
Egg Peritonitis Syndrome: A Painful and Prevalent Disease in Commercial Layers

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In 2013, the largest project on farm animal health and welfare funded by the European Union¹ was launched, with the overall goal of helping combat production diseases in animals raised intensively, namely those “*diseases which tend to persist in animal production systems and, typically, become more prevalent or severe in proportion to the potential productivity of the system*” [1].

The high prevalence of production diseases in the poultry industry is no surprise: productivity gains in this sector have stemmed predominantly from the selection of highly productive breeds, a strategy that has stretched the physiological limits of animals beyond those expected from naturally evolving biological systems. A high prevalence of physical injuries, diseases, and behavioral disorders is, therefore, the industry norm nowadays. Temple Grandin has referred to this problem as ‘biological system overload’ [2].

In a review of the literature and consultation with multiple stakeholders in the industry conducted as part of this initiative [3], salpingo-peritonitis (also referred to as egg peritonitis) was reported as the most common production disease in modern breeds of laying hens. It is also the leading cause of mortality in laying hens (Chapter 8 [4]). Salpingo-peritonitis is a reproductive disease characterized by the inflammation of the oviduct (salpinx) and abdominal cavity (peritoneum), often triggered by the presence of yolk as a result of partially or fully formed eggs reaching the abdominal cavity by reverse peristalsis of the oviduct, or by the retention or rupture of eggs in the oviduct (Figure 5.1). Yolk material by itself induces only a mild inflammatory response and may be reabsorbed, but because it is an excellent growth medium, secondary infections by bacteria such as *Escherichia coli* often occur [5]. As we discuss in this chapter, the condition is associated with poor welfare, leading to painful outcomes and often to mortality.

Since there is a lack of consensus in the nomenclature (Box 5.1), we have chosen to use the term ‘egg peritonitis syndrome’ (EGPS) as an umbrella term to capture the symptoms brought about by the presence of egg material in the abdominal cavity and oviduct. There are multiple interrelated conditions that affect the reproductive tract and may lead to egg peritonitis syndrome, frequently induced by the management conditions endured by commercial layers and intensive production requirements. As a result of selection for high prolificity (modern strains lay one egg nearly every day, compared to about 20 eggs per year in their wild ancestral) and early sexual maturity, reproductive disorders are now highly prevalent in commercial breeds. Examples include cystic ovarian disease, ovarian tumours and ‘erratic oviposition and defective egg syndrome’ (EODES), a

¹ The PROHEALTH Initiative had a total funding of €12 million and a consortium of 22 partners from the industry and academic sectors from six European countries.

condition resulting from high ovarian activity, an increased number of rapidly growing follicles and ovulation into the abdominal cavity [6]. Other conditions are of a purely mechanical nature, such as the rupture or torsion of the oviduct, the binding of the egg to the oviduct walls, trauma to the vent and excessive fat deposition.



Figure 5.1. Illustration of egg yolk peritonitis syndrome (EGPS) in laying hens, a common, painful and potentially fatal inflammation of the oviduct (dark pink in the illustration) and/or abdominal cavity (not shown), often triggered by the presence of yolk as a result of partially or fully formed eggs reaching the abdominal cavity or by the retention or rupture of eggs in the oviduct. The accumulation of leaked yolk can lead to fibrinous deposition (amorphous yellowish mass in the illustration) in the visceral cavity. The "penguin-like" stance adopted by the hen is typical in individuals afflicted by this condition, and is believed to be an attempt to relieve some of the intense visceral pain. Illustration: Olga Kurkina.

Prior research has been mostly focused on egg production losses due to EGPS-related mortality, with scarce data on the evolution of clinical symptoms of the disease at the individual level and its impact on the hen's well-being. In the next section we propose an operational classification for possible outcomes associated with EGPS. Because the proposed classification is only an approximation, it should be revised as more knowledge becomes available.

Box 5.1 Classification

Egg peritonitis has also been referred to as ectopic egg, coelomitis, salpingitis/peritonitis/salpingoperitonitis (SPS) [7], and used as a synonym of internal laying, with different authors aggregating these conditions in different ways. For example, Greenacre and others [8] mention that “*egg yolk peritonitis is an old term*” and give preference to the term “*egg related coelomitis*”, since birds have a coelom rather than a peritoneum, and the offending egg material is not restricted to the yolk.

