for synchronization of spore release with host anthesis.

Removal of stromata from sclerotia before they have liberated their ascospores results in the formation of a new crop of stromata. There appear to be a number of potential sites within a sclerotium from which stromata may be formed and these are stimulated into activity by a period of chilling. The larger the sclerotium, the more sites it is capable of supporting.[23] If left undisturbed, stromata mature and release ascospores, thereby utilizing the available energy reserves in the sclerotium.

There is a definite relationship between the amount of infection and the climate, the infection being favored by wet weather and reduced sunshine. Conditions such as these are favorable for the germination of the sclerotia and for the production and dissemination of the ascospores. During dry weather the flowering takes place rapidly and the possibility of infection is reduced.[110]

Within a few days after infection the injected florets produce conidia in a sticky, sweet exudate called "honeydew." Small flies are attracted to this exudate and carry the spores to healthy florets in the same head and to florets in the heads of other plants. Each sclerotium is the product of a separate infection. The fungus cannot spread by itself from one floret to another in the head.

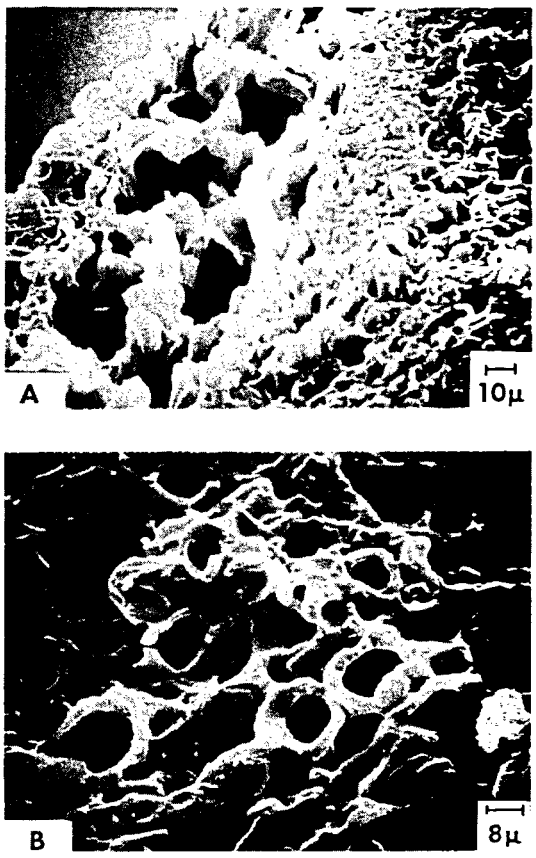


FIGURE 3. Scanning electron microscopy of ergot sclerotia. A = outer edge and B = center of cut surfaces of sclerotia.

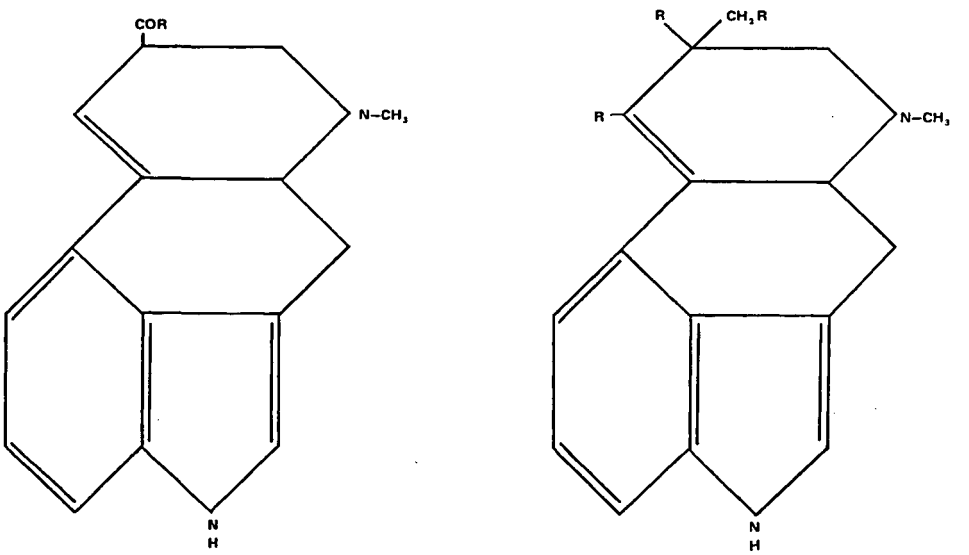
The mycelial mass gradually changes into the dry hard stage, in which form it may retain vitality for at least a year.[13,90] As the mycelium develops, it crowds out all the tissues that would normally constitute the grain. To complete the cycle, the ergotized grain grows to maturity, the ergot bodies fall to the ground and the life cycle is repeated.

CHARACTERISTICS OF SCLEROTIA

The external characteristics of the various species of ergot vary considerably. Sclerotia may vary in length from the 8 cm long sclerotia of *C. gigantea* to the 3 mm long ones of *C. microcephala*.[13] They also vary in weight. Tetra Petkus, a tetraploid rye, which produces larger heads and larger rye kernels than diploid rye varieties also produces larger size ergot sclerotia than the diploid varieties.[31] Deufel[31] reported a weight of 8.2 g for 100 sclerotia of 2n-rye and 24.5 g for 100 sclerotia of 4n-rye. There were no anatomical differences between the different sized sclerotia.

Structural variations between domestic rye and wheat ergot are limited to compactness of the pseudoparenchyma. Ergot of rye is more deeply fissured than ergot of wheat.[110]

Besides variations in size ergot sclerotia also vary in shape. They can be curved, straight, or round. Ergot sclerotia also differ in color from the white *C. tripsaci* to the



Group I. Derivatives with the General formula:

1) R = peptide
2) R = 2–aminopropanol : Alkanolamide
3) R = NH_2
4) R = $NHCHOHCH_3$: Carbinolamide

Group II. Derivatives with the General formula:

1) R = H
2) R = OH

Adapted from: Hofmann, A. (60) and Kröller, E. (74).

FIGURE 4. General formulae of ergot alkaloids. (Adapted from Kröller[74] and Hofmann[60].)

brown *C. glabra* to the yellow *C. hirtella* to the green *C. viridis* to the black to purplish brown *C. purpurea*.

It is the sclerotia of *C. purpurea* which we are mostly concerned about in cereal grains.

CHEMICAL COMPOSITION OF ERGOT SCLEROTIA

Alkaloids

A hundred years have passed since the first crystalline ergot alkaloid was isolated[130] and about 40 years since the structure of lysergic acid, the basic building block of the ergot alkaloids, was established.[67] The first to report the presence of alkaloids in ergot was Wenzell,[137] who in 1864 obtained two impure resinous preparations giving alkaloid reactions. Tanret,[130] however, was the first to obtain from ergot a crystalline alkaloid, which he named ergotinine. Today more than 40 individual alkaloids have been isolated from *Claviceps*.[107] One group is a series of ergoline derivatives, the clavine series, while another group includes derivatives of lysergic acid joined in amide linkage with a side chain. Basic chemical structures of these groups are shown in Figure 4. The different alkaloids and their chemical formulas are given in Table 2. Knowledge of their structure is due to the work of Barger,[9,10] Jacobs and Craig,[66,67] and, above all, to that of Stoll and Hofmann.[60,125]

The history of the discoveries of different ergot alkaloids has been described in great detail by Hofmann[60] and Bové.[13] The chemistry of alkaloid formation has been thoroughly reviewed by Weygand and Floss[138] and by Ramstad.[107]

The toxicity of ergot is due to these alkaloids. Total alkaloid content in ergot sclerotia ranges from 0.01 to 0.5%. The species of *Claviceps* differ in their capabilities to

TABLE 2

Ergot Alkaloids

Derivatives of lysergic acid

Alkaloid	Formula	
Ergometrine	$C_{19}H_{23}O_2N_3$	(ergobasine, ergonovine)
Ergotocine		
Ergostretine		
Ergosine	$C_{30}H_{37}O_5N_5$	(ergotine)
Ergocornine	$C_{31}H_{39}O_5N_5$	
Ergocryptine	$C_{32}H_{41}O_5N_5$	
Ergotamine	$C_{33}H_{35}O_5N_5$	
Ergocristine	$C_{35}H_{39}O_5N_5$	
Ergosecaline	$C_{24}H_{28}O_4N_4$	

Derivatives of isolysergic acid

Alkaloid	Formula	
Ergometrinine	$C_{19}H_{23}O_2N_3$	(ergobasinine)
Ergosinine	$C_{30}H_{37}O_5N_5$	(ergotinine)
Ergocorninine	$C_{31}H_{39}O_5N_5$	
Ergocryptinine	$C_{32}H_{41}O_5N_5$	
Ergotaminine	$C_{33}H_{35}O_5N_5$	
Ergocristinine	$C_{35}H_{39}O_5N_5$	
Ergosecalinine	$C_{24}H_{28}O_4N_4$	

Derivatives of dimethylergoline (clavine group)

Alkaloid	Formula	
Agroclavine	$C_{16}H_{18}N_2$	
Elymoclavine	$C_{16}H_{18}ON_2$	
Penniclavine	$C_{16}H_{18}O_2N_2$	
Isopenniclavine	$C_{16}H_{18}O_2N_2$	
Setoclavine	$C_{16}H_{18}ON_2$	
Isosetoclavine	$C_{16}H_{18}ON_2$	
Molliclavine	$C_{16}H_{18}O_2N_2$	
Festuclavine	$C_{16}H_{20}N_2$	
Pyroclavine	$C_{16}H_{20}N_2$	
Costaclavine	$C_{16}H_{20}N_2$	
Chanoclavine	$C_{16}H_{20}ON_2$	(secaclavin)

Other ergot alkaloids

Alkaloid	Formula
Ergine	$C_{16}H_{17}ON_3$
Isoergine	
Hydroergotinine	$C_{35}H_{41}N_5O_6$

Adapted from Kroller, E., *Dtsch. Lebensm. Rundsch.*, 66, 115, 1970.

form alkaloids. While some will produce a single alkaloid only, most will synthesize several of these compounds. A few *Claviceps* species are altogether incapable of alkaloid production. The amounts of the compounds formed are also dependent upon the location and the climate.[60,93]

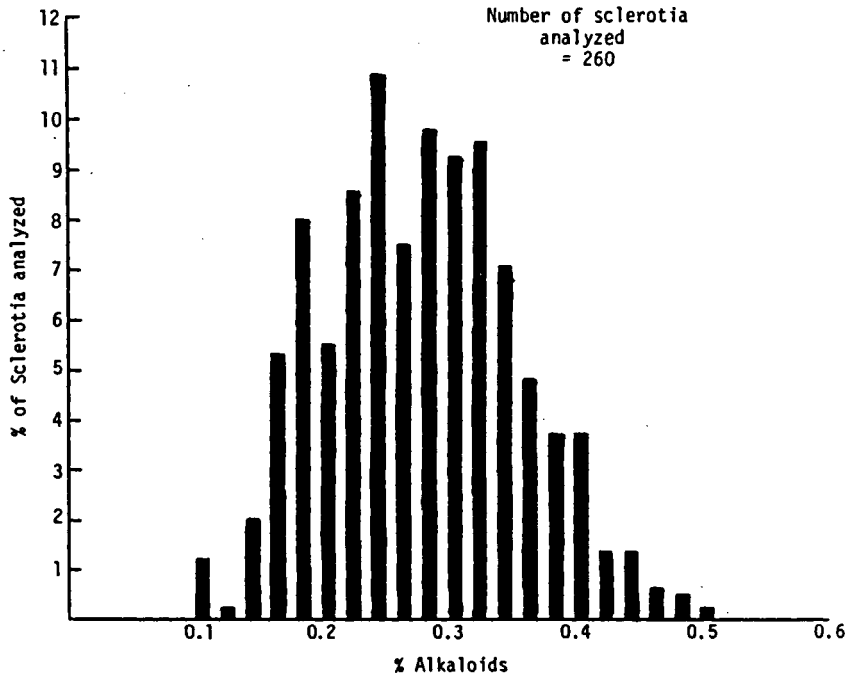


FIGURE 5. Alkaloid content of different ergot sclerotia within a sample. (Adapted from Silber, A. and Bischoff, W., *Pharmazie*, 9, 46, 1954.)

TABLE 3

Comparison of Alkaloid Content of Tetraploid and Diploid Rye Ergot

Rye variety	Wt of 100 sclerotia (g)	Fat content (g)	Alkaloid content (%)
Diploid — 2n	8.226	1.933	0.028
Tetraploid — 4n	24.516	5.761	0.035

Adapted from Deufel, J., *Naturwissenschaften*, 39(18), 433, 1952.

Only the sclerotial stage of ergot produces alkaloids. Neither the "honeydew" nor the conidia produce the chemicals. Alkaloids seem to be formed at the very moment of the formation of the sclerotial cells.[106]

Sclerotia of a given *Claviceps* species vary in alkaloid content. The small sclerotia tend to have lower alkaloid contents than the large ones harvested from the same host.[32,117] The considerable variability in alkaloid content is illustrated in Figure 5.

