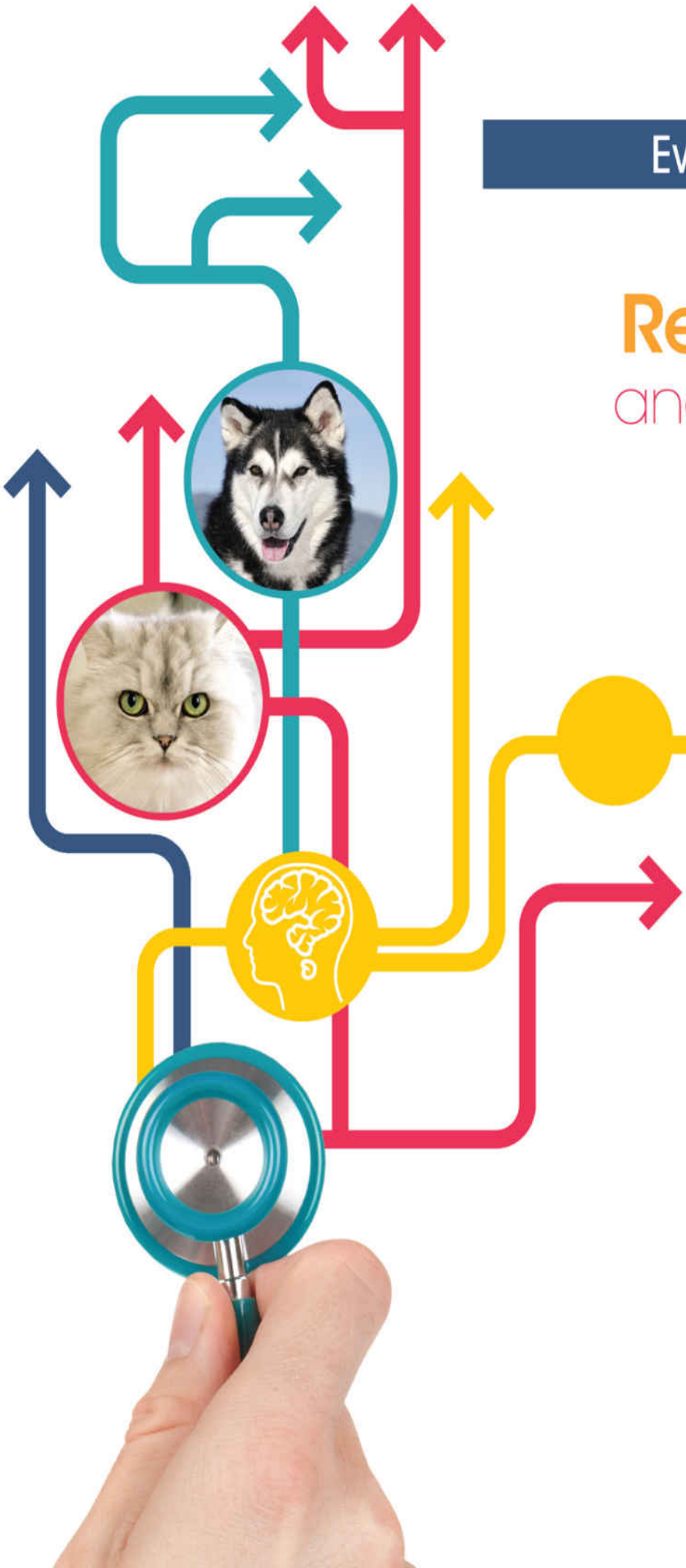
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Evaluate your skills

Clinical Reasoning and Differential Diagnosis

Josep Pastor Milán

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Clinical Reasoning
and Differential Diagnosis

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Warning:

Veterinary science is constantly evolving, as are pharmacology and the other sciences. Inevitably, it is therefore the responsibility of the veterinary surgeon to determine and verify the dosage, the method of administration, the duration of treatment and any possible contraindications to the treatments given to each individual patient, based on his or her professional experience. Neither the publisher nor the author can be held liable for any damage or harm caused to people, animals or properties resulting from the correct or incorrect application of the information contained in this book.

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PREFACE

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This book on reasoning is based on an idea that my great friend Enric Valladares and I conceived a few years ago, although I must stress it would have never seen the light of day were it not for Enric's insistence.

The basic concept that gave rise to this compilation of cases was the notable increase in the number of analytical methods, diagnostic imaging tests, and diagnostic algorithms being used in small animal veterinary medicine. All these resources have improved veterinarians' skills and the overall level of veterinary medicine; however, our perception was that the underlying theory was being lost during this process. In other words, not enough attention was being paid to the arguments used to choose between diagnostic tests, how an animal's clinical problems can be linked to the reasoning behind the algorithms which simplify our day-to-day clinical activities. What is more, the importance of a good clinical record and complete physical examination seems to be waning.