Other authors [7] make a distinction between ‘egg peritonitis’ as peritonitis (or salpingoperitonitis) caused by the spread of *Escherichia coli* into the abdominal cavity and “*E. coli peritonitis syndrome*” (EPS) as a more severe condition often accompanied by severe septicaemia. Wang and collaborators [9], in turn, aggregate peritonitis with salpingitis (inflammation restricted to the oviduct/salpinx) and oophoritis (inflammation of the ovary) based on an experimental model showing that infection with different *E. coli* strains via the salpinx can give rise to lesions in the salpinx, ovary, and peritoneum, hence their preference to group all lesions associated with the reproductive tract.

Here, we chose to use the term ‘egg peritonitis syndrome’ (EGPS) to capture all symptoms resulting from the presence of egg material in the peritoneum and oviduct. We adopt this term fully aware that this is at the cost of overlooking the physiopathological complexity behind the use of various terms, but we prioritize the value that a single umbrella term can provide for the understanding and discussion of this severe welfare issue in commercial egg-laying birds.

Clinical evolution of egg peritonitis syndrome in layers

Egg peritonitis syndrome can lead to different outcomes (Figure 5.2). Some experimental studies have demonstrated that the presence of egg yolk in the peritoneal cavity acts as a prerequisite factor to the development of egg peritonitis [10,11]. By itself, the presence of yolk material in the abdominal cavity results only in mild inflammation, which can resolve spontaneously as it can be reabsorbed completely by the peritoneum [12]. Under experimental conditions, hens inoculated intraperitoneally with sterile egg yolk did not present localized infection in the liver, heart, peritoneum, oviduct or ovaries, nor were there fatalities or signs of anorexia and depression [10]. We refer to this outcome as ‘aseptic peritonitis’.

However, if eggs are laid at a faster pace than yolk can be reabsorbed, there will be a build up of yolk in the abdominal cavity causing its enlargement, which may lead to diffuse abdominal pain and often difficulty breathing [13]. Since yolk is an excellent medium for bacterial growth, the chances of secondary bacterial infection are high. *Escherichia coli* is the most frequently isolated bacteria from affected birds [5], with other genus including *Klebsiella*, *Proteus*, *Staphylococcus*, *Salmonella* and *Streptococcus*. Infection can also spread to other organs, causing pancreatitis, hepatitis, splenitis, nephritis or even multi-organ failure and death. Although in the literature the problem is not referred to specifically as ‘bacterial peritonitis’, we use this term for the purpose of assessing the pain it causes in laying hens.

In chronic cases, the yolk will form clumps in the abdominal cavity, with possible adhesions in the peritoneum and almost all visceral organs [14]. This occurs in cases of permanent oviduct problems, leading to a life of discomfort. Often the chicken loses weight even though deceptively

appearing to have a good body condition due to the enlargement of her abdomen. We refer to this condition as ‘chronic peritonitis’.

Depending on host factors (e.g., immunological status, genetics, health), virulence characteristics of the pathogen and the presence of persistent partially resolved infections [5], egg peritonitis syndrome may progress from the acute to the chronic form, resulting in longstanding inflammation of the peritoneum, and varying degrees of scarification and fibrinous deposition on internal abdominal organs as revealed at necropsy examination [9]. Acute bacterial peritonitis can also progress to acute septic peritonitis due to factors such as the perforation of the intestine and subsequent spillage of intestinal contents into the abdominal cavity. The classification of egg peritonitis syndrome into either the acute or chronic states will therefore depend on the progression of the disease.