Deufel[32] observed that sclerotia from tetraploid rye, which are larger in size than sclerotia from diploid rye, contain more total alkaloids than those from the diploid rye, as shown in Table 3.

The alkaloids are concentrated in the outer layers of the sclerotia. The amount of these compounds decreases towards the center of the sclerotium.[117]

Without doubt, the alkaloids are the most important detrimental and beneficial components of ergot.

Amino Acids and Amines

The presence of amino acids in ergot sclerotia has been shown by several research-

TABLE 4

Amino Acid Composition of Ergot and a Semi-Dwarf Triticale[a]

	Semi-dwarf triticale kernels	Triticale ergot sclerotia	Ratio of amino acids in protein of ergot sclerotia and kernels of triticale
Kjeldahl nitrogen (%)	3.03	4.16	—
Aspartic acid	8.16	5.97	0.73
Threonine	2.90	6.35	2.19
Serine	6.32	4.62	0.73
Glutamic acid	27.55	11.95	0.43
Proline	9.10	5.10	0.56
Glycine	4.35	3.81	0.88
Alanine	4.22	4.62	1.09
Valine	1.76	5.16	2.93
Methionine	1.40	1.40	1.00
Isoleucine	3.22	4.70	1.46
Leucine	5.45	4.70	0.86
Tyrosine	4.53	4.97	1.10
Phenylalanine	5.16	4.51	0.87
Histidine	1.92	2.81	1.46
Lysine	3.61	7.91	2.19
Arginine	6.52	4.76	0.73

[a] Grams amino acid per 100 g amino acid recovered.

Adapted from Lorenz, K., *Lebensm. Wiss. Technol.*, 11, 70, 1978.

ers.[54,71] Early qualitative determinations were made by paper chromatography. Recently, the amino acid composition determined with automatic amino acid analyzers has been reported by several laboratories.[58,81,104] We know that almost every known amino acid is present in ergot of all types and at all stages of growth. These amino acids might be derived from protein. Some investigators believe that there is a connection between the amino acids, the amines, and the amount of alkaloids in ergot sclerotia. Others, however, disagree based on their laboratory results.[13]

Kjeldahl nitrogen of ergot sclerotia from several cereal grains including wheat, rye, triticale, oats, and barley ranged from 1.46 to 3.49% with an average of 2.47% in a study by Pomeranz et al.[104] Others reported Kjeldahl nitrogen values of over 4%.[58,81]

A comparison of the amino acid composition of sound kernels of triticale with ergot sclerotia harvested from the same grain is given in Table 4.

Of the essential amino acids, all but leucine and phenylalanine were present in higher amounts in ergot sclerotia than in the grains,[81] which is in agreement with the findings of Pomeranz et al.[104] A ratio of amino acids in protein of ergot sclerotia to kernels of triticale is shown in Table 4.

Glutamic acid and proline, which are the predominant amino acids in cereal grains, were present in considerably lower amounts in ergot sclerotia than in triticale. The rather high amount of lysine in ergot appears significant. Lysine is the first limiting amino acid in cereal grains. This amino acids is generally higher in triticale than in most other cereal grains and ergot contained more than twice the amount of lysine in triticale. Pomeranz et al.,[104] however, cautioned that increased amounts of amino acids in the sclerotia may be due, in part, to unknowns eluted in the same positions as the identified amino acids. In the study by Pomeranz et al.[104] at least five unidentified compounds appeared on the chromatogram. It is not known whether the unidentified components are related to the presence of any of the known alkaloids in ergot.

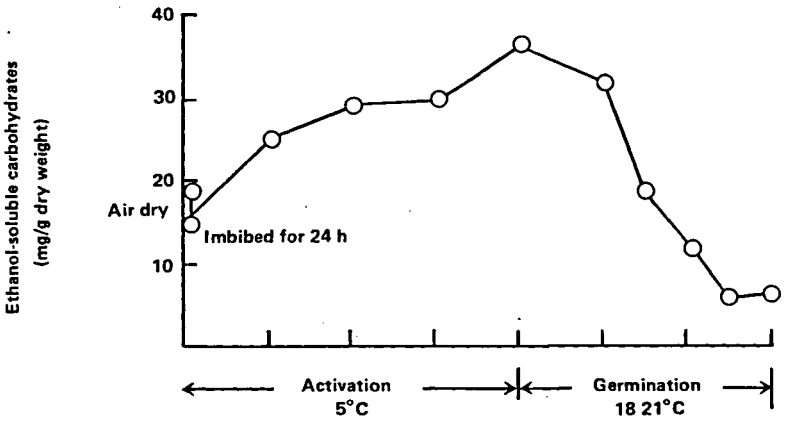


FIGURE 6. Changes in total sugars during activation and germination of ergot sclerotia. (Adapted from Cooke, R. C. and Mitchell, D. T., *Trans. Br. Mycol. Soc.*, 54, 93, 1970.)

Ergot sclerotia contain relatively high amounts of amines. Methyl-, trimethyl-, ethyl-, *n*- and isopropyl-, isobutyl-, isoamyl-, *n*-hexyl-, and phenylethylamine have been identified.[122,123] Other aliphatic amides in ergot sclerotia were discovered by ApSimon et al.[7] A cerebrin-like material, ergocerebrin, $C_{42}H_{83}NO_3$, and a known cerebrin have been isolated from ergot residues remaining after removal of the phenolic pigment.

Other nitrogen-containing compounds identified in ergot sclerotia include choline, acetylcholine, betaine, uracil, and guanosine.[54]

Carbohydrates

Sugar analyses of "honeydews" from infected hosts indicate that synthesis of the major sugars is controlled by the parasite and that sugar composition is distinct for each fungus.[94] The identity of the sugars in the "honeydews" of various cereal ergots has been reported by several investigators.[33,45,94,95] The types of sugars in "honeydew" include hexoses, alditols, fructofuranosylglucoses, and fructofuranosylalditols. Glucose and fructose are present in most "honeydews".

A number of soluble carbohydrates are present in sclerotia during both the dormancy phase and germination. Glucose, trehalose, mannitol, and arabitol were found in ergot sclerotia of *C. purpurea* and *C. nigricans*. Trehalose and mannitol are the major carbohydrates present. Quantitative determinations indicated that mannitol constituted about 1% of the dry weight of the sclerotium.[24] The sugars are synthesized via a lipid-consuming system activated during the low temperature dormancy breaking treatment. Carbohydrates are consumed during germination of the sclerotia.[24] They are the predominant components in the nutrition of the fungus.[78]

During activation (low temperature chilling) sclerotia show an increase in mannitol and trehalose. Subsequently, the levels of these carbohydrates decline during germination to an apparently constant level. The changes in total sugar during activation and germination, as reported by Cooke and Mitchell,[25] are shown in Figure 6. Total sugar rose from 15.9 mg/g to 35.8 mg/g at the end of the activation period and then declined rapidly as germination progressed.

Sugars and polyols are present within the sclerotium when it is formed and are utilized during dormancy. During activation by low temperature sufficient carbohydrates are formed to support germination and stroma production.[24]

The roles of arabitol and glucose are unknown. Arabitol disappears during either dormancy or activation and does not subsequently reappear.

TABLE 5

Fatty Acids in Ergot Sclerotia

Fatty acid		Fraction of unesterified fatty acids (%)	Fraction of esterified fatty acids (%)
Lauric	C-12	0.53	0.08
Myristic	C-14	0.52	0.36
Palmitic	C-16	32.66	33.37
Palmitoleic	C-16:1	4.66	4.03
Margaric	C-17	0.80	0.20
Stearic	C-18	4.89	5.11
Oleic	C-18:1	24.38	21.30
Linoleic	C-18:2	28.84	12.29
Linolenic	C-18:3	0.62	0.35
Octadecatetraenic	C-18:4	0.77	0
12-Hydroxystearic	C-18-OH	0.61	22.00
Arachidic	C-20	0.34	0.96
Behenic	C-22	trace	0

Adapted from Thiele, O. W., *Biochim. Biophys. Acta*, 84, 483, 1964.

A glucan consisting of a central chain of several hundred 1 to 3-linked β-D-glucopyranosyl units with branches has also been detected in ergot sclerotia.[101] The branches are single β-D-glucopyranosyl units attached by 1 to 6 linkages to every fourth unit of the central chain.

There are reports that ergot sclerotia also contain inositol and erythritol.[24] All the determinations of sugars and polyols in ergot sclerotia are qualitative in nature. Quantitative data are lacking.

Lipids

Total fat content of ergot sclerotia ranges from 10 to 45%.[79,81,131] Thin-layer chromatographic analysis indicated that the fat was composed mainly of triglycerides and smaller amounts of steroids and unesterified fatty acids.[68]

Composition of the fatty acids as determined by gas-liquid chromatography by Thiele[131] is shown in Table 5.

The glyceride oil of naturally occurring *C. purpurea* has long been known to contain 25 to 35% ricinoleic acid.[88] Ricinoleic acid has been identified as a metabolite in laboratory cultures of *C. purpurea* as the principal component of the triglyceride oils.[86] Thiele,[131] however, did not detect ricinoleic acid in his sample of ergot oil. The C-18 hydroxy acid, which he found, was shown to be 12-hydroxystearic acid.

Morris and Hall[92] demonstrated that the glycerides in ergot oil are of unusual structure in that the hydroxyl groups of the ricinoleic acid units are not free but are esterified with a variety of long chain fatty acids.

Pigments

Ergot sclerotia contain a number of pigments. A detailed history of the discovery of these compounds has been written by Bové.[13]

The pigments can be placed into two groups, according to Franck.[40,41,42] One is the orange-red group of pigments having anthraquinone carboxylic acids as their structure and the other is the group of bright yellow or ergochrome pigments. The pigments are listed in Table 6. They form dimers. Thus, secalonic acid A and B, or ergochromes AA and BB, are symmetrically stereoisometric. Secalonic acid C was shown to be nonsymmetric. The structure of a yellow pigment then can be identified by two letters to

TABLE 6

Pigments in Ergot

Group	Pigment	Color	Formula
1	Endocronin	Orange	1,6,8-Trihydroxy-3-methylanthraquinone-2-carboxylic acid
	Clavorubin	Red	1,5,6,8-Tetra-hydroxy-3-methylanthraquinone carboxylic acid
2	Ergochrome AA (4-4')	Yellow	Secalonic acid A — $C_{28}H_{26}O_{12}$
	Ergochrome BB (4-4')	Yellow	Secalonic acid B — $C_{28}H_{26}O_{12}$
	Ergochrome AB (4-4')	Yellow	Secalonic acid C — $C_{28}H_{26}O_{12}$
	Ergochrome CC (2-2')	Yellow	Ergoflavin — $C_{30}H_{28}O_{14}$
	Ergochrome AC (2-2')	Yellow	Ergochrysin A — $C_{56}H_{56}O_{24}$
	Ergochrome BC (2-2')	Yellow	Ergochrysin B — $C_{56}H_{56}O_{24}$

Adapted from Franck,[142] Bove,[13] and Stoll et al.[126]

indicate the monomeric unit and two numbers to indicate the C-C linkage. Ergot sclerotia contain yellow pigments ranging from 1 to 2% of total weight.[126]

Some researchers believe that there is a connection between these pigments and the alkaloid content of the ergot sclerotium, while others do not. The argument has not been settled. It is a fact, however, that several biosynthetic processes of the alkaloids and the pigments are the very same in the early stages of formation.[13]

Minerals

The ash content of ergot sclerotia ranges from 2.2 to 6.5%.[12,81] Twenty-seven mineral elements — aluminum, barium, beryllium, boron, calcium, chromium, cobalt, copper, gallium, germanium, iron, lead, lithium, magnesium, manganese, mercury, molybdenum, nickel, phosphorus, potassium, silicon, silver, sodium, strontium, titanium, vanadium, and zinc — have been identified in ergot sclerotia.[12]

The amounts of several mineral elements in ergot sclerotia in comparison with those of kernels of triticale variety from which the sclerotia were harvested are given in Table 7. Each of the mineral elements determined was present in higher concentrations in ergot sclerotia than in the sound kernels of triticale. Kybal[78] reported 0.50% P in sclerotia compared to 0.40% P in rye kernels.