This impression gave rise to the present work, which applies reasoning to a series of cases that are representative of the main problems encountered by veterinarians when treating cats and dogs. The clinical cases presented in this book have been gathered with help from other authors, advice from staff at the Autonomous University of Barcelona (UAB) Clinical Veterinary Hospital, and the participation of the Department of Diagnostic Imaging. Other vets at the UAB Clinical Veterinary Hospital have undoubtedly participated in the management of the cases described herein, so I would like to take this opportunity to thank them for allowing us to use these cases and for their professional work and teaching.

While developing this book, the aim was not only to produce reading material and a reference work for vets, but ultimately, through the clinical cases included as examples, to teach them how to actively apply clinical reasoning by acquiring and strengthening their practical skills when establishing a structured, logical, and efficient working method.

Without further ado, I hope this book helps you develop, inevitably thanks to daily practice, the habit of clinical reasoning – an art that must be cared for and cultivated throughout a veterinarian's career.

There is no such thing as a perfect book, and I am sure this one can be improved, but I hope you like it and may benefit from it.

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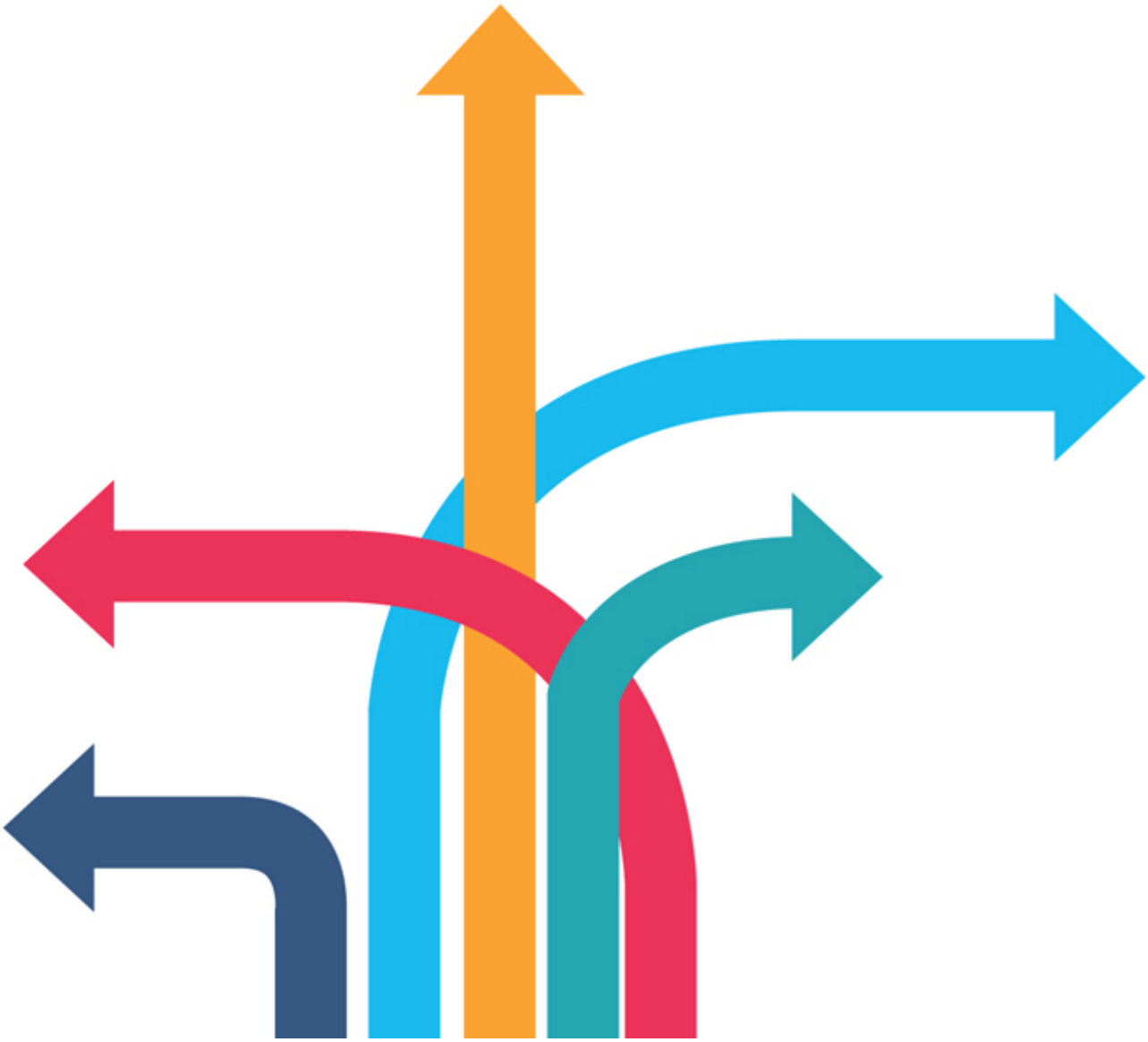
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Recommended reading

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1 HOW TO PERFORM DIFFERENTIAL DIAGNOSIS



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1 HOW TO PERFORM DIFFERENTIAL DIAGNOSIS

WHAT IS CLINICAL REASONING?