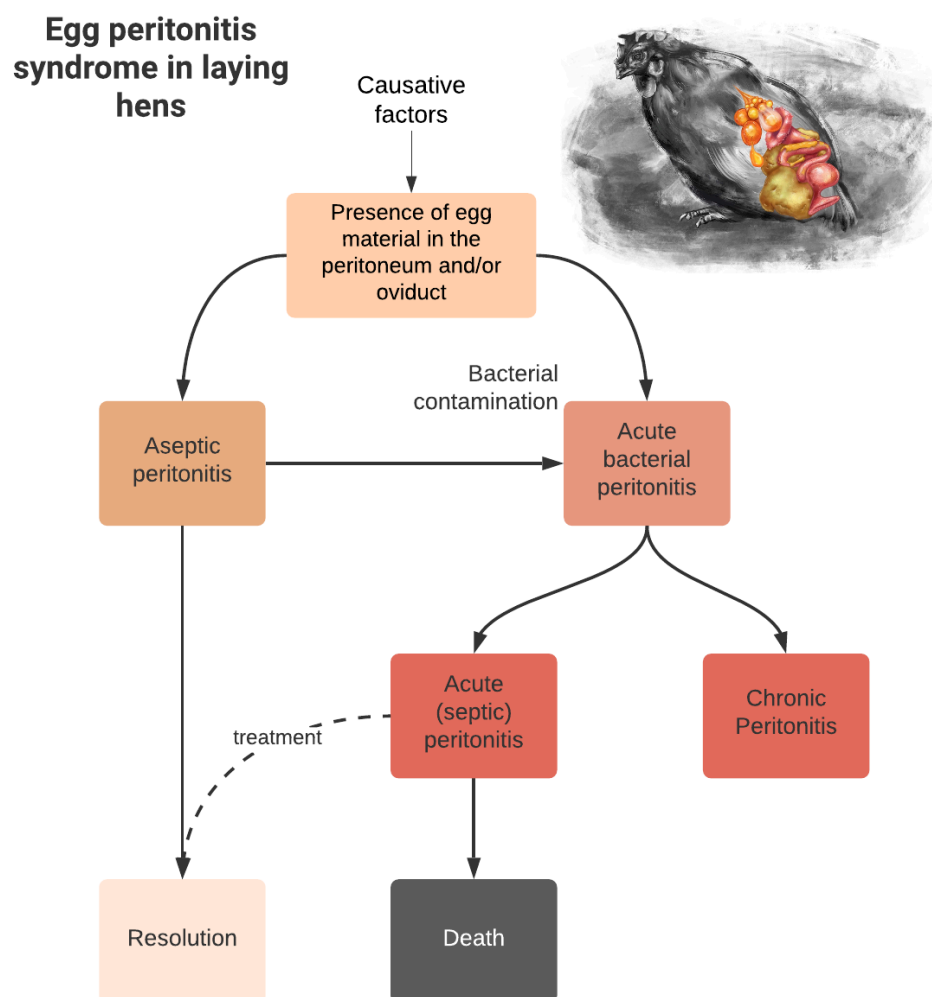


Figure 5.2. Proposed clinical evolution of egg peritonitis syndrome in egg-laying hens.

General Clinical Symptoms

The first sign of egg peritonitis syndrome is usually a decrease in egg production or its cessation altogether. The condition is also associated with multiple symptoms suggestive of substantial pain. These include fluffed feathers, lethargy, dyspnoea, lack of vocalizations, severe straining, depression, lameness, anorexia, pain signs on palpation of the abdomen and swollen vent, often soiled with yolk-coloured droppings or mucus discharge from the cloaca [8,15]. In the words of a backyard hen keeper, typical early signs would include “*pale, floppy comb, abnormal poo, standing with her feathers hunched up or standing with her tail down, no interest in food and water and separating herself (hiding) from the others*” [16].

In advanced stages, there may be severe abdominal distension, ascites (associated with diffuse abdominal pain), increased respiratory and heart rate [8], and neurological symptoms due to severe septicaemia. In broiler birds, a more common sequel is abdominal herniation due to increased intra-abdominal pressure and distension of the abdomen. In hens experimentally inoculated with *E.coli* similar symptoms have been observed, such as loss of egg production efficiency, severe anorexia, ascites and depression [10]. In humans, the presentation of spontaneous bacterial peritonitis can range from silent to overt [17]; however, human patients typically present nonspecific symptoms such as nausea, abdominal pain, malaise, fever, and mild confusion [18].