The element phosphorus (P) is of special significance. P supply is the limiting factor for ergot growth and ripening of the sclerotia of *C. purpurea*.[79]

Ergot sclerotia replace the grains in the heads of cereals; and are thus supplied with the same nutrients as the grain. A pronounced decrease in P content of ripening sclerotia, as shown by Kybal et al.,[79] indicated an insufficient supply of utilizable P from the host during the development of the parasite. Surplus nitrogen and sugar that cannot be assimilated due to lack of P during ergot development are excreted as "honeydew".[78]

Furthermore, Kybal[77] found that a high content of P is a limiting factor in the biosynthesis of ergot alkaloids. Total alkaloid content of ergot sclerotia was shown to have a statistically significant correlation with the numerical value of the ratio, total N:total P. At a low level of available P, the nitrogen source becomes the governing factor. Inversely, increasing amounts of P inhibit the response of availability of nitrogen.[77]

ERGOT AND DISEASE

Epidemics supposedly caused by the consumption of poisonous breads ravaged Europe from the 10th century up to modern times. It is believed that all of these epidemics were due to ergot contamination and specifically due to the alkaloids in ergot, but

TABLE 7

Mineral Content of Ergot and a Semi-dwarf Triticale

Mineral element (ppm)	Semi-dwarf triticale kernels	Triticale ergot sclerotia
Potassium	3713 ± 65	4750 ± 71
Magnesium	829 ± 20	914 ± 24
Sodium	156 ± 12	219 ± 18
Zinc	70 ± 9	89 ± 11
Iron	63 ± 4	97 ± 3
Manganese	65 ± 3	65 ± 4

Adapted from Lorenz, K., *Lebensm. Wiss. Technol.*, 11, 70, 1978.

some of the claims are disputable since nobody really knows when ergot was first mentioned in the literature and positively identified as the cause of the problems.[13]

Detailed descriptions of recorded outbreaks of ergotism throughout the history of civilization can be found in books written by Barger[10] and Bové.[13]

In these epidemics the average mortality was between 10 and 20% of those who became ill in the 10th through the 18th century. Higher mortality rates were reported in some instances. Ergotism of the 19th century yielded to medical treatment and the mortality was not as high. Children were more susceptible to the disease than adults.

While most of the epidemics in Germany, France, Ireland, Finland, Russia, and Belgium were due to ergot of rye, several cases in England were caused by ergotized wheat, in Sweden it was barley and oats which were contaminated, in Algeria it was barley, and in Colombia maize which contained the ergot.

Ergotism was rare in fertile districts which provided a variety of foods compared to areas with poor soil which only allowed cereal grain production. Farmers who had a supply of meat and dairy products and did not have to rely exclusively on cereals were less often affected than the poor laborers who could only afford to buy the contaminated flour from the miller. Poor families baked the ergotized flour not only into bread, but used it to prepare dumplings, pancakes, porridge, soups, and other foods. This almost exclusive use of rye flour explained the sudden outbreaks of ergotism, most of which came immediately after the harvest.

The food supplies of the previous year were often exhausted at the time of the rye harvest in late July or early August. Therefore, the grain which fell out during harvesting was milled immediately and this grain was especially rich in ergot. The ergot sclerotia became detached more readily than the rye grains. In some countries the government helped the poor in times of epidemics by supplying sound grain, but when this supply was exhausted, the peasants were again forced to use their own supplies, which resulted in reoccurrence of the disease.[10]

Ergotism was definitely a disease of the poor. The well-to-do separated the grain, but the poor could not afford to waste anything.

ERGOTISM IN MODERN HISTORY

During the last two decades there has not been a recorded outbreak of ergotism. Grain standards in all developed and most developing countries are very strict and do not permit grain, which contains ergot above a certain small percentage level, to reach commercial food channels. Only ignorance, carelessness, or gross negligence on the

part of a miller in a small community could cause another outbreak of ergotism in modern times.

The last reported outbreak of ergotism in the little river city of Pont St. Esprit in southern France in 1951 was due to gross negligence.[48] The miller admitted knowing that the grain was contaminated. He milled the ergotized rye and sold the flour to a baker in Pont St. Esprit who realized that it was of poor quality but did not suspect ergot. Due to the consumption of rye bread baked from the flour more than 200 people became ill. The doctors who treated those unfortunate people reported that one man plunged out of his window screaming hysterically that he was a jet plane. From a third floor hospital room a 68-year old women leaped to the ground to escape the flames she imagined engulfed her. Other sufferers insisted that they were being chased by wild beasts. Many victims were forcibly subdued and carried to hospitals.

The first symptoms appeared 6 to 48 hr after consumption of the bread and consisted of a depressive state with slight agitation followed by digestive disturbances. People experienced nausea with abdominal pains. In 30% of the cases vomiting and diarrhea were noted. Disturbances of the nervous system accompanied by digestive disorders followed. Gusts of warmth, followed by impressions of cold waves, were described. The patients were pale, had a weak pulse, rather muffled heart sounds, and low body temperatures. Thereafter, insomnia appeared, which lasted several days. The digestive disorders became worse, with burning sensations throughout the entire digestive tract, abundant sweating, and trembling of the extremities. Most patients had a disagreeable body odor.

The disorders developed more quickly in children, but also left them more quickly. For most patients in Pont St. Esprit the illness as described went no further. They recovered after several days.

In other cases, however, more severe disorders appeared, such as cramps, severe fainting attacks, tremors accompanied by fibrillary twitching, and hallucinations. In several of the patients these hallucinations were followed by dreamy delirium. Every attempt of restraint increased the agitation of the patients.

Four fatal cases were reported from the outbreak in Pont St. Esprit — three men and one woman. They died in muscular spasm and in a state of cardiovascular collapse.[48] The ergot epidemic in Pont St. Esprit received much publicity in the press.[3,4]

The amount of ergot in the flour used to bake the breads was not determined but it had to be a substantial amount. Ergot intake had to be considerably less, however, than that of a family in Haute Savoie in France in 1843. Father, mother, and seven children ate within 3 days 8600 g of bread containing 14% ergot. On the average each family member consumed 133 g of ergot. All suffered from severe convulsions lasting a month. A 10-year-old boy had both legs amputated, another child lost one leg. It was estimated that the dead child had consumed 125 g of ergot.[10] That is a large amount.

Correlation of grain inspection and medical statistics shows that the disease occurred when there was 1% or more of ergot in the cereal grain, 7% causing fatal poisonings. In many of the epidemics between the 10th and the 18th century the amount of ergot in the grain exceeded 30%.

TYPES OF ERGOTISM

From medical records of ergot epidemics, Barger[10] described in detail all the symptoms of the two different types of the disease. The following is a summary of these symptoms.

Convulsive Ergotism

The milder forms of convulsive ergotism are characterized by a feeling of fatigue, heaviness in the head and arms and legs, pressure and pain in the chest. Sometimes mild diarrhea, with or without vomiting, which lasts for several weeks, accompanied these symptoms. A very common early symptom was a tingling sensation. "Pins and needles" were experiences of many patients. After a few weeks convulsive muscular twitching and spasms of the limbs followed. These spasms might begin in the toes and then gradually extend upward. Other groups of muscles might also be affected, resulting in spasms of the face, the vocal cord, the esophagus, and the diaphragm.

In severe cases the whole body was attacked by extremely painful convulsions which returned at intervals of a few days and lasted from a few minutes to several hours. The first convulsions often occurred 2 to 3 days after eating the poisonous bread. A cold sweat covered the whole body. The knee-jerk was lost in all moderately severe cases and was restored after a lapse of several years.

Between convulsions many patients suffered little discomfort. They might have been sick only 1 day and working in the fields the next.

In severe cases people were extremely hungry. It had been suggested by Dale, cited by Barger,[10] that the severe hunger was the result of hypoglycemia due to ergotoxine poisoning, intensified by the disappearance of glycogen from the muscles during convulsions.

In severe, but nonfatal cases, the disease might have lasted 6 to 8 weeks. Convalescence took several months. Relapses occurred frequently, however, and were accompanied by epilepsy, gastric pains, permanent contractures of the hands and feet, and impairment of hearing. Sight was also impaired due to improper nutrition and cataract formation.

In extreme cases patients would lie for 6 to 8 hr as if dead, with paralysis of the lower limbs. Delerium and loss of speech often occurred. The patients then became unconscious and generally died on the third day after the onset of the first symptoms.[10]

For a long time it was believed that the disease was infectious, since often all the members of a family living on the same diet became ill at the same time.

Gangrenous Ergotism

The individual susceptibility to gangrene seemed to vary greatly. The pulse and appetite remained normal at first. The patients then began to complain of a general lassitude. There was slight vomiting. Pains in a limb followed. In a few weeks the affected part became swollen and inflamed and was attacked by burning pains. This feeling of intense heat alternated with one of icy cold. The patients would try to seek relief in the open air, but then felt so cold that they had to immerse their limbs in hot water. Gradually, the diseased part became numb and the pains stopped. Later, the part became black and all sensations were lost. It shrank, mummified, and dried. The gangrene then gradually spread upward.

The skin in general, but particularly the face, was yellow. The whole body was emaciated.

In severe cases the course of the disease was more rapid. There were violent pains and gangrene would set in suddenly. The separation of the gangrenous part took place spontaneously at a joint without pain or loss of blood. The extent of the gangrene varied from the loss of nail to that of fingers and whole arms or legs. After the loss of a single limb the patients often made a good recovery but were sometimes attacked again in a second epidemic.[10]

TABLE 8

Ergot on Cereal Grains (%)

Cereal Grain	Fargo, N.D. Planting date 4-14	Fargo, N.D. Planting date 5-7	Carrington, N.D. Planting date 4-23
Era wheat	0.00	0.01	0.01
Waldron wheat	0.03	0.25	0.13
Dickson barley	0.04	0.18	0.04
Lodi oats	0.01	0.01	0.00
Rosner triticale	ND*	0.53	0.06
Triticale 6-TA-203	0.21	0.39	0.18
Triticale 6-TA-204	0.37	0.92	0.25
Triticale 6-TA-209	0.20	0.86	0.47

* Not determined.

Adapted from Busch, R. H. and Wilkins, H. D., *N.D. Farm Res.*, 29(3), 29, 1972.

AGRICULTURAL CONSIDERATIONS

Grain Losses Due to Ergot

Ergot is very frequently found on cereals throughout the temperate regions of North America. Relatively high infections are occasionally observed on rye (*Secale cereale* L.) and durum wheat (*Triticum durum* Desf.) and in recent years have been common on triticales.[82] In most instances these infections have been below the tolerance maximum established for each cereal grain and therefore, have not received wide publicity. In Europe the ergot fungus has been at times troublesome on rye in certain years when conditions were favorable for the development of *C. purpurea*.

There always have been and always will be ergot infections and a possible danger to human health, but man has learned to minimize the effect and keep any contamination below the maximum levels permitted.

With an ergot infection cereal grain yields decrease due to the replacement of ergot sclerotia for grain kernels but also due to the fact that flowers remain sterile although they do not necessarily bear sclerotia. Therefore, there can be economic losses.

Field observations have shown that the actual damage is always greater than that based on the assumption that the loss caused by ergot is directly proportional to the number of sclerotia produced as the result of transformation of potential grain kernels into the corresponding number of poisonous sclerotia.[111]

Heavy infections with ergot, such as the ones which caused epidemics in the Middle Ages, are very rare in modern times, however, and arise only through a coincidence of several climatic conditions. The chief factor is a wet season for germination of the sclerotia. For the dissemination of the ascospores formed from the sclerotia, dry and windy weather is needed. When infection has taken place, the growth of sclerotium is favored by hot weather.[10] Only when all these factors are present do we see relatively high ergot contents in cereal grains. These are exceptional years.

Differences in susceptibility to ergot between cereal grain varieties grown at a given location are illustrated in Table 8. The level of infection varied with location. Ergot contamination was higher on triticales than on wheat and was affected considerably by the date of planting at Fargo.[18]

Often infections are observed in a small, isolated area. It may be a particular valley or even a single low-lying field which is heavily ergotized compared to the surrounding fields. Ergot is also generally more abundant along the edge of a field than in the middle, because plants on the periphery are not so readily pollinated and/or are more frequently visited by insects.[10]

In Russia the prevalence of ergot has been correlated with rainfall, relative humidity, and the number of overcast days in June and July,[109] and the percent contamination has been forecasted by determining the percentage of the ergotized plants in field, which is said to be about 43% as great as the percentage of ergot by weight in the unharvested grain.[73] During harvesting and threshing about half of the ergot is eliminated, which increases the prediction factor to 86. When this factor is applied to calculate the ergot in rye during the 1926 epidemic in Russia, in which 75% of the plants were infected, a value of 75/86, or 0.9%, is obtained. Actual contamination in samples of grain traded was 0.44% which at present grain standards would be above the tolerance levels in Russia and in the U.S.

The presence of ergot on wheat in England is rare and, when it does occur, the contamination is light and not widespread.[2] No heavy infections of the rye crop have been reported by member countries of the European Economic Community (EEC) in recent years.