When dealing with a sick animal or during a check-up, clinical reasoning allows us to identify the patient's specific problems and prioritise the most relevant points in their diagnosis. It also helps us determine whether the problems are interrelated, so we can define the significance and possible causes of the pathological process. In human medicine, it is believed that around 17 % of adverse events or incorrect decisions are due to errors in clinical reasoning. While no equivalent data have been published in veterinary medicine, the percentage is expected to be similar. These unfavourable results are due to a lack of knowledge, errors when obtaining appropriate information, and errors when processing the information.

Every single clinical case begins with a proper clinical record, a complete and thorough physical examination, without neglecting any organs or systems, and sometimes with an analysis of prior laboratory tests. This information forms the fundamental basis for optimal clinical reasoning and corresponds to the first step in the appropriate management of each case.

Using the information gleaned from the animal's signalment, clinical record, physical examination, and sometimes a prior blood test, the vet puts various lines of reasoning into practice to zero in on a diagnosis. The most common thought processes are:

1. Nonanalytical, intuitive, or based on disease patterns.
2. Based on analytical test results (as we do not know what the problem is, let's do some basic tests to get more information).
3. Clinical reasoning based on the identification of problems.

Each of these methods of reasoning has its own limitations and advantages; in some instances, all three methods should be applied to the same case.

KEY POINT

A good clinical record and a comprehensive and meticulous physical examination are the essential pillars of a correct clinical diagnosis. Even the best veterinarian in the world can make an incorrect final diagnosis if they have been working with inaccurate information from the outset.



1 INTUITIVE CLINICAL REASONING BASED ON THE IDENTIFICATION OF PATTERNS

This is the fastest model of reasoning and involves a subconscious effort to identify clinical patterns stored in our memory which we have studied or experienced in clinical situations. As a case in point, when faced with an adult dog with a history of polyphagia, polyuria, polydipsia, pendulous abdomen, hair loss on the trunk, weight gain, and constant panting, the most logical course of action would be to try and rule out Cushing's syndrome or hyperadrenocorticism because they are the most common diagnoses. Furthermore, this type of reasoning tends to impress the animal's owner if we reach the correct conclusion, portraying an assuring image of a great veterinarian. However, it presents a series of significant limitations:

- We tend to remember diseases that are easier to memorise rather than other more complex conditions that might have a greater prevalence.
- Atypical attributes that do not fit in with the chosen diagnosis, and which may or may not be related to the initial diagnosis, may be overlooked.
- Erroneous confirmation. This is possibly the most frequent clinical error and is based on the following reasoning: since the clinical picture suggests a specific diagnosis, the vet's mind searches for data to confirm this belief, ignoring any information or data that might oppose their clinical suspicion.

- Premature case closure. Our confidence in the diagnosis means we consider the clinical investigation to be complete before obtaining all the correct and appropriate information and without examining the possibility of unusual complications or a second, concurrent disease.

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As we can see, this model of clinical reasoning can guide the vet to a lot of initially satisfactory results, but it may also lead to significant clinical errors. Additionally, it is excessively reliant on our knowledge of diseases, how up to date that knowledge is, our information retrieval capacity, and our clinical "intuition".

2 CLINICAL REASONING BASED ON LABORATORY TESTS

This line of reasoning is applied when the vet is unable to determine a specific disease pattern after examining the animal, so the next step is to request general blood tests to learn more about the patient's problem. This rationale may work in certain situations: for example, an animal with kidney disease whose increased creatinine and urea levels point us towards the correct diagnosis. Nevertheless, this model is significantly limited in disease processes that do not produce evident analytical changes, including respiratory tract diseases, heart disease, digestive disorders, and neurological diseases.

This method of clinical reasoning has become more sophisticated with the advent of diagnostic imaging tests. The line of thought is now something like: since we are unsure what is troubling this patient, let's take an abdominal ultrasound and chest X-ray to see if we can detect any alterations that might steer us towards a diagnosis. This approach often yields information, but if the veterinarian has not already applied clinical reasoning as a basis upon which to establish a differential diagnosis, then they may simply be requesting tests that increase the cost of the clinical procedure without any benefit for the patient. However, as mentioned earlier, in some cases reasoning based on laboratory tests is a good means of reaching a diagnosis.