Temporal Evolution of Pain

To our knowledge, there have been no published investigations on the clinical course of egg peritonitis syndrome (EGPS), the duration of its different stages and their corresponding symptoms. Studies conducted on commercial poultry have focused predominantly on histopathological findings upon necropsy examination. In general, clinical signs are described only vaguely and mortality is reported as sudden. Veterinary manuals (e.g. Merck) directly report EGPS as a condition diagnosed at necropsy, with the appearance of a contagious disease given its seemingly rapid evolution and high fatality rate (in fact, the classification of EGPS and related conditions as a necropsy finding further discourages research on its clinical evolution). Case reports by veterinarians of pet hens are more thorough, but biased towards cases which have progressed to severe stages. Yet, reports from backyard poultry keepers (described in the next sections), who follow the birds more closely, indicate that death is far from sudden, with various clinical phases prior to aggravation or death, neglected in the study of commercial poultry. In the next two sections we explore the possible temporal evolution of the pain associated with the most likely outcomes of egg peritonitis syndrome (Figure 5.2). Aseptic peritonitis is not discussed for being unlikely to be associated with pain.

Acute Bacterial Peritonitis (fatal)

In Pain-Track 5.1 we propose a tentative scheme for the temporal evolution of the pain associated with the acute (septic) form of peritonitis, partitioned into five time segments. Given the absence of clinical signs noted in experimental trials where hens were inoculated intraperitoneally with sterile yolk [10], the mild inflammatory response caused by yolk material inside the peritoneum is unlikely to cause noticeable pain in most hens. This is also supported by studies in humans, where 75% of patients with sterile ascites presenting peritonitis were asymptomatic [17], hence the 25% probability assigned to the annoying category in segment *i*. Since egg yolk is an excellent culture medium, and bacterial infection can spread in a few days should the egg material fail to be reabsorbed rapidly, bacterial contamination of the yolk fluid is assumed to occur in up to a week

(2-7 days). The infected fluid will build up, causing inflammation (phase *ii*), the swelling of the abdomen, and diffuse abdominal pain [8]. Other symptoms associated with this outcome include fluffed feathers, dyspnoea, lethargy, lack of vocalizations, depression, lameness, anorexia and swollen vent [15], which would suggest that the the pain most likely endured is at least of a hurtful nature as defined in Chapter 1 [19], although possibly interspersed with bouts of higher pain intensity (represented by the 20% likelihood of pain at a disabling level in *ii*) as based on the severity of these symptoms (alternatively, these percentages may be interpreted as the temporal variation in the levels of pain over the period). Anecdotal reports by backyard hen keepers [16,20] suggest that it may take up to two 8 weeks from this stage until development of a more severe picture (sepsis, *iii*).

Pain-Track 5.1. Hypothesis for the temporal evolution of the pain associated with the fatal (septic) form of acute bacterial peritonitis (for the definition of intensity categories, see Chapter 1 [19]).

	i. Infiltration of egg material	ii. Inflammation	iii. Sepsis (initial symptoms)	iv. Severe sepsis (organ failure)	v. Septic shock
Excruciating				30%	
Disabling		20%	90%	40%	10%
Hurtful		70%	10%	30%	80%
Annoying	25%	10%			10%
	2 - 7 days	2 - 8 weeks	12 - 24 hrs	5 - 10 hrs	2 - 4 hrs

Sepsis (phase *iii*)

In human medicine, sepsis is defined as the manifestation of a systemic inflammatory response in the presence of infection. Clinical diagnosis of sepsis requires finding a focus of infection that is accompanied by at least two signs of systemic inflammation, which include fever, tachycardia, tachypnoea and high white blood cell counts. However, in poultry, the clinical diagnosis of sepsis is not well-defined [21].

Progression from sepsis to severe sepsis (when sepsis is accompanied by major organ failure) and septic shock has been well established in humans. Still, direct extrapolation of temporal parameters from humans to poultry is made difficult by the employment of several treatment strategies in humans, which affect the time course of the disease. Therefore, we rely predominantly on models of sepsis in rodents. These models suggest that death due to sepsis, including the development of severe sepsis and septic shock, takes 24 to 48 hours, from the onset of symptoms (phase *iii* in Pain-Track 5.1) until death following septic shock (phase *v*)².