In the U.S. the FDA conducted a comprehensive survey in 1951 of grains from all sections of the U.S. This was done immediately after the Pont St. Esprit epidemic in France had received much publicity. Of 1700 samples of wheat received from mills, terminals, and other elevators, the FDA did not find one instance of the presence of ergot on wheat or rye. That was reassuring. With our preoccupation with matters of ecology and our passion for pure air, water, and food, high levels of ergot in grains would give our consumer advocates something to write about for many years.[5]

A few cases have been reported, however, in which ergot contamination has caused some losses in the U.S. Farmers of the northwestern U.S. suffered some losses in the durum wheat crop of 1921.[136] A moderate infection of the Northern Spring and Hard Winter wheat occured in 1946.[2] The 1971 crop of the U.S. Northern Hard Spring wheat was sufficiently high in ergot to call for an investigation, although average contamination in North Dakota was only 0.08%, which is still below the 0.3% level required for the wheat to be graded "ergoty".[6]

The cereal industry was concerned, however, and reminded again that the contaminant is likely to proliferate whenever conditions are right and that there is always a potential threat requiring constant vigilance.[6]

Development of a hybrid cereal with greatly improved yield may lead to its widespread acceptance and create a potential ergot problem.

There should never be a problem, however, in the U.S. or anywhere else in the world, if industries handling and processing grain adhere to the established standards.

Ergot Tolerances

Ergot tolerances have been established in many but not all countries. These tolerances differ between countries and often between cereal grain types.

Wheat and rye containing 0.3% ergot and triticale with 0.1% ergot are graded "ergoty" in the U.S.[35,74,133]

The Canadian Grain Act specifies that the highest grades of wheat and rye intended for milling should be free of ergot. Grain samples containing more than 0.33% ergot sclerotia by weight are graded "ergoty".[143]

Countries of the EEC, have set a limit of 0.1% of ergot for wheat[74] and 0.5% for "Black Besatz" in rye which includes weeds, seeds, unsound kernels, smutty kernels, chaff, and other impurities as well as ergot. The EEC has at present no legal standards for triticale.

TABLE 9

Response of Wheat Cultivars Inoculated With *Claviceps Purpurea*

Cultivar	Florets with sclerotia (%)	Size of sclerotia[a]	Amount of honeydew produced[b]
Manitou	70	2	3
Kenya Farmer	26	1	1
Stewart 63	78	3	4
Carleton	42	1	2

[a] 1 = very small; 3 = considerably larger than grain kernels.
[b] 1 = no honeydew; 2 = honeydew within glumes; 3 = honeydew exuding from florets in small drops; 4 = large drops of honeydew running down the head.

Adapted from Platford, R. G. and Bernier, C. C., *Nature (London)*, 226, 770, 1970.

In countries with a high rye bread consumption, which do not belong to the EEC, national laws generally do not permit the use of rye with ergot contamination higher than 0.2%.[35] The U.S.S.R. established a 0.15% level for rye.[10] Japan set a very low limit of 0.04% of ergot in wheat.

The specific tolerances established by different countries became quite important in international grain shipments.

Prevention of Ergot on Grains

Cereal grain growers carry a considerable responsibility in producing ergot-free crops. They cannot become careless or complacent.

To minimize ergot infection, good farm management is essential. This means clean seeds, clean fields, removal of weeds and grasses from areas adjacent to fields, and crop rotations. Seed selection should be based on sound judgment for local adaptation, plant disease resistance, and appropriate quality characteristics.[50]

A homogeneous crop, in which all plants flower at the same time, is desirable.

Housekeeping practices on the farm can be improved in many instances to lessen the likelihood of infection. Wild grasses near the grain fields should be cut, because these flower early and become a source of infection before the grain flowers.

Planting varieties of wheat or rye less prone to ergot can correct the problem. As shown in Table 9, the wheat variety Manitou was about three times as susceptible as Kenya Farmers and the durum variety Stewart 63 about twice as susceptible as Carleton. Platford and Bernier[103] expressed the resistance by a decrease in the number of sclerotia formed, by the reduction of the amount of honeydew produced, and by the size of the sclerotia. They stated that the number of sclerotia produced per head was a fairly accurate index of the degree of infection. The resistance to ergot of the varieties of Kenya Farmer and Carleton was considered quite adequate. Although infection may occur when planting these varieties, honeydew production would be small and secondary infections minimal. Since only low numbers of very small sclerotia are produced the amount of primary infection in the following year should be reduced.

The wheat variety Chris was found to be less susceptible to ergot than the variety Waldron in a different study.[49]

Recently, a new high yielding cultivar of spring rye named Gazelle appeared to be less susceptible to ergot infection than other cultivars of spring rye.[119] In a subsequent study, Gazelle spring rye was consistently lower in percentage of ergot sclerotia in seed samples from plots grown at seven locations in 1973 and 1974 in companion with other

TABLE 10

Percentage by Weight of Ergot Sclerotia in Seed Samples from Experimental Plots at Four Locations in Saskatchewan (1974 Harvest)

Spring rye cultivar	Saskatoon	Indi	Indian head	Arcola	Average (1973—74)
Gazelle	0.65	0.41	0.57	0.01	0.24
Prolific 1	1.70	0.53	1.23	0.04	0.65
Prolific 2	1.82	0.68	1.66	0.05	0.77
S6204	1.46	0.93	2.10	0.06	0.79

Adapted from Sosulski, F. and Bernier, C. C., *Can. Plant Dis. Sur.*, 55, 155, 1975.

spring rye varieties. The 1974 harvest data of Sosulski and Bernier[120] are shown in Table 10.

Ergot infection of some spring rye plots exceeded 1.0% during the 1974 tests because of small plot size and close proximity to roadways sown to perennial grasses. The 1973—74 averages, however, were all below 1.0%.

The lower incidence of ergot observed in Gazelle was apparently due to a better flowering habit which allowed the variety to escape infection to a greater degree than other spring cultivars.[120]

From these few examples, it is obvious that it is possible to select cereal grain varieties which under given agronomic and climatic conditions are less susceptible to ergot than others.

Rotation of crops is also very effective. Sclerotia do not germinate generally after one year and only cereal grains are attacked.

How about the ergot sclerotia left on the ground after the harvest? How do we prevent them from ergotizing the cereal crop the following year if another cereal group is being produced on the same land? There are two possible ways to do that. One is to pick up the sclerotia and destroy them, which just is not feasible. The alternative is to bury them deeply (10 to 12 in.) which requires deep plowing. At that depth, germination or spore production of ergot is impossible.[13]

Removal of Ergot from Contaminated Cereal Grains

Ergot bodies remain intact when cereal grains are in storage. When grains are transported, ergot tends to break into smaller fragments, however, since ergot is less sound structurally than grain kernels. During transport, these ergot fragments tend to rise towards the top of the transporting vehicle, because of their lower density, creating the impression that these fragments have increased in number. This, however, is only the result of breakage of the relatively large ergot bodies into smaller fragments during loading, transport, and unloading.[50]

Removal of intact ergot bodies as part of the "dockage" — the material that can be readily removed from the grain by prescribed mechanical means — with conventional grain-cleaning equipment such as sieves and separators is relatively easy, since they are larger in size than cereal grain kernels.[50] Up to 82% of ergot removal is generally possible by this process.[113] Remaining ergot particles can be removed by use of a flotation technique using 20% sodium chloride solutions, or 32% potassium chloride solutions which do not damage the seeds, and could ultimately be used as a fertilizer.[49]

TABLE 11

Percent Recovery of Ergot in Mill Streams

	Buhler mill ergot in wheat (%)			Pilot mill ergot in wheat (%)		
Mill stream	0.3	0.6	5.0	1.0	5.0	15.0
Bran	74.2	72.3	74.1	2.5	1.2	0.5
Shorts	18.4	19.7	19.2	76.8	80.0	76.1
Break flour	1.7	2.2	2.9	3.9	3.0	2.4
Reduction flour	5.1	4.6	3.5	8.5	8.3	5.5
Low grade flour	0.7	1.1	0.3	8.2	7.6	5.5

Adapted from Shuey, W. C., Connelly, F. J., and Maneval, R. D., *Northwest. Miller*, 280(3), 10, 1973.

ERGOT IN CEREALS AND CEREAL-BASED PRODUCTS

Milling of Ergoty Wheats

Shuey et al.[113,114] milled a wheat mix containing different percentages of added ergot on a Buhler experimental mill and on a Pilot mill, respectively, to determine if ergot contamination would influence the milling characteristics of the wheat mix and to express the distribution of ergot in the different milling streams. Their results are shown in Table 11.

The distribution in percent of ergot for the two mills indicated that it is possible to control the streams containing the most ergot. Between 80% and 90% of the ergot could be directed to the feed streams — bran and shorts. The absolute amount would depend on the mill flow, flour extraction, and initial ergot contamination. That mill flow will affect ergot distribution is apparent from the data in Table 11, the Buhler mill producing highest ergot recovery in the bran fraction while the Pilot mill showed the highest amounts in the shorts.

In a later study, Shuey et al.[115] showed that flour extraction decreases with increased ergot contamination. The change in flour extraction with addition of ergot is shown in Figure 7. The percent ergot recovered vs. the percent flour extraction is shown in Figure 8. The decrease in flour extraction and proportional percent recovery of ergot demonstrates the deleterious effect of ergot on the milling properties of wheat.[115]

Effect of Ergot on Rheological Properties of Flours

Amylograph viscosities decreased at all reference points as the level of ergot reached 1% or higher in flour which is, however, considerably higher than the 0.3% level, or the 0.1% level of ergot permitted by U.S. and ECC grain standards,[81] respectively. Lower amounts of ergot produced only insignificant changes in viscosity as shown in Table 12.

Farinograph characteristics were not significantly affected up to a level of 0.5% ergot in flour as shown in Table 13. Replacing 1% or more of the wheat flour with ergot resulted in increased absorption and in decreases in farinograph peak times, stabilities, and departure times. It required 5% of ergot in flour to affect the mixing tolerance index.[81]

This indicates that ergot contamination at levels above those permitted by the grain standards cannot necessarily be detected by the normal evaluation of a flour in a cereal chemistry laboratory. Only when the level of ergot in the flour reaches 1% will rheological characteristics of a flour as determined with the farinograph or the amylograph deviate from the normal behavior of the flour in these instruments.[81]

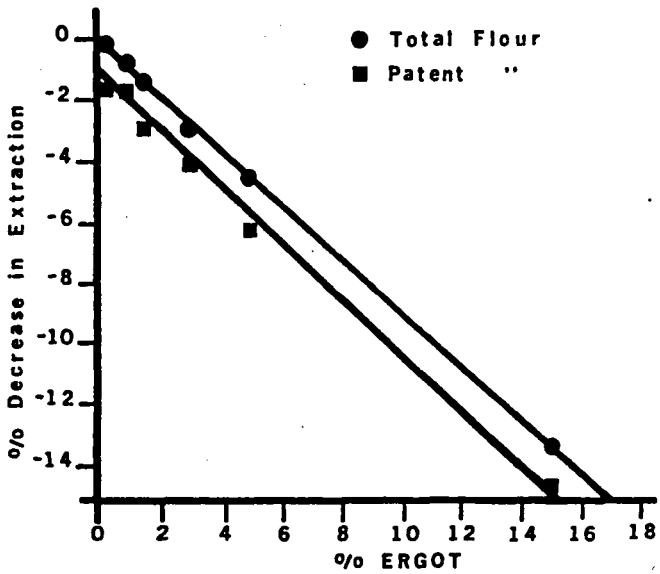


FIGURE 7. Percent decrease in flour extraction vs. percent ergot contamination in wheat mix. (From Shuey, W. C., Sibbitt, L. D., and D'Appolonia, B. L., *Cereal Chem.*, 52, 101, 1975. With permission.)

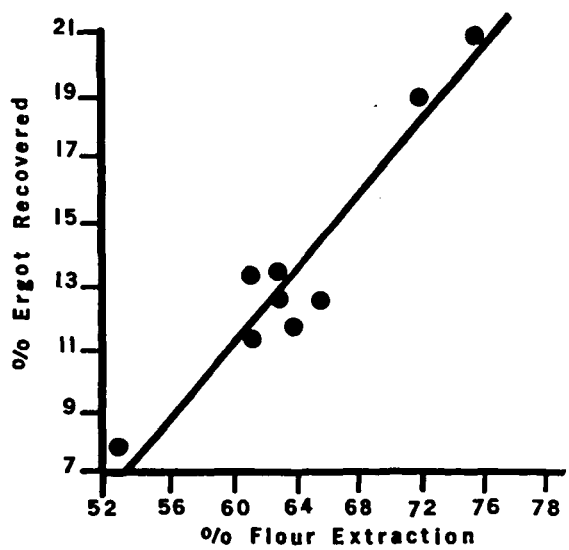


FIGURE 8. Percent of total ergot recovered vs. percent flour extraction. (From Shuey, W. C., Sibbitt, L. D., and D'Appolonia, B. L., *Cereal Chem.*, 52, 101, 1975. With permission.)

