UDC 619:616.61
DOI https://doi.org/10.32851/2226-0099.2022.125.27

RETROSPECTIVE REVIEW OF RISK FACTORS ASSOCIATED WITH FELINE LOWER URINARY TRACT DISEASES (FLUTD)

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The article presents the results of analysis of information sources concerning main risk factors associated with feline lower urinary tract disease (FLUTD). The relevance of the study of feline lower urinary tract diseases is associated with changes that have occurred in populations. While at the beginning of the 20th century most cats did not live up to 8 years, and a 15-year-old cat was considered a long-liver, presently the number of cats neutered, spayed, aged 10+, has increased; almost all animals survive to the age of 7+; most cats are kept indoors and consume industrial food, lead a sedentary lifestyle, and there is a problem of maintaining life expectancy and identifying risk groups for the most common and dangerous diseases.

Clinical disorders of the lower urinary tract occur in cats more often than throughout 1970s and 1980s, their incidence has increased from ~1% to ~8.90–15.00% of cases of non-communicable disease, in total, the FLUTD-related mortality rated ~20% of cases. Among the cases of feline lower urinary tract diseases (FLUTD), the vast majority belonged to urolithiasis (60.0–70.0%) and feline idiopathic cystitis (FIC). Urinalysis has been the main diagnostic method, when using it identified various feline lower urinary tract diseases.

Among the diseased animals prevailed male cats (81.30%, 82.20% of them neutered), among female cats – spayed animals (80.00% of them), indoor-housed cats (65.90%). The urolithiasis risk group cats included indoor-housed male cats, especially neutered; female cats, especially spayed; between 2 and 6 years of age, Persian and British cats. In the studies of different feline populations, struvite and calcium oxalate uroliths comprised > 90% of all uroliths submitted. The feline idiopathic cystitis (FIC) risk group included young- to middle-aged female cats, especially Persian, British, Scottish and outbred.

Key words: *male cats, female cats, feline lower urinary tract diseases (FLUTD), urolithiasis, feline idiopathic cystitis (FIC), risk groups, incidence.*

Соболь О.М., Криця Я.П. Ретроспективний огляд факторів ризику, пов'язаних із котячими захворюваннями нижніх сечових шляхів (FLUTD)

У статті наведено результати аналізу джерел інформації щодо основних факторів ризику, пов'язаних із захворюванням нижніх сечових шляхів у котів (FLUTD). Актуальність вивчення захворювань нижніх сечовивідних шляхів у котів пов'язана зі змінами, що відбулися в популяціях. Якщо на початку 20 століття більшість котів не доживали до 8 років, а 15-річний кіт вважався довгожителем, зараз зросла кількість кастрованих, стерилізованих котів у віці 10+; майже всі тварини доживають до 7+ років; більшість кішок утримуються в закритих приміщеннях і вживають промислові корми, ведуть малорухливий спосіб життя і виникає проблема збереження тривалості життя та визначення груп ризику по найбільш розповсюдженим та небезпечним захворюванням.

Клінічні захворювання нижніх сечовивідних шляхів котів (FLUTD) зустрічаються у кішок частіше, ніж протягом 1970-х і 1980-х років, їх частота зросла з ~1% до ~8,90–15,00% випадків серед неінфекційних захворювань, загалом, FLUTD -пов'язана смертність становила has increased from 20% випадків. Серед випадків захворювань нижніх сечовивідних шляхів котів переважна більшість припадала на сечокам'яну хворобу (60,0–70,0%) та котячий ідіопатичний цистит (FIC). Основним методом діагностики, за допомогою якого виявляли різні захворювання нижніх сечовивідних шляхів котів, був аналіз сечі

Серед хворих тварин переважали коти (81,30%, з них 82,20% кастрованих), серед кішок – стерилізовані тварини (80,00%), коти на без (65,90%). До групи ризику розвитку сечокам'яної хвороби належали коти, які утримувалися в закритих приміщеннях, особливо

кастровані; кішки, особливо стерилізовані; від 2 до 6 років, персидські та британські коти. У дослідженнях різних популяцій котячих переважали струвітні та оксалатні уроліти, вони становили > 90% усіх поданих сечових каменів. У групу ризику котячого ідіопатичного циститу (FIC) входили кішки молодого та середнього віку, особливо персидські, британські, шотландські та безпородні.