In animal models of sepsis, systemic and local inflammation is often regarded as a major source of pain [22]. In a study that inoculated mice with fecal flow in the abdominal cavity to induce peritonitis and sepsis, the first signs of sepsis (phase *iii*) included hunched posture, piloerection, lethargy, and diarrhea, with death occurring after 48 hours. In another model where sepsis was induced by an intraperitoneal injection of stool, 75% of mortality occurred within 24 hours [23]. During the first 12 hours, septic mice progressively manifested symptoms that included increasingly laboured breathing and minimal response to auditory and tactile stimuli, indicating the disabling nature of the pain.

² This estimate also seems to be with the observation that human patients with severe sepsis do not take long to reach septic shock, usually 48 to 72 hours (Dr. Pedro Salinas, MD, *personal communication*), even those who receive some therapeutic support. Without treatment, the time is bound to be shorter.

The Centers for Disease Control and Prevention lists “extreme pain or discomfort” as a potential sign of sepsis, with an estimated 70% of patients developing peripheral neuropathy (when peripheral nerves are damaged), which often results in intense pain [22]. Intravenous morphine is routinely used for pain relief, providing an indication of the level of pain endured. Sepsis also involves changes on endothelial tissues and microcirculation, primary and secondary immune tissues, coagulation, parenchymal tissues and neurological disturbances that directly affect microglial cells and neurons [24]. Furthermore, systemic inflammation has been linked to generalized hyperalgesia [22], hence the high likelihood that pain is experienced at a disabling category in phase *iii*.

Severe sepsis (phase *iv*)

The term ‘severe sepsis’ denotes sepsis that is accompanied by major organ failure, whereas ‘septic shock’ refers to the added complication of unresponsive cardiovascular collapse [21]. Sepsis-associated inflammation has been linked to pulmonary, cardiovascular, renal, haematological, hepatic and neurological dysfunction. In broiler chickens, septicemic carcasses are frequently associated with hemorrhages on the heart, liver, kidneys, muscles and serous membranes. The kidneys, liver and spleen are often swollen and with excess blood. Muscles are also compromised, as described in this passage: *“Very few birds with septicemia survive catching and transportation to make it to the processing plant alive. If the bird prior to catching has had a septicemia event, often the muscles have wasted away and have broken down because of changes in muscle metabolism”* [25].

In humans, this stage is marked by severe muscle pain, with pain described as extreme (“I feel like I might die”; “My sepsis felt like my body was on fire, burning from the inside out”) [26,27]. Therefore, we assume that pain is experienced at the excruciating level for 30% of the time during this phase (given the duration of the segment, affected hens would spend from 1.5 to 3 hours at a level of pain equivalent to that of severe burning events - we consider that longer durations would not be possible without the neurological system shutting down).

On the other hand, the pathophysiologic consequences of sepsis may reduce pain perception. For instance, sepsis-associated encephalopathy is implicated in brain damage of regions related to nociceptive modulation [28]. Because the resulting decrease in cognitive and nociceptive sensitivity may attenuate pain responses [21], we attribute the same likelihood (30%) to a less intense (hurtful) category. The remaining proportion is allocated to the intermediate intensity category. The homogeneous spread of probabilities in three categories of pain intensity in this phase reflects not only the likely heterogeneity of the phenomenon, but also the current lack of knowledge about its manifestation at the individual level. As the reader of this book may notice, we.

Septic shock (phase *v*)

Individuals who fall into septic shock usually die within hours. In humans, a maximum of one day has been reported [24], although this time is frequently shorter than 12 hours [29]. In both humans and animals, multiple organ failure will be associated with severe refractory hypotension, which leads to rapid death [24].

At this stage, brain inflammation is believed to profoundly alter the local synaptic circuitry, resulting in reduced nociception [28]. During sepsis, especially in septic shock, there is a deterioration of the small nerve fibers responsible for the transmission of pain, reducing the ability to experience pain [30]. A similar phenomenon, referred to as critical illness polyneuropathy, was also described, with up to 70% of human patients in septic shock having their ability to feel pain affected [31]. In general, there seems to be a general reset of the pain pathways when the end is near [32]. Very few patients in septic shock, around 10%, maintain their state of