Baking with Flours Containing Ergot

Reports on the effects of using ergot-contaminated flours on bread-baking performance are very few in number.[82,115]

Shuey et al.[115] observed discoloration in the flour as ergot levels in the wheat increased. Flours containing 1.5 and 3.0% ergot appeared to be mixed with black pepper, while ergot in amounts of 0.3% was hardly noticeable. This discoloration carried over

TABLE 12

Effect of Ergot in Wheat Flour on Amylograph Viscosity (Brabender Units)

Amount of ergot in wheat flour (%)	Viscosity at peak	Viscosity at 92°C	Viscosity after 30 min at 92°C	Viscosity cooling to 35°C	Viscosity after 60 min at 35°C
None (control)	1020	260	110	360	1630
0.3	990	260	110	380	1620
0.5	980	250	120	370	1650
1.0	910	230	100	340	1350
3.0	840	230	110	330	1200
5.0	740	210	100	310	1090

From Lorenz, K., Baking properties of ergot-containing flours, unpublished data.

TABLE 13

Effect of Ergot in Wheat Flour on Farinograph Characteristics of Flour-Water Doughs

Amount of ergot in wheat flour (%)	Absorption (%)	Arrival time (min)	Peak time (min)	Stability (min)	Departure time (min)	Tolerance index (B.U.)*
None (control)	66.0	3.5	8.0	15.5	19.0	20
0.3	66.0	3.0	8.0	13.0	16.0	20
0.5	66.2	3.0	8.0	14.0	17.0	20
1.0	67.0	2.5	7.5	13.0	16.0	20
3.0	68.0	4.5	7.0	7.0	11.5	20
5.0	68.5	4.5	7.0	6.0	11.5	50

* Brabender units.

From Lorenz, K., Baking properties of ergot-containing flours, unpublished data.

into the dough when the high ergot flours were baked into bread. The baking results showed no apparent influence on the baking properties of flours milled from a wheat containing 0.3% ergot, the maximum amount permitted under the U.S. grain standards.

Breads baked from flours containing different amounts of ergot are shown in Figure 9. Ergot contamination is not necessarily recognizable by the consumer when present in amounts up to 0.5% in white bread.[82] It becomes even more difficult to detect in whole wheat breads or rye breads which are considerably darker in crumb color than white breads.[82] There are no differences in bread volume due to ergot as shown in Figure 9. Crumb color, however, becomes quite dark at higher levels of ergot in flour.

The average daily intake of flour from all sources is approximately 135 g.[2] If this quantity contained 0.1 g of ergot, the degree of contamination of the flour would be 0.07%. Taking the highest figure recorded for the proportion of ergot in wheat that might get into the flour (20%), a contamination of 0.07% in a flour of 72% extraction would correspond to a contamination in the wheat of 0.25%.[2]

A maximum level of 0.05% has been suggested for an acceptable safety-in-use rating of flour for human consumption.[2]

It has to be remembered, however, that the pharmacologically active alkaloids of *C. purpurea* are rather unstable. The alkaloid components deteriorate slowly in whole ergot. The milling of ergot sclerotia greatly increases the rate of deterioration by increasing the surface area to volume ratio. Therefore, any ergot in flours for baking and cooking may contain somewhat less of the active alkaloids.[85]

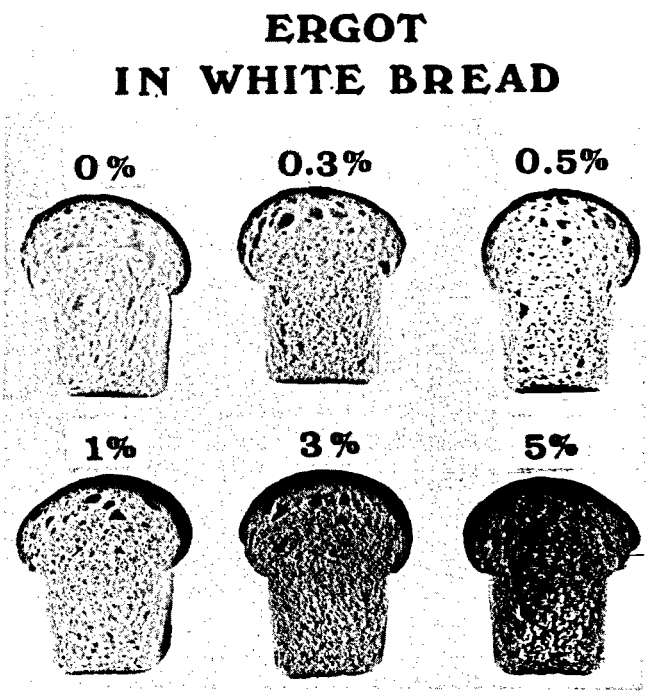


FIGURE 9. Ergot in white bread. (From Lorenz, K., Baking properties of ergot-containing flours, unpublished data.)

Based on the results of Shuey et al.[115] and Lorenz,[82] it has to be assumed that the breads consumed during the ergot epidemics in Europe through history must have shown definite signs of contamination. These breads, however, were eaten because of widespread food shortages and the ignorance of the potential dangers of ergot.

This should not happen today — at least not in the developed countries. Modern techniques of farm management, milling and baking, and close laboratory control of our basic raw materials for bakery production should preclude any possible danger. But that is precisely what was said before the latest major epidemic in Pont St. Esprit in France in 1951.

All involved in cereal grain production and utilization should be cognizant of the potential danger.

DETECTION OF ERGOT IN FLOURS AND BREADS

Available methods for the detection of ergot in cereal products are not completely satisfactory. Good chemical methods are needed to replace the reliable but rather complex biological methods which have been developed.[74,87]

For the determination of the ergot content of cereal grains or their milling products, the following methods are available today:

1. Color tests and simple colorimetric methods
2. Microscopic determination of ergot fragments
3. Chemical determinations of total ergot alkaloids
4. Determination of the pigment content of ergot
5. Biological determinations of the effects of ergot alkaloids in cereal products on experimental animals

Not mentioned in this review, however, are the many different tests which have been developed to analyze samples of ergot grown and harvested specifically for pharmacological use. These tests have been described in detail by Barger[10] and Bové.[13]

Color Tests and Simple Colorimetric Methods

Rye bread containing 3% or more of ergot is easily recognizable by a slight violet color and by its odor of trimethylamine. At lower levels of contamination the bread is darker than usual and might show a few dark specks, but ergot contamination is not necessarily obvious.[10] In a white bread lower percentage levels (1.5%) are detectable by inspection.

There are several simple colorimetric methods for the detection of ergot. None of these can be considered a standardized test, however. Jacobj, cited by Bové,[13] reported that flour or bread containing ergot produces a pinkish red color when dilute sulfuric acid is added. Using ergot-free flour as the control to which then known amounts of ergot are added, a more or less quantitative measurement of the ergot content of the test sample is possible.

Hofmann[61] developed a more sensitive test which permits the detection of ergot when present in amounts even as low as 0.01%. The flour is moistened with potassium hydroxide, then extracted with acidic ether, and treated wtih sodium bicarbonate. A color measurement is then taken.

Microscopic Determination of Ergot Fragments

Under the microscope, fragments of ergot are characteristically different from any other particles of the flour. They consist of closely packed hyphae, resembling polygonal cells, as was shown in Figure 3. Ergot particles are highly refractive because of their oil content.[10] They also may show the characteristic pigment of ergot especially when the particle was part of the outside wall of the sclerotium. A rough quantitative estimate may be obtained by comparison with flours of known ergot content. Counting of ergot particles of various sizes does not provide sufficient information, however, to state the precise percentage content of ergot nor give an indication of the toxicity of the sample.

Different stains have been suggested for making ergot particles more obvious under the microscope. The starch in the flour should be hydrolyzed first since it can cause some interference. This can be done by boiling the flour with dilute acid or by using an enzyme treatment. The remaining cellulose will stain blue with iodine while the cell walls of ergot sclerotia appear yellowish brown, making contaminations as low as 0.01% recognizable.[59]

Ergot contamination of bread can be shown microscopically. The bread is soaked in water for 24 hr. The starch is then hydrolyzed by boiling in 1 to 1.5% hydrochloric acid after which the residue may be examined directly or first washed with alcohol and centrifuged. Amounts as low as 0.05% of ergot have been detected by this method.[10]

Chemical Determination of Total Ergot Alkaloids

Barger[10] and Bové[13] described the many colorimetric methods for total alkaloid content of ergot developed up to the 1960s. Recent chemical determinations of ergot alkaloids involve fluorometric,[55,56] spectrophotometric,[91] or colorimetric methods.[134] Any method, however accurate, establishing the total alkaloid content to estimate ergot contamination of cereal grains will only give little information on the biological activity of the sample tested, since it will include, together with the active alkaloids, inactive alkaloids as well as other hydrolysis products.

The van Urk method,[134] with modifications as summarized by Michelon and Kelleher,[91] is probably the most widely used method today for total alkaloid determinations

of food- and feedstuffs. It involves a color reaction (blue) between alkaloids extracted from cereal grains and flours and *p*-dimethylaminobenzaldehyde. The values obtained by this method can vary greatly, however, depending upon the alkaloid composition of the sample.[74] The van Urk reaction depends on the presence of the indole structure for a positive reaction and cannot distinguish between active lysergic acid- and relatively inactive isolysergic acid derivatives. The alkaloids of the lysergic acid group are considerably more toxic than all derivatives of the isolysergic group. Furthermore, pigments and other compounds, e.g., tryptophan, interfere with the van Urk reaction.[135] Decomposition of the alkaloids also results in loss of toxicity within approximately 1 year.

Total alkaloid content is, therefore, not a very meaningful indication of the toxicity of a particular grain sample. The van Urk test is still, however, one of the simplest and most sensitive for the detection of ergot.

The only possibility for an exact chemical determination of each of the different ergot alkaloids in a sample and an assessment of its potential health hazard would be by chromatographic separation. Paper-, thin-layer, and electrophoretic methods have been developed.[1,13] Such methods are, however, too time-consuming and simply not practical for use in the cereal industry.

Determination of the Pigment Content of Ergotized Cereals

Ergot detection methods based on pigment content have been criticized in the past. However, that was before the structures of the ergot pigment were known.[87] Marine Font et al.[37] state that the pigment content of ergot is proportional to its alkaloid content and that a measurement of the pigments, therefore, provides a method of measuring the toxicity of a sample.

The test developed by Marine Font et al.[87] calls for an ether extraction of the flour sample to remove carotenoids and fat followed by a chloroform extraction to isolate the ergochromes. After evaporation of the chloroform, the residue is dissolved in ethanol and absorbance is measured at 370 nm. A 10% $AlCl_3$ solution is added and the absorbance is measured again after 10 min. The quantity of ergot in the flour is calculated from the difference in the absorbance readings. The residue of the flour sample after extraction is treated with 1% hydrochloric acid and the clavorubin extracted with methanol for separation and measurement by thin-layer chromatography. Since clavorubin is specific for ergot, this method can be used to confirm the ergochrome test results.

The authors[87] are aware that cereal grains and the ergot growing on them are natural products and, therefore, susceptible to considerable variations in pigmentation and that the pigments of ergot sclerotia also depend on the state of conservation which would influence the results.

The method of pigment determination for an estimation of the ergot content was not applicable to bread.[87] It is believed that the ergot pigments are partially destroyed during fermentation and exposure to the high heat during baking or that they form stable complexes with the protein or starch, which makes extraction impossible.

Biological Methods of Ergot Detection

There are no other methods which can predict the toxicity of a cereal grain or cereal-based product as effectively as a biological method. Such methods are, however, rather costly and time consuming.

The first investigators fed ergotized cereal grains to pigs and chickens to see if they would die. These tests were actually toxicological and not biological.[13]

In a biological test involving experimental animals, it is recommended to utilize a specific pharmacological property of ergot such as the reversal or abolition of the

motor and inhibitor effects of adrenaline on a number of organs.[10] Furthermore, measurements should be comparative, with reference to an accepted standard, which are available, and in order to reduce the effect of individual variations in a population of experimental animals, it is advisable to compare the known and unknown on the same animal.

Biological methods have not been used often to assess the toxicity due to ergot of cereal products.

ERGOTISM IN ANIMALS

While human ergotism is a disease of the past, ergotism in animals is still frequently being observed today. At times farmers permit their livestock to feed on fields or pastures with ergotized plants without realizing it until it is too late or they might feed their animals the by-products of cereal grain milling operations, such as bran and shorts fractions, which will contain high amounts of ergot when ergotized grains are milled into flour. Up to 90% or even more of the ergot will end up in the feed fractions as was shown in Table 11. Contaminated cereal grain dockage has also been the cause of ergotism.

Poisoning of livestock, attributed to the ingestion of sclerotia of *Claviceps* spp., has been known for many years and has been reported from many parts of the world. A range of clinical signs of ergotism in animals has been described, including gangrene, abortion, convulsions, agalactia, hypersensitivity, lameness, and ataxia.[141] Ingestion of the sclerotia may result in adverse physiological changes affecting peripheral circulation, fertility, lactation, or general behavior due to several of the alkaloids occurring naturally in the sclerotia.[85]

There is a need for additional data on the dosage levels of ergot sclerotia necessary to present a danger to livestock under various conditions under which farm animals are raised. Furthermore, the possibility of microbial modification of the alkaloids due to fermentation in the ruminant to produce more or less potent derivatives needs to be considered.[85]

Economically, the principal animals which are potentially at risk are cattle, pigs, sheep, and chicken. Experiments on small laboratory animals such as mice and rats have indicated certain pharmacological properties of ergot sclerotia, but such experiments may not necessarily be directly related to the large ruminants.