3 CLINICAL REASONING BASED ON THE IDENTIFICATION OF PROBLEMS

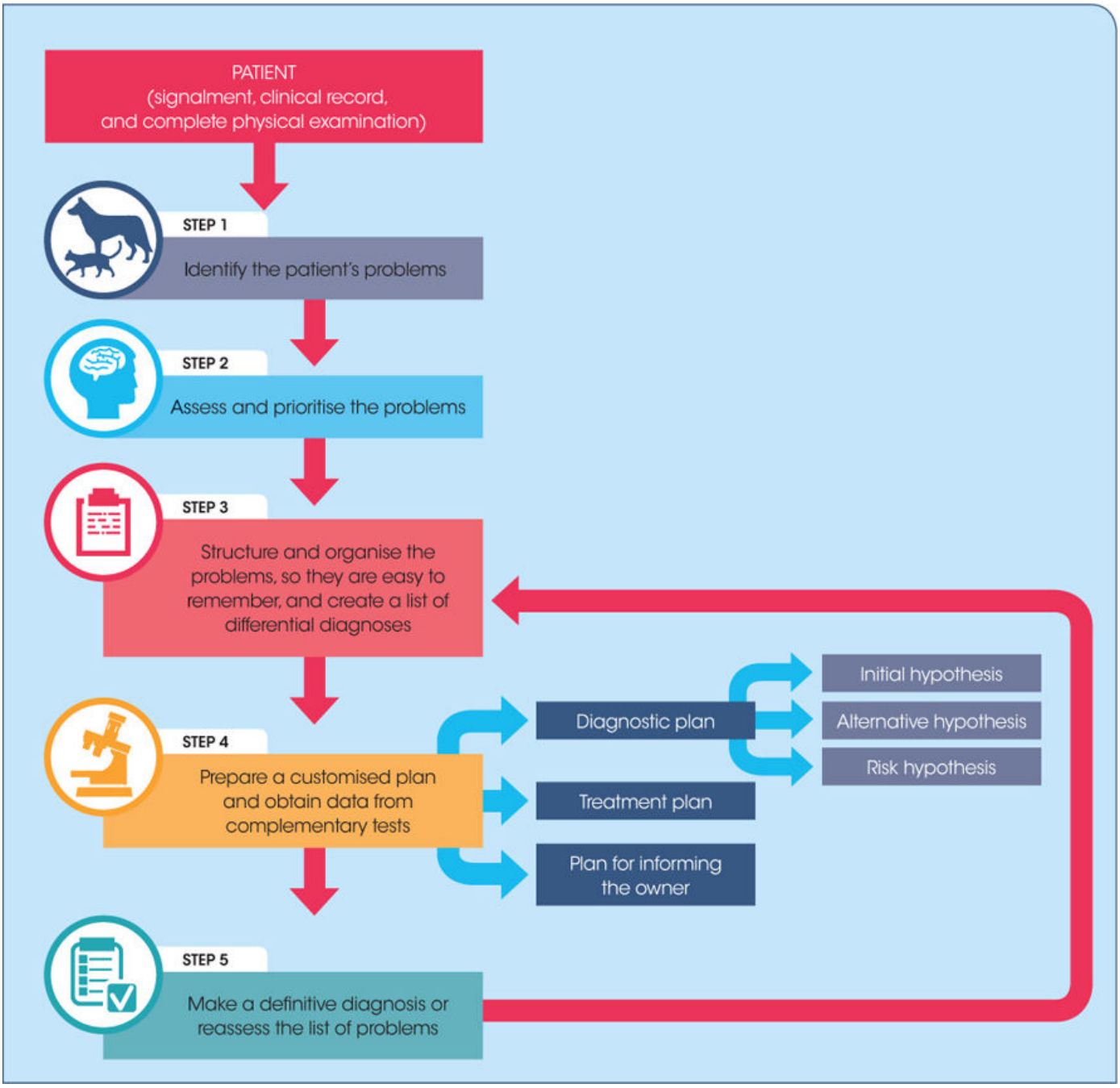
There is no such thing as a perfect approach to clinical reasoning. But for relatively inexperienced vets, vets working on complicated referrals, and, in general, to nurture our clinical reasoning, the problem-based model is the most complete method. It is not a perfect model and will be unnecessary in obvious cases, yet it is essential for our training as professionals and for us to become true "clinical detectives", as well as being motivational (although it may initially take longer).

We intend to explain this clinical reasoning model throughout the book and will illustrate the steps involved using clinical cases to represent the described problems.

STEPS OF PROBLEM-BASED CLINICAL REASONING

The following diagram summarises the steps implemented during clinical reasoning that relies on problem identification, problems which will be described in more detail later in the book.

WORKFLOW ALGORITHM FOR PROBLEM-BASED CLINICAL REASONING





IDENTIFICATION OF CLINICAL PROBLEMS

When tackling a clinical case, it is important that we recognise the animal's problems. To do this, firstly we must define what is a clinical problem.

KEY POINT

A clinical problem is any alteration that interferes with the animal's quality of life and requires medical or surgical intervention.

Problems can be classified as concerns held by the owner, findings from a physical examination, abnormal lab test results, chronic problems (e.g. diabetes, leishmaniasis, inflammatory bowel diseases, etc.), acute clinical signs, or significant past diseases such as a neoplasm. With this approach, it is vital to identify the patient's problems correctly and subsequently update them during each consultation until they are resolved.

STEP 2



PRIORITISE THE PROBLEMS

Insofar as possible, each animal's problems must be prioritised according to their importance or seriousness. As a case in point, if an animal manifests vomiting, anorexia, and weight loss, it is reasonable to believe that the vomiting is responsible for the anorexia and weight loss, so the vet should focus on a differential diagnosis of the vomiting. On the other hand, if a patient manifests with the same clinical signs plus jaundice, then the latter may be the cause of the vomiting and other clinical signs and we should concentrate on a differential diagnosis for jaundice. This decision-making exercise is known as prioritisation of problems. If there is no relationship between one problem and the others, it should be dealt with individually.