Ключові слова: *коти, кішки, котячі захворювання нижніх сечовивідних шляхів (FLUTD), сечокам'яна хвороба, котячий ідіопатичний цистит (FIC), групи ризику, захворюваність.*

Problem statement. Between humans and other species forged a strong bond. Our relationships with animals can take different forms. On one hand, animals serve instrumental purposes; on the other hand, human–animal relations are social. The clearest example is pet keeping, and people attributing a special status to their companion animals [1]. Cats are among the most popular companion animals in the world, feature of this species is the growing an adaptive push-and-pull between the wild and the domesticated traits of cats, which is aligning with their dual societal roles as companions and pest controllers [2].

Despite the decline in interest in the utilitarian function of cats, their popularity and value as pets has only increased over time, and therefore there is increasing attention to the problem of keeping animals healthy and happy for as long as possible. At the beginning of the 20th century, most cats did not live up to 8 years, and a 15-year-old cat was considered a long-liver, injuries were the main cause of premature death, non-communicable diseases were practically not studied [3].

Under the modern conditions, most domestic cats die at the age of 10 years and older; now there are more and more cats aged 20-22 years and even 25 years old, that is, animals began to live longer, thanks to an increase in living standards in general [4]. Today cats are living much longer now than was even 20 years ago, thanks to better feeding, veterinary and care, accordingly, feline ages and life-stages have been redefined. In most cases, a veterinarian will deem a cat to be a senior when she is 7-10 years of age, by the time cat is 10 years or older, a common term uses to describe your cat is "geriatric." Among feline breeders, cats are considered to be elderly once they reach 11 years with senior cats defined as those aged between 11-14 years and super-senior cats 15 years and upwards [5].

The attitude of a person towards animals has also changed, today owners are ready to take care of cats even in critical situations, while spending significant funds [6]. The modern domestic cat is descended from the African Nubian cats (*Felis lybica Forster*), and has retained some of their features, such as the ability to concentrate urine. For cats living indoors and deprived of the normal habitat for their physiological characteristics, this creates the prerequisites for the development lower urinary tract diseases, which, if severe, end in death.

Thus, the proportion of animals in the feline lower urinary tract disease (FLUTD) risk group increases and today, diseases of the urinary organs are one of the most common pathologies. They occur in cats more often than pathologies of the cardiac and respiratory systems [7].

Thus, the study of urolithiasis in 465 cats and 32 cases of urolithiases in Algeria from 2016 to 2018 showed that the lower urinary tract urolithiasis appeared to be more frequent in European and Siamese cats. In addition, cats aged between 4 and 8 years old were the most affected. Male cats (87.50%) were more affected than female cats. On the whole, the lower urinary tract urolithiasis was more frequent in cats, which consumed the commercial pet food, previously castrated, and confined inside the house [8]. Based

on the foregoing, over the past 20 years there have been serious changes in the domestic cats' populations: the number of cats neutered, spayed has increased; most cats consume industrial food and lead a sedentary lifestyle, which leads to obesity; the number of cats aged 10+ increases in the population, almost all animals survive to the age of 7+. Analysis of large datasets of uroliths is necessary to illustrate the prevalence and risk factors of urolithiasis. Due to the sharp increase in the risk group animals and the occurrence of the feline lower urinary tract disease (FLUTD), the issues of their study and prevention are becoming increasingly relevant, which led to the choice of this research topic by us.

Analysis of the latest studies and publications. Clinical disorders of the lower urinary tract of cats are not new phenomena, although in a series of over 1000 cats seen at the Royal Veterinary and Agricultural College in Copenhagen throughout the 1930s and 1940s there was no examples of "real stone formers"; "sedimentation" of the urine was reported, however, in ~1% of cases. More recently in Europe and the U.S. (1977–1985) reported about 0.64 and 0.85%, today's incidence fluctuates within ~8,90-11,80% of cases [7].

Later in 1970 the term feline urological syndrome (FUS) was coined to unite syndromes characterized by dysuria, urethral obstruction, urolithiasis and hematuria. Thus, the term FUS describes the presence of signs of lower urinary tract disease without implying any specific cause. Subsequent studies identified many risk factors associated with FUS – dietary influences, for example, the fact that struvite (the stone most commonly associated with FUS) is composed of magnesium, ammonium and phosphorus led toward the conclusion that most cases of FUS were diet induced and away from investigation of other potential causes [9].