A discussion of the effects of ingestion of ergot on different species of animals follows.

Cattle

The ingestion of sclerotia of *C. purpurea* has been reported to be the cause of reduced feed intake and weight gain, decreased milk production, gangrene of the feet, tail, and ears, and possibly of the lameness syndrome and abortion in cattle.

Effect of Ergot on Feed Intake and Milk Production.

Many researchers[34,39,64,89] have observed a reduced performance feeding cattle diets containing ergot.

A study by Ingalls and Phillips[65] in which 50 dairy calves were fed diets containing 0, 0.07, 0.14, and 0.28%, respectively, of ergot taken from triticale and added to a complete barley diet, showed reduced feed intake of diets containing the ergot. The ergot-free diets produced greater weight gains. Feed efficiency, however, was not affected.

Dinnusson et al.[34] reported that, compared to control groups of animals, there was a 20% reduction in feed intake and, consequently, reduced weight gain when finishing

TABLE 14

Effect of Ergot on Feed Intake and Weight Gain of Cattle

	Beef heifers % ergot in finishing rations			Fattening cattle: Crossbreeds % ergot in barley rations		Fattening cattle: Beef breed % ergot in barley rations	
Weight (lb)	0	0.5	1.0	0	0.5	0	0.5
Initial weight	591	603	586	538	520	382	372
Final weight	623	572	571	1056	1011	817	761
Average daily gain	0.65	−0.06	−0.31	2.19	2.12	1.88	1.68
Feed per day	11.10	8.00	7.77	17.20	15.20	13.40	11.70

Adapted from Dinnusson, W. E., Haugse, C. N., and Knutson, R. D., *N. D. Farm Res.*, 29(2), 20, 1971.

rations containing two levels of ergot were fed to heifers and about a 12% reduction in feed intake when fattening cattle were placed on barley rations containing 0.5% ergot. The results of the study are presented in Table 14.

Additional signs of ergot toxicity included wet pens as the result of greater water intake and urination, heavier hair coats and an inability to shed the winter coats, increased respiration, and some discomfort on warmer days.[34]

The detrimental effect of ergot on milk production was shown by Drink[36] with a herd of milking cows that had access to a field of rye heavily ergotized with *C. purpurea*. The first symptom was a fall in milk yield 6 days after the herd had been turned into the field. Shortly thereafter 16 of the 43 cows became lame. This affected mainly the older, heavier milking cows, and was confined to the hind feet. The ears and tails were unaffected. Only 9 of the 16 sick animals recovered. The remaining 7 had to be slaughtered.[36]

Dinnusson et al.[34] mentioned that there have been cases of complete agalactia.

Lameness and Gangrene

A definite relationship between ergot ingestion and the lameness syndrome in cattle has not been established.

In England, the lameness syndrome had been tentatively associated with ergotism in cattle by Jones,[69,70] Hughes,[63] Barron and Kidd,[11] and Edwards.[38] Medication was required to treat affected animals to relieve intense and continuous vascular constrictions, presumably caused by the active alkaloids of ergot. Post-mortem examination of affected animals showed extensive necrosis of the fore- and hind limbs and ulceration of the skin. Observed lesions were not localized in any particular area.[38,69] The diagnosis of ergotism was circumstantial since intake of ergotized feed could not be proven.

Barron and Kidd[11] were more certain of their diagnosis since the pastures were actually found to have a heavy ergot infection. Affected animals had elevated temperatures. Of 25 calves, 6 showed the lameness syndrome and 4 others were slightly lame. Lesions were found on the feet but also on the muzzle of at least 9 animals. At first foot- and mouth disease was suspected but could not be confirmed and the disease was explained as ergotism.

Cunningham,[28] however, argues that if ergot poisoning were the cause of lameness, a strict seasonal occurrence of the disease would be expected. In his experience there is no evidence of a seasonal incidence of the disease.

It has been suggested by Greatorex and Mantle[52] that ergot is most toxic to rumi-

nants under field conditions. The reports from England were field observations, which might explain why in some controlled experiments the lameness syndrome was not observed. Furthermore, the source of the ergot and the active alkaloid content of the sample would have to be taken into consideration. Many of the reported field observations do not specify the type of ergot, the percent of ergot consumed, nor the percent of active alkaloids in the sample.

Gangrene has been observed in cattle due to ingestion of ergot.[38,85,141]

Daily doses of 150 to 250 mg of alkaloids from ergot produced the lameness syndrome within 10 to 14 days, which then progressed to peripheral gangrene.[27] No alimentary lesions were observed. It has to be realized, however, that the development of any lesions would be greatly influenced by both the digestibility of the fodder and the physical environment.[85]

More recently Woods et al.[141] correlated a severe gangrenous syndrome in cattle with an epidemic of *C. purpurea*. In this outbreak, though the ergotized field was not naturally wet, climatic reports for the period the cattle grazed the pasture showed that rain fell on most of the days keeping the ground wet and that there was relatively little sunshine during those days. The normal physiological response to low external temperature is peripheral vasoconstriction, a condition which ergot ingestion would cause. If a heavily ergotized pasture is grazed under cool conditions, less vasoconstrictor would be necessary to reduce circulation to the extremities than would be required under warm conditions. The additional vasoconstrictor effect due to ergot could severely reduce circulation resulting in gangrene.

Sheep

Experimental results of the effects of ergot do not always agree with observations made under field conditions. This has been reported with other animal species as well.

Spratling[121] reported that 40 of a flock of about 500 lambs showed signs of ergotism due to the consumption of rye grasses heavily contaminated with *C. purpurea*. Dry gangrene of the tips of the ears was observed but not of the feet or tails. The extent of ergot contamination was not determined nor the percent of ergot ingested. It had to be a rather high amount, however. The wheat harvest during that year in the same region contained about 2% ergot.

In a controlled study by Cunningham et al.,[27] sheep received a ration which contained ergot with a total alkaloid content of 0.2 to 0.6 mg/kg body weight. While some of the sheep were not affected, others developed alimentary and tongue lesions which the authors thought were caused by a local effect of the ingested ergot, due presumably to the alkaloid component. For a few animals the ergot level was lethal, but no peripheral gangrene developed.

Greatorex and Mantle[52] mention a suspected epidemic of ergot poisoning of sheep in which 41 of 120 pregnant ewes aborted 7 to 10 days after feeding on rye grass containing ergot at a level of 4%. Many of the sheep developed diarrhea and about half of the animals which aborted died. Post-mortem examinations showed inflamed GI lesions.

A study by Burfening[17] did not produce the same results as those mentioned by Greatorex and Mantle.[52] The level of ergot included in the diets differed, however, which might explain the differences in results. Burfening[17] fed 6-year-old ewes ground barley with either 0, 0.1, or 0.5% of crude ergot. Ewes receiving ergot during the prebreeding and/or gestation period had a lower percentage lambing than did those that received no ergot. Data of the study are shown in Table 15. No abortions were observed in the study. The percentage of ewes lambing or lambs born per ewe bred did not differ between those receiving 0.1 and 0.5% ergot in their rations. The author[17] suggested that this may indicate that there is a threshold level above which increasing

TABLE 15

Effect of Feeding Different Levels of Ergot to Ewes During the Gestation Period

	Ergot in feed (%)		
	0	0.1	0.5
Number ewes	51	51	50
Number lambing (%)	34 (67)	24 (47)	24 (48)
Lambing rate			
Per ewe bred	1.02	0.78	0.87
Per ewe lambing	1.51	1.69	1.85

Adapted from Burfening, P. J., *Theriogenology*, 3, 193, 1975.

the concentration of ergot in the ration has no more effect on reproductive performance. He made no attempt to define the physiological cause of the reproductive failures observed.

Greatorex and Mantle[53] fed milled ergot (*C. purpurea*) containing ergotamine (0.25%) or alkaloid-free ergot to pregnant sheep, either orally or through a ruminal cannula. The daily dosage of ergot sclerotia was 0.4 g/kg body weight. The milled ergot, irrespective of route of administration, produced severe illness, which involved vascular disturbance, especially in the tongue, and extensive intestinal inflammation. The tongue lesions were shown to be not due to a topical effect as had been suggested earlier. Variability in the response of the individual animals to ergot was demonstrated with one sheep which, though showing transitory clinical effects, maintained an uninterrupted pregnancy and produced normal lambs. By contrast, alkaloid-free ergot had no effect when the daily dosage was increased by 50%. Dosage of animals under field conditions gave either an immediate or delayed response which resulted in acute illness in the ewe but did not affect pregnancy. Dosage of animals under loose box conditions at later stages in pregnancy resulted in less acute illness in the ewe but caused death in some animals beyond the 3 1/2 month-stage of pregnancy.

It is generally agreed that ergoty grains should not be fed to breeding-age sheep.

Pigs

Ergot contamination of feeds has caused reduced feed intake, slower weight gains, reduced pregnancy rates, lower birth weights, abortions, and agalactia in pigs, when compared with the performance of animals on control diets. However, different researchers have not always been able to come to an agreement concerning specific effects of various levels of ergot and ergot obtained from different sources when fed in diets to animals. The discrepancies in reported results are in many instances impossible to explain. Generally, however, it appears that ergot sclerotia are not as toxic to pigs as to ruminants. The pig seems to eliminate the alkaloids more efficiently. Furthermore, ergot poisoning is not as readily diagnosed in the pig from the characteristic external change seen in other species of animals.[85,139]

Effect of Ergot on Feed Intake and N Retention

Friend and MacIntyre[43] fed two grades of rye to pigs at 0, 30, and 60% of the ration. One of the rye samples contained 0.03% and the other 0.20% of ergot. Inclusion of the ergot-contaminated grain reduced body weight gain. The effect was more pronounced with the higher level of ergot.

TABLE 16

Effect of 0.10% Ergot in Ration on Digestibility and Retention of Nitrogen by Growing Pigs

	Barrow		Gilt		Average	
	Control	Ergot	Control	Ergot	Control	Ergot
Number pigs	3	3	3	3	3	3
Weight gain, g/day	428	484	431	390	430	437
N digestibility, %	86.3	86.3	85.6	84.6	85.9	85.4
N balance, g/day	13.7	13.0	14.0	11.6	13.8	12.3
N retention	29.7	27.9	33.9	27.8	31.8	27.9

Adapted from Friend, D. W. and MacIntyre, T. M., *Can. J. Comp. Med.*, 34, 198, 1970.

TABLE 17

Effects of Ergot Contamination of Swine Feeds

	All barley	50% Barley 50% Triticale (uncleaned)	All triticale (uncleaned)
Number of pigs	6	6	6
Average initial weight, kg	55.7	55.8	56.6
Average final weight, kg	192.8	172.8	157.5
Average daily gain, kg	1.51	1.29	1.11
Average daily feed consumption	5.37	4.50	4.20
Feed/gain ratio (lb. req/100 lbs. gain)	356	350	379

Adapted from Harrold, R. L., Dinnusson, W. E., Haugse, C. N., and Buchanan, M. L., *N.D. Agric. Exp. Stn. Farm Res.*, 28(3), 34, 1971.

In a later study the same authors[44] showed that severe reduction in feed intake and growth of rate of growing pigs accompanied the inclusion of 1 to 2% of ergot in the pig ration. Levels of 0.05 and 0.1% ergot even affected the performance of the animals. A subsequent experiment with growing-finishing pigs also showed reduced feed intake and growth performance on rations containing 0.05 to 1.0% ergot. A nitrogen balance study showed that the control pigs retained 1.54 g more N daily than pigs fed 0.1% ergot. Digestibilities of the rations and the N-retentions of the pigs are given in Table 16.

The total alkaloid content of the ergot used in these experiments was 0.29%, the predominant alkaloid being ergocristine, which is known to constrict, selectively, smooth muscle and many blood vessels.[44]

Weight reduction due to ergot was also reported by Harrold et al.,[57] who fed rations containing 86.9% barley, 43.5% barley and 43.5% triticale, and 86.98% triticale, respectively, to growing-finishing swine. All three rations were supplemented with 10.9% soybean meal, vitamins, and minerals. Their results are shown in Table 17.

The triticale had not been cleaned and contained ergot. Inclusion of uncleaned triticale at either 50 or 100% of the grain in rations for growing -finishing swine caused a considerable reduction in feed intake and average daily gain. The most severe reduction in performance was observed when triticale was the sole component of the grain mix. Efficiency of feed utilization has not changed significantly by using triticale, indicating that palatability was probably causing the decreased feed consumption, with the reduction in weight gain resulting from the decreased feed intake.