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KEY POINT

Vets should seek connections between the animal's problems; the main problem is that which explains the other alterations. However, one animal can manifest several main problems, or their problems may be unrelated, in which case they should be treated individually.

STEP 3



ORGANISE THE PROBLEMS ACCORDING TO THEIR IMPORTANCE AND CREATE A LIST OF DIFFERENTIAL DIAGNOSES

The vet must structure the most important classifications or steps, so they are easy to remember, especially the set of differential diagnoses. It is possible to memorise a long list of causes for a particular problem, but it is not the most appropriate strategy, as it is hard to remember all the differential diagnoses. Therefore, the first thing is to place the problems in categories which are easily remembered and clinically relevant. This type of structuring can be anatomical, by organ or system, based on pathophysiology, or according to key points. Reorganising the problem into subgroups facilitates the creation of shorter lists of differential diagnoses, so the vet can develop a more focused, case-specific diagnostic plan. The subclassification must assist with clinical reasoning; therefore, one of the methods used in this step is to pose decisive questions that guide the problem towards different subgroups. For example, with an animal suffering from vomiting, the case can be divided into gastrointestinal or extragastrointestinal groups, and if a patient has convulsions, it could be an intra- or extracranial problem.

To this end, veterinarians can use published algorithms, books on differential diagnosis, or books on clinical reasoning. However, it is very hard to remember all the information available in these lists. As each vet has their own way of working, the first time they confront a problem it is a good idea to reason and organise it in a logical, easy-to-remember structure. The veterinarian should therefore consider their own format which they can memorise and allows them to structure the problem associated with each new situation. Subsequently, as they acquire more

clinical experience, the vet will add to their repertoire of differential diagnoses and diagnostic plans.

KEY POINT

The structuring of problems into subgroups makes it easier to remember differential diagnoses and the corresponding complementary tests.

STEP 4



INDIVIDUALISE THE DIAGNOSTIC PLAN

When applying problem-based clinical reasoning, every effort should be made to limit the differential diagnosis using key points or dichotomous questions in line with the signalment, clinical record, examination data, and prior laboratory findings (if any). This information is then used to choose the most logical differential diagnosis for the animal. As mentioned earlier, in some cases diagnosis may be straightforward, as the clinical picture may fit a pattern encountered previously, but in many other cases, complementary tests are required to reach a definitive diagnosis.

The diagnostic plan should consider an initial hypothesis, an alternative hypothesis, and a hypothesis that should not be disregarded or underestimated because of the risks it could imply for the patient.

KEY POINT

After completing the differential diagnosis, the vet should study any necessary additional tests to confirm their hypotheses, determine a treatment plan if the case is urgent or the animal critically ill, and implement an owner information plan to explain the veterinarian's reasoning and the strategy they will employ to treat the patient.



ESTABLISH A DEFINITIVE DIAGNOSIS OR REASSESS THE DIFFERENTIAL DIAGNOSIS

In this step, the vet obtains the results from any complementary tests that were requested. If the results lead to a conclusive diagnosis, a specific treatment and individual prognosis can be established. If the tests reveal more information but do not confirm a definitive diagnosis, the list of problems should be reconsidered and expanded, and further tests selected and requested.

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2 CLINICAL REASONING IN A CASE OF FEVER/ HYPERTHERMIA



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2 CLINICAL REASONING IN A CASE OF FEVER/HYPERTHERMIA

CLINICAL CASE
FEVER/HYPERTHERMIA

***M* is a 5-year-old, entire male Beagle brought to the practice with a 10-day clinical history of anorexia and apathy. The owner reported no previous medication or access to toxic substances. The physical examination did not reveal any significant alterations, except for mild tachycardia (110 beats per minute), tachypnoea (30 breaths per minute), and a temperature of 40 °C.**



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REASONING APPLIED TO THE CASE

Based on the available information, go through the first two steps of clinical reasoning:
1. Identify the animal's problems.
2. Prioritise the problems.





1. IDENTIFYING THE ANIMAL'S PROBLEMS

The patient has anorexia, apathy, tachycardia, tachypnoea, and a temperature of 40 °C.



2. PRIORITISE THE PROBLEMS

In this case it appears reasonable to assume that the anorexia and apathy are secondary to the fever/hyperthermia. Similarly, the mild tachycardia and tachypnoea could be a response to the stress of visiting the consultation room or due to the fever/hyperthermia. It is unlikely that the tachycardia and tachypnoea are the primary problems because of the absence of crackling sounds, cough, and previous tiredness. The most notable factor is the high temperature, so it seems logical to think that *M* 's main problem is probably fever.

Take these premises and proceed with the next two steps in the clinical reasoning procedure:
3. Structure and organise the animal's problem.
4. Individualise the diagnostic plan.





3. STRUCTURING AND ORGANISING THE PROBLEM (DIFFERENTIAL DIAGNOSIS)

To structure a differential diagnosis for a high temperature, we can consider the body's temperature regulation mechanism in physiological terms, where body temperature is the result of the balance between heat production and loss. Initial questions would be: What are the organism's sources of heat production? How do cats and dogs dissipate heat?