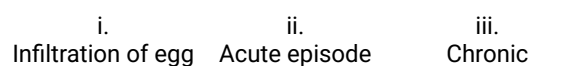
consciousness unaltered until a few minutes before dying. In these cases, the cause of death is related to multiple organ dysfunction without neurological compromise. Accordingly, we consider that pain is more likely felt at the hurtful level during this phase, with few individuals (10%) able to feel pain at a higher (disabling) intensity. We also consider the possibility that, due to the impairment reported, some individuals only experience an annoyance (10%)

Chronic Peritonitis

Chronic lesions associated with peritonitis, commonly reported during necropsies [9], are an indicator that longstanding inflammation of the peritoneum has occurred. We hypothesize that egg peritonitis syndrome can also progress from an episode of acute inflammation to a chronic stage due to persistent partially resolved infection. Hens with chronic peritonitis will present with respiratory disease, swollen abdomen, and organ inflammation [33], suggesting that -at the very least- some discomfort is likely present. Adherence of almost all visceral organs, air sacculitis and fibrinous deposits [14] are also present. Some studies report that hens with chronic peritonitis appear to be generally in good condition, but are frequently emaciated [7,34], though the extent to which emaciation during the chronic phase is a result of weight loss during the acute episode endured, loss of appetite (anorexia) or the reduction of feeding due to pain is not clear. For example, in horses chronic peritonitis often results in recurrent colic episodes, along with weight loss and intermittent abdominal pain. In humans, the condition has been described in the following way *“Pain is a very frequent symptom in chronic peritonitis. It may be mild, severe, of short duration, or persistent. Its variability depends often on the degree of irritation or congestion. Acute attacks are frequent when there is cause for exacerbation”* [35]. Other reports in humans associate the onset of pain only with specific events, such as exertion, exercise, eating [35] or the onset of the menstruation [36], which if generalized to the case of laying hens could translate into daily bouts of pain.

These observations suggest that pain is likely best represented as an intermittent phenomenon in individuals affected by the chronic condition, with most periods spent with discomfort (annoying level) or no pain³, interspersed with bouts of more intense abdominal pain (hurtful level). We also consider the possibility of acute colic events in a very small fraction (1%) of the time (corresponding to one episode of acute colic, lasting 4-5 hours, once per month). The distribution of probabilities can be also understood as the variation in the intensity of pain across individuals, as a result of differences in the extent of adherence and inflammation. Due to the chronic nature of this condition, we assume that it will be present until depopulation (60-80 weeks). If the acute episode has its onset, on average, at mid-lay (30-40 weeks), an average flock member would experience the chronic condition for 12 to 48 weeks. The wide uncertainty interval reflects both existing uncertainty on the onset and duration of this challenge, as well as the possible heterogeneity in its duration.

Pain-Track 5.2. Hypotheses proposed for the temporal evolution of the pain endured as a result of chronic peritonitis.



³ Notice that the percentages in Pain-Track 5.2 do not add up to 100%, to account for periods/cases of no pain.

	material	Inflammation
Excruciating		
Disabling		10%
Hurtful	80%	20%
Annoying	25%	60%
	2 - 7 days	2 - 8 weeks

Burden of Pain in Affected Individuals

As discussed by Donald Broom [37] “...*much remains to be discovered about the magnitude of the effects of disease on welfare. Little is known about how much suffering is associated with different diseases*”. In this section we attempted to quantify the time spent in the four categories of pain as a result of a common and fatal condition among laying hens, egg peritonitis syndrome. Only hours spent awake (16 hours/day) are considered. Pain-Tracks 5.1 and 5.2 are used as reference, reflecting the most likely estimates for the time endured at each category of pain intensity, as discussed throughout the Chapter. The results presented in Figure 5.3 consider the uncertainty regarding intensity of pain and duration of each healing phase, as depicted in the Pain-Tracks. However, if the reader wants to change any of the assumptions regarding the durations and intensity of the pain, an interactive web application can be used for this purpose, available at <https://pain-track.org/hens>.

The burden of pain in birds affected by chronic peritonitis is shorter, but almost on par with that due to the keel fractures (Chapter 3 [38]) endured over a hen’s life. Overall, 89 [50-129] hours of disabling pain, 1,120 [636-1604] hours of hurtful pain and 2,090 [880-3300] hours of annoying pain (nearly half of the laying cycle) are expected on average as a result of this condition.