Urinary tract diseases affect animals of any age, breed and gender. Among the diseases that affect this system, urolithiasis is the second largest cause of clinical signs compatible with feline urinary tract disease. The term urolithiasis refers to the presence of uroliths in any region of the urinary tract, but it is more commonly seen in the bladder and urethra.

The disease can occur asymptomatic, or show nonspecific clinical signs, so the diagnosis can be difficult. Urolithiasis is a consequence of various disorders: dietary, metabolic, genetic and infectious causes. Factors that potentiate the chance of development of uroliths are considered breed, age, sex, age range, obesity, sedentary lifestyle, geographic region and climate. The assessment of these factors makes it possible to identify susceptible populations, which facilitates the diagnosis and treatment of patients with urolithiasis [10].

For example, during research in the Czech Republic a total of 214 cats with signs of feline lower urinary tract disease (FLUTD) were assessed in this study (81.30% males (82.20% of them neutered) and 18.70% females (80.00% of them spayed) with an age range from 9 months to 17 years). Most of the cats (51.90%) were diagnosed with feline idiopathic cystitis (FIC); in 26.60% cats uroliths were detected. A urinary tract infection (UTI) as well as urethral plugs were diagnosed in 10.75% cats. In 46.72% cats, a non-obstructive form of feline lower urinary tract disease (FLUTD) was present; in 53.28% cats (exclusively males) a urethral obstruction was diagnosed. Most of the cats (65.90%) were indoor-housed. Haematuria was the most common laboratory finding within the urinalysis which was diagnosed in 84.60% cats [11].

As mentioned above, feline lower urinary tract disease (FLUTD) are one of the most common pathologies in cats today, and the incidence of these diseases is increasing (Fig. 1). So, according to the data of 2015, such diseases occurred in 6.0%, in 2020

already in 15.96% of animals, while the incidence of such a serious disease as Polycystosis renis increased. A study was conducted to examine the epidemiological data and identify the causes of feline lower urinary tract disease (FLUTD).

The population consisted of 177 cats presented with lower urinary tract disease signs was included in the study at the Small Animal Clinic of the University of Veterinary and Pharmaceutical Sciences Brno. 41 (23%) cats were diagnosed with a urethral plug, 26 cats (14%) with a urinary tract infection (UTI), 9 cats (5%) with urolithiasis and 101 cats (57%) with feline idiopathic cystitis (FIC).

Figure 1

Characteristics of the incidence of non-communicable feline diseases

Disease	2015 [12]	2020 [13]	
		absolutum; head	certis; %
Helminthosis	19,1	49	26,06
Allergies	8,7	28	14,89
Urolithiasis, idiopathic cystitis	5,6	21	11,17
Conjunctivitis	10,1	14	7,45
Stomatitis	4,5	14	7,45
Neoplasmata	12,9	11	5,85
Aeksema	1,2	11	5,85
Otitis media et aurem interiorem	1,0	10	5,32
Polycystosis renis	0,4	9	4,79

The cats diagnosed with UTI were significantly older than the cats with FIC, urethral plugs and urolithiasis. Urinary tract infection was diagnosed significantly more often in patients older than 10 years, and in female cats, that is to say the causes are significantly age and sex-related [14].

Studies conducted in veterinary clinics in 14 states revealed that among the cases of feline lower urinary tract diseases (FLUTD) with a severe and unsafe course of the disease for the patient, the vast majority belonged to urolithiasis (60.0–70.0%), FIC was diagnosed less frequently, consequences of kidney disease, in particular, chronic kidney disease (CKD), chronic kidney failure (CDF), polycystic kidney disease (PCKD).

The diagnosis of urolithiasis was epietiological, often chronic, characterized by the formation of uroliths in the bladder, painful and frequent urination, sometimes with blood impurities, in acute cases, blockage of the urethra occurred with a complete absence of urination. Female cats were susceptible to urolithiasis at any age, most often between 2 and 6 years of age. In spayed cats after 7 years, urolithiasis was practically not diagnosed, less often this disease occurred in cats under 1 year old (up to 2.8%) [15]. In other studies, feline urolithiasis represented only 15% of the lower urinary tract disease incidence in cats, approximately 50% of feline uroliths were struvite-containing [16].