While this structuring is physiologically relevant and fundamental, it is hard to remember and tends to be forgotten, and even though these aspects are important for our understanding of what is happening to the animal, they are of little help when establishing a differential diagnosis and diagnostic plan.

An alternative approach is to consider the clinical definition of fever/hyperthermia or how a high temperature is classified in a patient. So, the first question the veterinarian must answer would be: **How should I define or classify a high temperature?** The answer being fever, hyperthermia, or fever of unknown origin (FUO).

The second question would be: **How can I establish this classification?** This would mean taking into account different definitions:

- **Fever** occurs when pyrogens (both exogenous and endogenous pyrogens such as interleukin-1, IL-1, and tumour necrosis factor alpha, TNF-α) stimulate the thermoregulatory centre in the anterior hypothalamus, prompting an increase in body temperature. Febrile animals may manifest raised hackles, a tendency to look for warm places, and tremors.
- **Hyperthermia** is not associated with a change in body temperature tasked by the thermoregulatory centre, so the animal will usually make a greater physiological

and behavioural effort to reduce its temperature by panting or seeking out cool areas, for example. Hyperthermia could be the result of exercise (especially in hot, humid climates), difficulty dissipating heat in obese animals or patients with breathing difficulties, an increase in muscle activity (convulsions, tremors due to hypocalcaemia, stress), an increase in metabolic activity (hyperthyroidism), poisoning (cocaine), drugs (ketamine, trimethoprim/sulfamethoxazole, etc.), or malignant hyperthermia.

- **Fever of unknown origin** is any fever that lasts for 2 or 3 weeks, has not responded to antibiotics, has an unknown aetiology following basic laboratory tests (blood count, blood chemistry, urine analysis), and therefore, after several visits, the vet establishes that it is of unknown origin.

Other important questions would be: **What is the normal temperature for a cat or dog? Is there a temperature for concern?** A normal temperature is 38–39 °C, but during consultations this can range up to 39.7 °C. A body temperature in excess of 41.1 °C can result in neurological damage or trigger disseminated intravascular coagulation or metabolic abnormalities with potentially fatal consequences, so the veterinarian must act rapidly to reduce the temperature.

In the present case, the duration of the patient's clinical signs (10 days), the anorexia, apathy, temperature of 40 °C, and the absence of drugs or toxic substances in the clinical record seem to indicate the problem is fever. We should look for behavioural changes during the examination and in the clinical record to support our hypothesis. In anamnesis, the owners mentioned that in the last few days *M* has sought out heat sources and trembled.

A FUO should be ruled out given the duration of the clinical signs and because there are still no results from any complementary tests to suggest using the concept of a FUO. We know that *M* has a fever and it is caused by the presence of exogenous pyrogens or the release of endogenous pyrogens, so we should focus on these mechanisms to develop a differential diagnosis. To do this, we can use the VITAMIN D mnemonic device to sort through possible causes (Box 1).

We can also search review articles for causes of fever in animals and discover that the most common ones in dogs are infections, immune-mediated diseases, neoplasms, or intoxications, in that order. Less has been published on the causes of fever in cats, but we know infections are the leading motive followed by neoplasms.

BOX 1. Key to the mnemonic acronym VITAMIN D for determining the origin of the problem.

V ascular: embolisms, haemorrhages.
I nfectious: bacterial, fungal, viral, or protozoan.
T oxic: endogenous (uraemia, hepatic encephalopathy) or exogenous.
T raumatic.
A bnormalities.

M etabolic: due to altered metabolism.

I mmune-mediated (noninfectious) inflammations.

N eoplasms: primary or metastatic.

D egenerative.

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4. INDIVIDUALISE THE DIAGNOSTIC PLAN

As a physical examination could not reliably determine the definitive cause of the fever and the clinical signs apparently developed more than 10 days ago, the next step should be a series of laboratory tests to rule out the most likely causes, such as a blood count to identify any active inflammatory processes (Table 1), blood chemistry (Table 2), and a urinalysis (Table 3). Additionally, if the patient lives in an endemic area, the vet could also order serological tests for *Ehrlichia* and *Leishmania* , then, depending on the results, the corresponding diagnostic imaging tests.

In *M* 's case, a rapid test for *Ehrlichia* , *Dirofilaria* , and *Anaplasma* gave negative results. The result of the serological assay for *Leishmania* was also negative.

How do we interpret the results?



The blood count reveals mild, nonregenerative anaemia indicative of chronic disease. However, the white blood cell count shows extreme neutrophilia with acute inflammation, which suggests an infectious, paraneoplastic, or immune-mediated process. Blood chemistry indicates slight changes in potassium and sodium, possibly related to the patient's hydration levels. Of note in the urine test results is the specific gravity of 1.020, which may suggest a decreased ability to concentrate urine or it could be secondary to the fever.