TABLE 18

Nitrogen Balance for Pigs Fed a Control Diet or a Diet Contaminated with 0.5% of Milled Ergot Sclerotia

	Control	Contaminated with 0.5% ground ergot
Urinary N loss (g/day)	20.1	17.7[a]
Retention of N (g/day)	11.1	13.6[b]
Retention/N intake	31.4	39.4[b]
Retention/digested N	34.8	43.6[b]

[a] $P < 0.05$.
[b] $P < 0.01$.

Adapted from Whittemore et al.[139,140].

The reduction in feed intake and growth rate has again been demonstrated in a very recent study by Whittemore et al.[140] The authors fed a considerably higher level of ergot (2.5%) to pigs than was used in earlier experiments and observed, besides the reduction in feed intake and growth rate, also lesions in the stomach, intestine, and liver of the animals.

As has been shown, there is agreement among researchers that ergot causes decreased feed consumption and subsequently reduced weight gain. There is disagreement, however, as to the effect of ergot on the N retention of pigs.

Whittemore et al.[140] offered diets contaminated with 0.5% milled ergot sclerotia to pigs and observed decreased N losses and improved efficiency of N retention. The data, presented in Table 18, are contrary to earlier evidence.

Results of Friend and MacIntyre[44] and earlier findings of Whittemore et al.[139] had shown increased urinary N excretion and reduced efficiency of N utilization. The ergot sample used by Whittemore et al.[139,140] in the two separate studies was obtained from the same source and contained the same amount of alkaloids, but produced opposite results. The authors were unable to furnish an explanation for the contradictory nature of the results. There obviously had to be a change in the composition of the ergot sample during storage. It is known that the activity of ergot alkaloids decreases with age.

Effect of Ergot on Pregnancy Rates and Abortions

In a study by Campbell and Burfening[19] gilts were mated to boars known to be fertile and were assigned at random to a barley ration containing 0.53% ergot or to an ergot-free control barley ration. At 38 days post-breeding, some of the females from each group were sacrificed. The remaining animals were kept for a total of 76 days postbreeding. The number of pregnancies and the weights of the embryos at 38 and 76 days postbreeding are given in Table 19.

There were no statistically significant differences in pregnancy rates among gilts due to the ergot in the ration. However, the pregnancy rates tended to be lower in the gilts receiving the ergot-contaminated feed (94 vs. 72%). The 38- and 76-day-old embryos from the ergot-fed gilts were heavier than those from the control animals. These results are not in agreement with those of Nordskog and Clark,[97] who reported that offsprings of ergot-fed gilts had lighter birth weights than those from the control gilts. There is no explanation for the difference in the results.

It has been stated by Norkskog and Clark[97] and Mantle[85] that ergot in the rations

TABLE 19

Effects of Ergot in Barley on Prenatal Development in Gilts

	% Ergot in Ration	
	0	0.53
No. pregnant/No. bred	15/16 (93.7%)	13/18 (72.2%)
Mean weight of 38-day old embryos (g)	8.8	10.5
Mean weight of 76-day old embryos (g)	348.8	462.1

Adapted from Campbell, C. A. and Burfening, P. J., *Can. J. Anim. Sci.*, 52, 567, 1972.

of pregnant sows can lead to abortions. There are other researchers, however, who disagree.

Bailey et al.[8] fed rye ergot sclerotia containing 0.25% ergotamine to gilts at doses of 5 and 80 g a day for 11-day periods during early pregnancy. The first treatment period covered the preimplantation and implantation stage and the second period the stage just after implantation. Untreated gilts were used as controls. Results were assessed after slaughter of the gilts on the 30th day of pregnancy through measurements of embryos, their organs, and placentae. The ergot treatment did not interfere with maintenance of pregnancy; neither did it have any adverse effects on blastocyst implantation or on organ weights of embryos.[8]

The abortions, linked to ergot in earlier reports, might have been caused by infections,[85] or they may have been due to a higher active alkaloid content of the ergot samples used. Until sound additional evidence is obtained, it is probably wise to avoid feeding ergotized diets to pregnant animals.

Agalactia

An agalactia of sows causing the death of new-born piglets was observed by Shone et al.[116] The piglets were born alive. They were healthy but died of starvation within a few days after birth due to failure of the mammary glands of the mother sow to develop normally during the last few weeks of pregnancy. Death of the piglets was due to absence of milk in the mother. By controlled feeding experiments, it was shown that the agalactia resulted from feeding pregnant sows pearl millet (*Pennisetum typhoides*) contaminated with 0.67% ergot. Nordskog and Clark[97] reported that levels of 0.1, 0.5, and 1.0% in sow rations produced agalactia.

The affected sows showed no other signs of illness other than the retarded development of the mammary glands due to ergot ingestion. Over a period of several years, during which agalactia was observed, no cases of lameness, necrosis, or gangrene of the extremities occurred even though ergot contamination was as high as 2%.[84]

Agalactia is believed to be a type of ergot poisoning different from ergotism caused by *C. purpurea* (Fr.) Tul. The alkaloids of the ergot of *Pennisetum typhoides* (*C. fusiformis*) belong to a group of alkaloids which are distinct from those associated with *C. purpurea*.[84]

Chicken

Two chick feeding trials were conducted by Bragg et al.[15] to test the effect of dietary triticale ergot on growth, feed per gain, and mortality of broilers. Eight levels of triticale ergot (0, 0.2, 0.4, 0.8, 1.6, 3.2, 6.4, and 12.8%) were added to a basal wheat ration containing 64.5% ground wheat, 25.0% soybean meal, 3.0% fish meal, 3% soybean oil, 1% alfalfa meal, and vitamin and mineral premixes. At the end of 28 and

TABLE 20

Effect of Dietary Triticale Ergot on Performance of Broiler Chicks

	28 days of age		56 days of age	
Ergot levels (%)	Weight gain (g)	Feed/Gain	Weight gain (g)	Feed/Gain
Control	543ab	1.79a	1541a	2.28
0.2	552a	1.78a	1539a	2.24
0.4	499ab	1.76a	1433a	2.29
0.8	496b	1.68a	1473a	2.13
1.6	251c	2.35a	808b	2.35
3.2	118d	2.88	—	—
6.4	74de	3.31a	—	—
12.8	39e	7.24b	—	—

Note: Means, followed by different letters differ significantly ($P < 0.01$).

From Bragg, D. B. , Salem, H. A., and Devlin, T. J., *Can. J. Anim. Sci.*, 50, 259, 1970. With permission.

56 days of feeding, average weight gain, feed per gain, and percent mortality were calculated. The results obtained by Bragg et al.[15] are shown in Table 20.

There were no significant differences in weight gain between chicks on the control diet and those fed 0.4 and 0.8% ergot at 28 days of age. A severe depression in weight gain occurred when 1.6% ergot was fed and growth almost completely stopped at 12.8% ergot in the ration. At the lower levels of dietary ergot (0.2 to 0.8%) feed utilization was not affected. Higher levels, however, caused a very poor feed/gain ratio as the result of both a decrease in weight gain and a voluntary feed restriction by the chicks. Chicks fed ergot diets from 29 to 56 days of age showed the same growth pattern as observed during the first 28 days.

Ergot toxicity was characterized by an initial depression in growth, poor feathering, nervousness, loss of coordination, and finally, lack of ability to stand. Mortality, as shown in Figure 10, was insignificant at ergot levels below 3.2% for the first 28 days, but increased to 60 and 93% at 6.4 and 12.8% ergot levels, respectively. At 48 days of age, the 3.2% ergot group showed 100% mortality, indicating that ergot, which is quite frequently found in triticale, has a cumulative effect on chicks and interferes with survival at levels above 0.8% in the ration.

The critical levels of ergot in feed established by Bragg et al.[15] do not completely agree with those found previously by O'Neil and Rae,[99] who determined an ergot tolerance of 0.30% for chicks. Growth depression and mortality resulted if higher levels were included in the ration. With hens, 0.20 to 0.40% ergot appeared to be critical with respect to feed consumption, maintenance of body weight, and egg production. Mortality was not observed when as much as 9% ergot was fed to hens.[99]

The discrepancies are likely due to differences in active alkaloid content of the samples of ergot used in the experiments.

Ducks

Ergotism in poultry is rare. If it occurs, the usual symptoms are necrosis of the womb, wattles, and tongue. Mortality has also been reported due to ingestion of ergot-infected grains.[129]

Swarbrick and Swarbrick[129] described a case of ergotism in a flock of Muscovy ducks which had been fed wheat dockage, later found to contain 1.17% of ergot sclerotia. After ingestion of the contaminated feed, several of the youngest ducks were listless

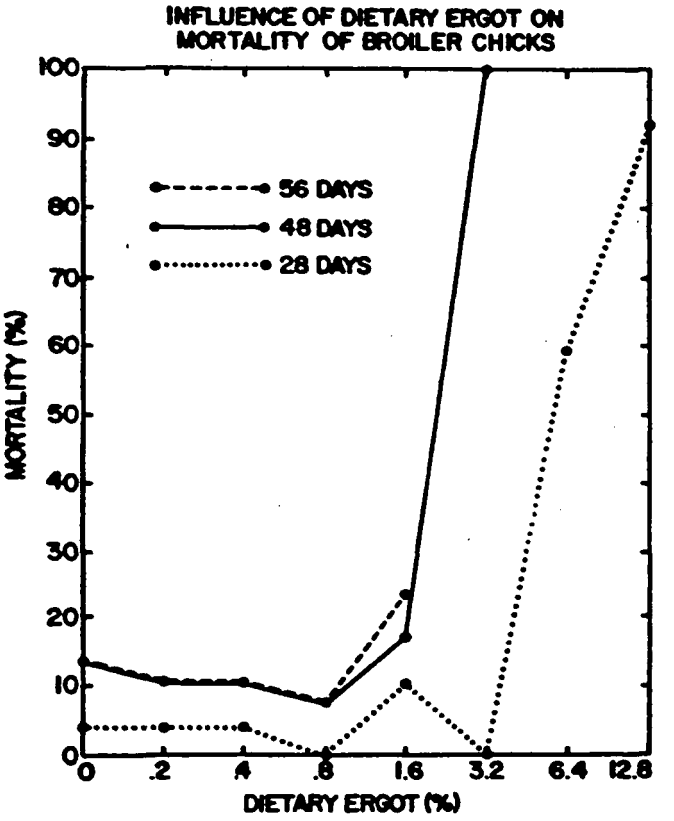


FIGURE 10. Influence of dietary ergot on mortality of broiler chicks. (From Bragg, D. B., Salem, H. A., and Devlin, T. J., *Can. J. Anim. Sci.*, 50, 259, 1970. With permission.)

and lethargic. They would not move unless driven and did not continue to eat or drink. Some of the birds developed diarrhea. All affected birds died within 24 to 48 hr after the onset of symptoms. During the week that followed 27 of 35 ducklings in the 8- to 12-week age group had died. The older birds, however, were not affected. Ergotism was suspected, since post-mortem examinations showed that the livers of the ducks were engorged with blood and that the kidneys were congested.[129]

It is frequently difficult to substantiate any poisoning and the diagnosis in this case was based largely on circumstantial evidence. Other possible reasons for the incident, however, had to be discarded considering the symptoms.

This outbreak emphasizes the dangers of indiscriminate feeding of dockage to livestock and poultry.

Rats and Mice

Ingestion of ergot sclerotia containing sufficient quantities of active alkaloids by mice can induce fertility problems during the conception and gestation period.[85]

Campbell and Burfening[19] studied the effects of feeding pregnant mice a ration based on barley which contained 0.53% ergot. They observed that the ability of the embryo to survive after implantation was affected. There were losses of whole litters, which agrees with previous reports by Carlson et al.,[21] which indicated that ergot alkaloids (lysergic acid derivatives) can cause complete termination of pregnancy. A single injection of ergocornine caused abortion.[21] A single subcutaneous injection of ergotoxine isolated from ergot also terminated pregnancy in rats.[112]

TABLE 21

U.S. Imports of Ergot and Ergotamine Compounds

Year	Ergot[a]		Ergotamine compounds[b]	
	lb	value ($)	lb	value ($)
1965	261,487	24,205	67	134,598
1966	157,698	12,571	56	50,487
1967	171,134	34,699	67	80,769
1968	101,506	28,804	NA[c]	NA
1969	97,829	18,323	334	133,477
1970	64,416	9,007	994	233,880
1971	51,786	6,660	254	51,064
1972	31,550	4,497	86	172,942
1973	26,843	NA	108	239,072
1974	NA	NA	80	274,000
1975	1,039	9,000	50	124,000

[a] Suppliers: Canada, Portugal, Netherlands, Spain.
[b] Suppliers: W. Germany, Switzerland, Finland, England, Czechoslovakia, France, Poland.
[c] Not available.

From U.S. Department of Commerce, U.S. Foreign Trade — Imports, TS USA Commodity by Country, FT 240, 1965—1975.