During two detailed investigations of specific causes of signs of feline lower urinary tract disease (FLUTD), in the Ohio State University urology service have been reported. The first study (1982–1985) described 143 cases of hematuria and dysuria, urethral plugs were present in 32 cases, urolithiasis without urinary tract infection (UTI) in 30 cases, UTI alone in two cases and UTI with uroliths in two cases and 77 cases were classified as idiopathic (was present in ~69% of the nonobstructed cats).

In a more recent study, 132 cats with signs of lower urinary tract disease were evaluated. 12 of these cats had urethral obstruction, 11 had concurrent systemic disease.

Specific causes for the signs of lower urinary tract disease were identified in 29 of the remaining cats. Urolithiasis (8 struvite, 7 calcium oxalates, one unknown) was present in 16 cats (14.7% of nonobstructed cats without concurrent systemic disease), anatomic defects in 12 (this included 1 of the cats with urolithiasis), neoplasia in 2 (this included 1 cat with urolithiasis), and urinary tract infection in 1 case. 10 cats were considered to have behavioral abnormalities and 70 had FIC (64.2% of nonobstructed cats without concurrent systemic disease).

It is interesting that the proportion of nonobstructed cases with idiopathic disease was similar in both studies, despite the 10-y gap between them. The more recent study does show, that urolithiasis remains an important cause of lower urinary tract disease in cats: two types of urolith predominate (struvite and calcium oxalate) [17].

Chronic kidney disease (CKD) is most affected geriatric cats (>12 years of age), that creates a special problem in connection with the increase in the proportion of senior and aged animals. Thus, frequency of the diagnosis of CKD in cats has increased in recent decades, although a variety of primary renal diseases have been implicated, the disease is idiopathic in most cats [18; 19]. In addition, the ever-increasing number of cats develop a disease without any obvious underlying cause – so-called 'feline idiopathic cystitis' or FIC. As these cats exhibit signs of cystitis but have no obvious underlying cause, it is possible that there is more than one (as yet unidentified) underlying condition that causes FIC. FIC is a bladder syndrome that only affects female cats. It occurs as the culmination of unknown factors causing a non-bacterial, sterile bladder infection that can cause urinary stones in cats. Episodes of FIC seem to occur mainly in susceptible cats in combination with a deficient environment [20].

Possible risk factors associated with FIC and compared different clinical presentations in 64 cats with FIC evaluated in the retrospective, case-controlled study. Several risk factors involved in FLUTD were identified as playing a role in FIC. Of the stressful situations considered, most occur with increased frequency in cats with a house move. FIC occurs most often in young- to middle-aged cats that are less than 10 years old. An obstruction was significantly more likely in cats with struvite-containing uroliths; urethral plugs were an important cause or contributing factor of obstruction in FIC [21].

Due to the increase in the frequency of FIC, there is increasing interest in assessing the severity of the outcome of the disease. Despite years of research, the aetiology is still incompletely understood and, subsequently, diagnostic markers and consistently effective treatment are lacking. Data regarding recurrence of signs of feline lower urinary tract disease (FLUTD) and FLUTD-related mortality in cats diagnosed with FIC between 2003 and 2009 were obtained through structured telephone interviews with the cat owners from December 2018 until February 2019.

At the time of the interview, only 12% cats were still alive. The FLUTD-related mortality rate was 20%; 23 cats (46%) had no recurrences, t3 cats (6%) were euthanized after diagnosis, 18% had 1-3 recurrences, 6% cats had 4-6 recurrences and six 12% had >6 recurrences. For the remaining 6 cats, the number of recurrences was uncertain.

The long-term prognosis for cats diagnosed with FIC, based on the results from the present study, is fairly good, as approximately 70% of the cats either recovered without additional episodes, experienced only a few recurrences, were still alive after a minimum of 10 years since inclusion in the study, or were euthanized for reasons unrelated to FLUTD [23].

Breed factors also play a role. Outbred and Persian cats were almost equally susceptible to feline lower urinary tract diseases (FLUTD) and were sick significantly more often than Siberian cats – by 28.62 and 28.44%, Cornish Rex – by 26.4 and 26.22%,

Siamese – by 26, 2 and 26.02%, Exotic – by 23.06 and 22.88%, and Scottish – by 21.52 and 21.34%, respectively. At the same time, outbred, Persian and British were most predisposed to the development of urolithiasis, Persian, British, Scottish and outbred – to FIC, outbred and Persian – to acute renal failure (ARF), outbred – to chronic kidney failure (CDF), Persian – to nephritis, to polycystic kidney disease (PCKD) – Persian and exotic [23; 24].