In view of the results:

5. Establish a diagnosis or reconsider the list of problems.





5. ESTABLISH A DEFINITIVE DIAGNOSIS OR REASSESS THE DIFFERENTIAL DIAGNOSIS

A differential diagnosis cannot be established with the information obtained so far, but a low urine specific gravity, nonregenerative anaemia, and a white blood count indicative of severe inflammation can be added to the list of problems. Considering the most likely causes of fever are of an infectious, immune-mediated, or neoplastic origin, further tests are required to totally rule out these processes. For this purpose, a more complete study can be conducted with chest X-rays, abdominal ultrasound, and urine and blood cultures.

Neither the chest X-ray nor the abdominal ultrasound revealed any significant alterations.

FINAL TREATMENT PLAN AND EVOLUTION

While waiting for the results of the blood and urine cultures, treatment was initiated with amoxicillin/clavulanic acid. During treatment, *M* showed no signs of improvement and the fever persisted. When completed, the blood culture returned a negative result, but the urine culture contained a Gram-negative bacteria, *Pseudomonas aeruginosa* , which is resistant to ampicillin, amoxicillin/clavulanic acid, cephalexin, nitrofurantoin, tetracycline, trimethoprim/sulfamethoxazole, and kanamycin; with an intermediate response to enrofloxacin and cefoperazone; and susceptible only to amikacin and marbofloxacin. Based on the cultures, marbofloxacin was selected for antibiotic therapy.

M responded very quickly; the patient's temperature normalised within 24 hours and the blood count was normal 4–5 days after changing the antibiotic.

TABLE 1. Blood count results.

Parameter	Value	Reference range

Erythrocytes (× 10^6 /µl)	**5.39**	5.5–8.5
Haemoglobin (g/dl)	13	12–18
Haematocrit (%)	**34**	37–55
MCV (fl)	71.9	62–77
MCHC (g/dl)	36.6	33–47
MCH (pg)	24.1	21.5–26.5
Reticulocytes (cells/µl)	12,936	0–60,000
White blood cells (cells/µl)	**50,050**	6,000–17,000
Lymphocytes (cells/µl)	4,505	1,000–4,800
Monocytes (cells/µl)	**1,502**	150–1,350
Segmented neutrophils (cells/µl)	**43,544**	3,000–11,500
Band neutrophils (cells/µl)	**501**	0–300
Eosinophils (cells/µl)	**0**	100–1,500
Basophils (cells/µl)	0	0–200
Platelets (× 10^3 /µl)	301	200–500

TABLE 2. Blood chemistry results.

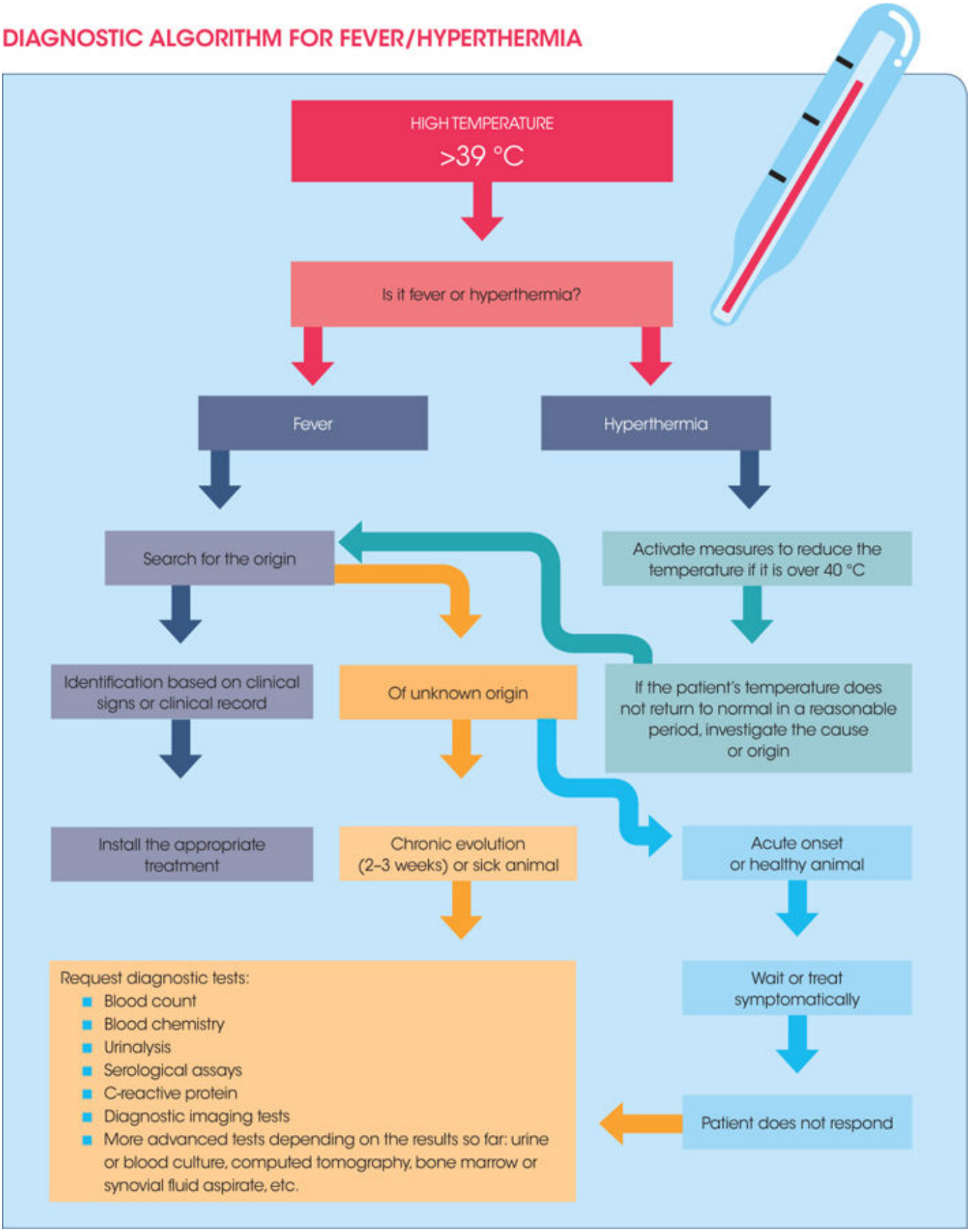
Parameter	Value	Reference range
Creatinine (mg/dl)	1.46	0.5–1.5
Urea (mg/dl)	34.5	21.4–60.0
Cholesterol (mg/dl)	269.5	135–270
Glucose (mg/dl)	109.4	65–118
Total protein (g/dl)	6.4	6–8
Total bilirubin (mg/dl)	0.16	0.1–0.5
Alkaline phosphatase (IU/l)	107.7	20–156
GGT (IU/l)	**1**	1.2–6.4
ALT (IU/l)	38	21–102
CK-NAC (IU/l)	125.8	10–150
Calcium (mg/dl)	9.5	9.0–11.3
Phosphorus (mg/dl)	4.73	2.6–6.2