More troublingly, acute cases of peritonitis - the leading cause of mortality in layers - are associated with extreme suffering in affected birds. Victims of this form of the disease are estimated to endure approximately 131 [64-199] hours of disabling pain, and over 2 [1.5-3] hours of excruciating pain due to the progression of the disease to severe sepsis (one of the most painful conditions known in human medicine).

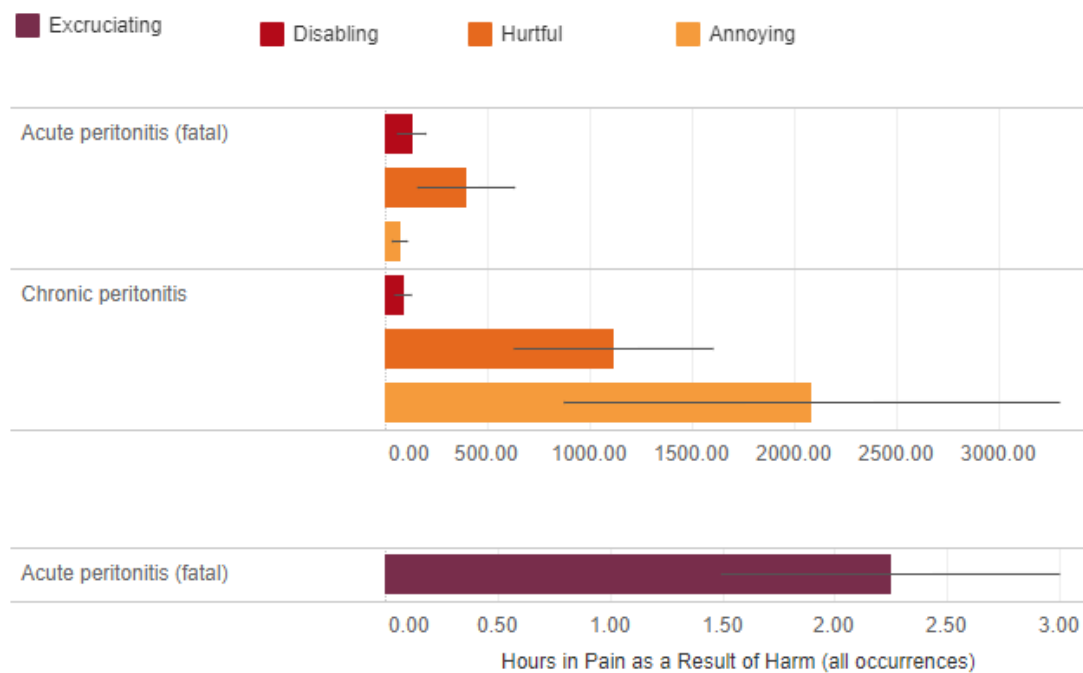


Figure 5.3. Time endured at each level of pain intensity (hours) resulting from chronic and acute (fatal) peritonitis syndrome. Error bars represent 95% confidence intervals.

Research Gaps

- ❑ Although egg peritonitis syndrome is the leading cause of mortality in layers, a major source of pain and of revenue loss for the egg industry *“there is little information about the onset and process of the disease in the field and the successes or failures of treatments implemented...It appears that this problem has been kept out of the research scope, and people who experience it only talk about it to close associates”* [39].
- ❑ Studies conducted on commercial poultry that report the occurrence of egg peritonitis syndrome have focused predominantly on histopathological findings upon necropsy examination. However, there seems to be no published investigation on the clinical course of the disease, the duration of its different stages and their respective severities. Similarly, little information is available on its prevalence, and case-fatality ratio.
- ❑ There is no consensus definition for the problem. Egg peritonitis syndrome has also been referred to as salpingitis/peritonitis/salpingoperitonitis, ectopic egg, coelomitis as well as used as a synonym of internal laying and egg bound, with different authors aggregating the condition in different ways.
- ❑ In poultry, neither is the clinical diagnosis of sepsis well-defined, nor are its symptoms and time course described. Sepsis is associated with extreme levels of pain during the laying period. Given the large number of animals affected, and the major burden of pain likely inflicted, further research is critically needed.

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