For a long period, the main diagnostic method for feline lower urinary tract diseases (FLUTD) has been urinalysis – the examination of normal and abnormal constituents of urine. It is an easy, cheap, and vital initial diagnostic test for veterinarians. Complete urinalysis includes the examination of color, odor, turbidity, volume, pH, specific gravity, protein, glucose, ketones, blood, erythrocytes, leukocytes, epithelial cells, casts, crystal, and organisms.

Semi-quantitative urine analysis with urine dipsticks, as well as an automatic analyzer, provides multiple biochemical data. Well-standardized urinalysis, when correlated in the context of history, clinical findings, and other diagnostic test results, can identify both renal and non-renal disease [25]. Uroliths can have a different composition (Figure 2).

The formation of uroliths is a complication of several disorders. Some abnormalities can be identified and corrected (for example, struvite uroliths due to infection); others can be identified but not corrected, and for most cats with calcium oxalate urolithiasis, the cause is unknown. In any case, these disorders can occasionally cause a supersaturation of the urine with one or more crystal precursors, leading to the formation of crystals [26].

Calcium oxalate-containing uroliths can have very sharp edges. Struvite-containing uroliths can dissolve and disappear after a change in the cat's diet, when the pH of the urine changes, but oxalate stones cannot. Struvite-containing uroliths occur in a pronounced alkaline environment. As a rule, male cats suffer from this type of pathology. Oxalates form in an acidic environment with an excess of calcium and often occur in aged animals [27].

Figure 2

Comparative characteristics of calcium oxalates- containing and struvite-containing urolith submissions from cats

Types of uroliths	Calcium oxalates	Struvites
Minerals, the excess of which leads to their formation	magnesium, phosphorus	calcium, urate, oxalate salts
Urine reaction	alkaline	acidic
Structure, density	solid	fragile
The form	smooth	with sharp edges
Prevalence	occur in 80% of urolithiasis cases, predominantly in cats under 6 years of age	more common in older animals

In studies of different feline populations, struvite and calcium oxalate uroliths comprised >90% of all uroliths submitted. Oxalate submissions outnumbered struvite submissions from the Canada, Hong Kong, Denmark, and the United Arab Emirate feline populations. In cats from the Australian feline population, struvite submissions

outnumbered calcium oxalate submissions. In Canada, the majority of urolith submissions were from domestic cats followed by Himalayan, Persian, and Siamese cats. Male cats were more likely to form calcium oxalate uroliths and female cats were more likely to develop struvite uroliths. Compared to domestic short-haired (DSH) cats, Tonkinese, Burmese, Devon rex, Himalayan, Persian, and Siamese cats were significantly associated with calcium oxalate urolith submission Egyptian Mau [28].

Although in the past mainly struvite stones were encountered, today we are seeing an increase in the occurrence of oxalate crystals and calcium oxalate uroliths. So, of 3940 urolith submissions from cats, 1820 (46.2%) were calcium oxalate-containing uroliths and 1856 (47.1%) were struvite-containing uroliths. A significant nonlinear decrease in the proportion of calcium oxalate-containing uroliths occurred over time from 50.1% in 2005 to 37.7% in 2018. In contrast, the proportion of struvite-containing uroliths increased significantly in a nonlinear fashion over this period from 41.8% in 2005 compared to 54.5% in 2018.

Of calcium oxalate-containing uroliths, 64% were from male and 36% were from female cats. The proportion of calcium oxalate-containing uroliths among male cats (49.8%) was significantly higher compared with the proportion among female cats (40.7%). Of cats with struvite-containing uroliths, 47.1% were submitted from female cats and 52.9% – from male cats. The proportion of struvite-containing uroliths among female cats (55.0%) was significantly higher than the proportion among male cats (41.8%).