Mantle[85] reported that mice fed millets containing 2% ergot failed to establish a pregnancy. Ovulation and conception occurred but implantation of the blastocysts was prevented. Once implantation was complete the same diet had no effect on the pregnancy except for the development of agalactia, already mentioned in pigs. This is in disagreement with the findings of Campbell and Burfening,[19] who did observe abortions due to ergot after embryo implantation. It has to be realized, however, that different alkaloids are involved. The main alkaloid component of the millet ergot fungus (*C. fusiformis*) is agroclavine, belonging to the clavine group of alkaloids, while lysergic acid derivatives are the main active components in the ergot from barley.

The condition of agalactia in mice due to ergot has been shown to be caused by the main alkaloidal component of millet ergot, agroclavine. A 2% millet diet fed during the latter part of a pregnancy inhibited mammary hypertrophy and prevented lactation. A 5% ergot diet was lethal in 5 to 8 days.[85]

ERGOT IN MEDICINE

Once a dreaded poison, ergot now is regarded a treasure house of drugs. There are only very few natural substances which can be used effectively in so many different medical applications as the ergot alkaloids. The therapeutically most important ergot alkaloids are the amides of lysergic acid (amides of the peptide type). The clavine series was shown to be of little importance in medicine.[62]

Ergot of rye is still the chief ergot for medical use although plants other than rye produce ergot with physiological activities. Rye ergot is rather large, however, and easier to separate from grain and such a factor influences commercial availability. The fungus is grown in isolated areas of the wheat- and rye-producing areas which have become important sources of supply. Although considerably more ergot develops every year in the rye-, triticale-, and wheat fields of other areas of the country, only a very small amount of this domestic supply actually enters the drug market. Farmers prefer

to burn or bury the fungus rather than compete with the foreign market or to run the risk of ergot-contaminated grain crops destined for food use.[142]

Relatively large quantities of ergot were imported into the U.S. for drug use every year up to approximately 1965. Thereafter, imports decreased year after year. Table 21 shows U.S. imports of ergot and ergotamine compounds for the years 1965 through 1975 as well as the supplying countries.

When the medical importance of the ergot alkaloids was realized, many attempts were made to produce them by growing the *Claviceps* fungus in vitro, instead of on rye. These attempts have been successful within the last decade. Furthermore, all the naturally occurring active alkaloids can be synthesized today. They are also modified and in that form have shown to be even more powerful in medical applications.[62]

Pharmacological Activities of Ergot Alkaloids

The use of ergot in medicine spread rapidly in the U.S. as soon as the beneficial effects were recognized. Its adaptation in Europe was delayed, but that is understandable considering the sufferings which high amounts of ergot alkaloids have caused for many years.

The major therapeutic uses of the ergot alkaloids fall into three categories:

1. Applications in obstetrics
2. Treatment of migraine
3. Treatment of hypertension

In addition, there are numerous miscellaneous uses. The therapeutic uses will be discussed only briefly. For an in-depth and authoritative coverage of all medical applications of ergot, which is beyond the scope of this review, the reader is referred to publications by Barger,[10] Bové,[13] Nickerson,[96] Brazeau,[16] and Hofmann.[60,62]

The different pharmacological activities of ergot alkaloids are summarized in Table 22. Central effects occupy an important place in the activity spectrum of the ergot alkaloids. The site of action is the medulla oblongata and the midbrain. Neurohumoral effects are antagonism to adrenaline and to serotonin. The peripheral action on smooth muscle is manifest as vasoconstriction and uterine contraction.[62] The pharmacological actions of the alkaloids are varied and complex; some actions are completely unrelated and some are even mutually antagonistic.

Absorption of Ergot Alkaloids

Ergot alkaloids are poorly absorbed after oral administration. An effective oral dose is usually 8 to 10 times the intramuscular dose and the resulting action is delayed and unpredictable.[96] The alkaloids are rapidly degraded in the body. They seem to be detoxified in the liver. Insignificant amounts are excreted in the urine and not more than 5% of an i.v. dose has been accounted for. Penetration of significant amounts of the ergot alkaloids into the brain and the cerebrospinal fluid has not been demonstrated.[96]

Prolonged administration of any of the natural ergot alkaloids is not recommended. It can cause vascular insufficiency and gangrene of the extremities, a prominent feature of the epidemics of ergot.[10,13]

Specific Effects on the Cardiovascular System

The marked effects of ergot alkaloids and ergotamine specifically on the cardiovascular system are due to simultaneous peripheral vasoconstriction, depression of central vasomotor centers, and peripheral adrenergic blockage.[16] Adrenergic blocking agents inhibit all effects stimulated by adrenaline or by the sympathetic nervous system. Ischemic changes in the ECG are often associated with coronary vasoconstriction caused

TABLE 22

Pharmacological Activities of Ergot Alkaloids

Effect	Site of Action	Symptoms	Effects clinically exploited for
Central-nervous	Medulla oblongata	Lowered blood pressure, bradycardia Inhibition of vasomotor center and pressoreceptor reflexes	Sedative effect, to potentiate effects of sedatives and hypnotics — especially barbiturates and tranquilizers
	Hypothalamus	Excitatory syndrome Mydriasis Hyperglycemia Hyperthermia Hyperreflexia	Analytical psychotherapy, Experimental studies of psychoses
Neurohumoral	Myoneural junctions	Seratonin antagonism	Prophylaxis for migraine treatment of rheumatic affections
		Adrenergic blockage	Treatment of high blood pressure, cerebral circulatory disorders, functional peripheral vascular disorders, cervical syndrome
Peripheral-muscular	Blood vessels	Vasoconstriction	Treatment of Migraine Treatment of low blood pressure
	Uterus	Uterine contraction	To hasten childbirth To arrest hemmorrhage

Adapted from Bové,[13]; Brazeau,[18]; Nickerson,[96]; Hofmann,[40,41].

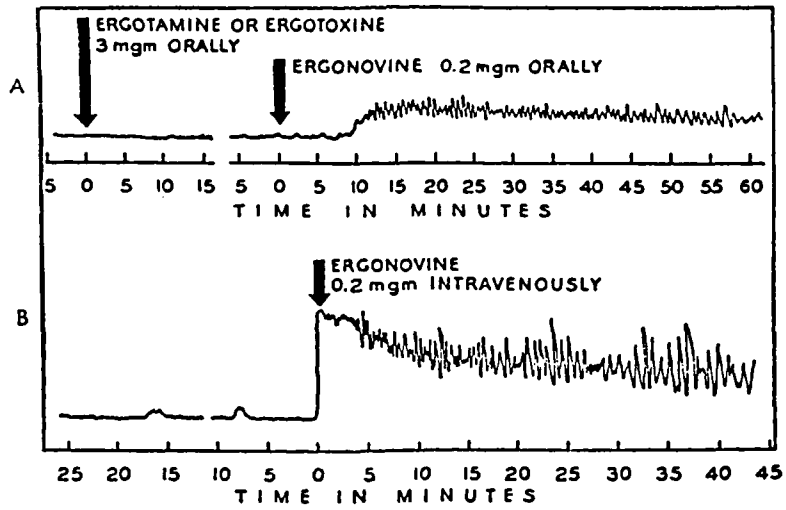


FIGURE 11. Effect of ergot on the human uterus. (From Davis, M. E., Adair, F. L., and Pearl, S., *JAMA*, 107, 261, 1936. Copyright © 1936, American Medical Association.)

by ergotamine. All the natural ergot alkaloids cause a significant rise in blood pressure as the result of the direct peripheral vasoconstriction.

GI Effects

Ergotamine increases peristaltic activity and rate of passage of solid material along the GI tract in man and animals.[96]

Effects on the Central Nervous System

Depression of the vasomotor center reduces peripheral sympathetic tone and appears to be responsible for vasodilation, fall in blood pressure, hypotension, and decreased reflex vasomotor responses.[96]

Cardiovascular responses to baroreceptor and chemoreceptor stimulation are inhibited caused by ergot alkaloids. There is also an impairment of temperature regulation as the result of action on the hypothalamus.[96]

Ergot Alkaloids in Obstetrics

All natural alkaloids of ergot increase the motor activity of the uterus. Contractions are increased in force or frequency. They are followed, however, by a normal degree of relaxation. The mechanism of action is one of direct muscular stimulation.[16] The effect of ergonovine on the human uterus is shown in Figure 11. All natural ergot alkaloids have qualitatively the same effect on the uterus, but they exhibit important differences in potency. Ergot alkaloids will also arrest hemorrhages.

Remedy for Migraine Headaches

Certain ergot alkaloids, notably ergotamine, are effective in relieving migraine headaches. Their action is directly related to the pathological physiology of migraine. The intensity of the pain is related to the amplitude of pulsations of the cranial arteries. When ergotamine induces relief of migraine, there is a parallel decline in the amplitude of arterial pulsations as shown in Figure 12. The ergot alkaloids are ineffective in the relief of headache other than migraine.[16]

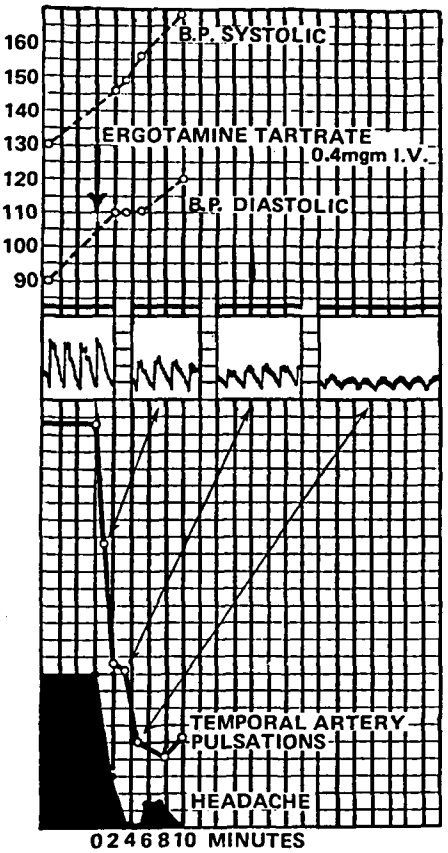


FIGURE 12. Graphic representation of the response of migraine to ergotamine. The solid line with open circles represents the average amplitude of pulsation of the temporal artery before and after the intravenous administration of 0.4 mgm of ergotamine tartrate. Pulsation of the artery was measured by means of a tambour, the movements being photographically recorded. The individual pulsations are shown in the inserts of representative photographic records. Note the rapid decline in intensity of headache (shown at bottom in solid black) after ergotamine, which is parallel both in time and degree with the decline in amplitude of pulsation of the temporal artery. The blood pressure rise seen here is not a constant feature of ergotamine therapy of migraine. Relief of headache is attributed to constriction of cranial vessels by the drug and consequent reduction in amplitude of their pulsations. (From Graham, J. R., and Wolff, H. G., *Arch. Neurol. Psychiatry,* 39, 737, 1938. Copyright © 1938, American Medical Association.)

Necessary Precautions in Usage of Ergot Alkaloids

The alkaloids of ergot are extensively employed in therapeutics and poisoning from their administation is not rare.[16] Poisoning is usually due to an overdose.

Patients with peripheral vascular disease are extremely susceptible to the vascular complications of ergotamine therapy.[16] The drug should also not be used in patients with arteritis, marked arteriosclerosis, coronary artery disease, or thrombophlebitis. Diseases of the liver and kidney are also contraindications.

SUMMARY AND CONCLUSIONS

Ergot is caused by a fungus (*Claviceps* species) which has been found on hundreds of plants in almost every country of the world. The fungus can adapt itself to form many different varieties. New species of the fungus and new hosts are still discovered today.

The alkaloids in ergot have caused hundreds of thousands of deaths in the Middle Ages after consumption of contaminated cereal grains, but during the last two decades there has not been a recorded outbreak of ergotism. Grain standards in most countries are very strict and do not permit grain which contains ergot to reach commercial food channels. All involved in cereal grain production and utilization should be cognizant of the potential danger, however, since ergot contamination at levels above those permitted by grain standards cannot necessarily be detected by the normal evaluation of a flour sample in the cereal chemistry laboratory.

There always have been and always will be ergot infections and a possible danger to human health, but man has learned to minimize the potential problem by using proper agricultural practices. Furthermore, techniques for the removal of ergot from contaminated grains have been developed.

While human ergotism is a disease of the past, ergotism in animals still occurs frequently. The problem is not a simple one because of many unanswered questions. What is the tolerance of different breeds or species of livestock to ergot? What are the effects of low level long term ingestion of ergot on livestock? What is the difference in toxicity to animals of ergot from different cereal grain varieties? What is the effect of storage and processing of cereal grain product on the potential ergot toxicity?

The last and most important chapter in the history of ergot concerns ergot as a source of pharmacologically useful alkaloids which have found applications in internal medicine and obstetrics. The future promises to bring some new ergot alkaloids and some new uses. Recent research data indicate the possibility of using ergot alkaloids in contraceptives, which would be truly remarkable.

Ergot alkaloids have killed millions of people in the Middle Ages, later were used in many million childbirths and now might be used in the future to prevent the births of even more million people.

The history of ergot has been fascinating.

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