Approximately 2/3 of calcium oxalate -containing uroliths were submitted from cats between 7 and 15 years of age. The proportion of calcium oxalate-containing uroliths was significantly higher in cats ≥7 years of age (56.5%) compared to the proportion in cats <7 years of age (31.2%). Struvite-containing uroliths most often were submitted from cats between 4 and 10 years of age (63.1%)? their proportion among cats <7 years of age (61.3%) was significantly higher compared to the proportion of struvite-containing uroliths from cats ≥7 years of age (38.0%).

Breeds at higher risk of developing CaOx-containing uroliths compared to the DSH were Burmese (5.3%) and Persian (1.7%). The domestic medium hair (DMH) was the only breed at significantly higher risk of developing struvite-containing uroliths compared to the DSH (1.4%). Several breeds were at lower risk of developing struvite-containing uroliths compared with the DSH, including Bengal (0.2%), Ocicat (0.2%), and Persian (0.6%) [29].

Since 2000, more cases of feline urate urolithiasis have been reported. The associations between feline urate urolithiasis and breed, age, gender, and urine composition retrospective case control study at Canadian Veterinary Urolith Centre (CVUC) between 1998 and 2007 years has been done. There were 10083 feline uroliths examined, including 385 ammonium urate, 13 uric acid, and 21 mixed struvite/urate uroliths. The Egyptian Mau, Birman, and Siamese breeds were significantly predisposed to urate urolithiasis [odds ratio (OR) = 118, 95%]. Urate urolithiasis was more frequent in younger cats (mean age 6.3 versus 7.1 y in cats with other uroliths) and in male cats (P = 0.024). The association between Egyptian Maus and urate urolithiasis was remarkable [30].

In this study, uroliths from veterinary practitioners in the Netherlands between 2014 and 2020 were analysed. Between 2014 and 2020 the distribution over the different types of uroliths remained similar over time. Female cats, obese cats, Domestic Shorthair cats had an increased risk for struvite. Neutered cats, all cat breeds except Domestic Shorthair had an increased risk for calcium oxalate urolithiasis [31].

Conclusions and suggestions. Among the cases of feline lower urinary tract diseases (FLUTD) with a severe and unsafe course of the disease for the patient, the vast

majority belonged to urolithiasis (60.0–70.0%), FIC was diagnosed less frequently, consequences of chronic kidney disease (CKD), chronic kidney failure (CDF), polycystic kidney disease (PCKD).

The causes and groups of animals predisposed to feline lower urinary tract diseases (FLUTD) have not been fully elucidated. In general, among the diseased animals prevailed male cats (81.30%, 82.20% of them neutered), among female cats – spayed animals (80.00% of them), most of the cats (65.90%) were indoor-housed.

Breed factors also played a role: outbred and Persian cats were almost equally susceptible to feline lower urinary tract diseases (FLUTD); outbred, Persian and British were most predisposed to the development of urolithiasis, Persian, British, Scottish and outbred – to FIC. Female cats were susceptible to lower urinary tract diseases at any age, most often between 2 and 6 years of age. In spayed cats after 7 years, urolithiasis was practically not diagnosed, less often this disease occurred in cats under 1 year old (up to 2.8%).

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UDC 636.087:636.034:636.52:637.4:575
DOI https://doi.org/10.32851/2226-0099.2022.125.28

GENETIC STRUCTURE OF EGG CROSSES AND EFFECT OF FEED SUPPLEMENT ON EGG PRODUCTION

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Egg crosses are hens whose main purpose is to lay eggs. Breeders have done a lot of work, which has resulted in highly productive species capable of laying up to 320-330 eggs in the first year of life.

It has been scientifically proven that cross females are more hardy, better adapted and have higher productivity. However, such efficiency is observed only in the first generation.

The right choice of laying hen crosses is a guarantee of high productivity.

Breeding companies offer poultry farmers a wide variety of egg crosses of chickens, which differ in productivity, maintenance technology, requirements for the quantity and quality of feed consumed by birds and the level of productivity. Today, one of the most productive crosses of hens is the poultry of German breeders Lohmann Tierzucht GmbH, hens: Lohmann Brown, Lohmann White (LSL Classic), Lohmann Sandy. Chickens with high egg production and egg quality are the result of many years of work by German geneticists Lohmann. At the beginning of the creation of new crosses of chickens, it was assumed that their habitat would be only the mild climate of Europe, but today they are widely kept in industrial poultry for cost-effective profitable poultry farming around the world. These crosses of laying hens have proven themselves in poultry farms in Ukraine.