Potassium (mmol/l)	**3.98**	4.37–5.35
Sodium (mmol/l)	**138.9**	141–152
Chloride (mmol/l)	110.9	105–115

TABLE 3. Urine test results (cystocentesis).

Parameter	Value
Specific gravity	1.020
pH	8
Proteins	0
Blood	1+
Sediment	No evidence of cells or bacteria

DIAGNOSTIC ALGORITHM FOR FEVER/HYPERTHERMIA



BRIEF REVIEW OF…

URINARY TRACT INFECTIONS

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Lower urinary tract infections have multifactorial origins which depend on:

- The individual animal: anatomical variations, the characteristics of their urine, or immunological factors.
- The virulence of the pathogen involved in the infection: uropathogenic bacteria usually originate in the enteric bacterial flora and ascend the urethra to the urinary bladder.

Urinary tract infections can be caused by bacteria, fungi, or parasites. The majority of cases are bacterial infections, so this review will concentrate on them by trying to answer a series of typical questions.

WHAT IS BACTERIURIA? IS IT SYNONYMOUS WITH A URINARY INFECTION?

One of the basic elements in a urinary tract infection (UTI) is the identification of bacteria in the urine (bacteriuria). Nevertheless, bacteriuria is not synonymous with a urine infection. At the same time, animals with bacteriuria may have clinical signs of a UTI (pain in the caudal abdomen, pollakiuria, strangury, dysuria, or haematuria) or they may not manifest any clear signs in the case of subclinical bacteriuria.

It is estimated that 2.1–8.9 % of dogs and 10.0–28.8 % of cats may have subclinical bacteriuria, in which *Escherichia coli* and *Enterococcus faecalis* are isolated more than any other bacteria.

CAN ANY BACTERIA ISOLATED FROM THE URINARY TRACT PRODUCE CLINICAL SIGNS OF A UTI?

The presence of clinical signs depends on the genetic characteristics of the bacteria that has colonised the urinary tract. For example:

- Bacteria with genes that are resistant to multiple antibiotics are usually found in chronic urinary infections and this characteristic means they are normally less virulent.
- On the other hand, Gram-negative bacteria have a greater affinity for the kidneys than Gram-positive bacteria.
- Some bacteria, such as *Enterococcus* or *Streptococcus* spp., do not usually affect the upper urinary tract.
- Adhesion molecules have been reported, mainly in uropathogenic *E. coli* bacteria, that are known to determine the site of bacterial colonisation. As such, type 1 fimbrial expression (coded by the *fim* gene) is observed in 100 % of bacteria that cause pyelonephritis and in 77 % of cases of asymptomatic bacteriuria, while P fimbrial expression is noted in 78 % of pyelonephritis-causing bacteria and 22 % of those that cause cystitis.

Most UTIs are caused by Gram-negative bacteria and *E. coli* is isolated the most often.

WHAT IS THE BEST WAY TO IDENTIFY A BACTERIAL URINARY INFECTION?

The best samples for determining the presence of a urinary infection are those obtained by sterile cystocentesis for culture under aerobic conditions. A urinalysis, particularly the study of urinary sediment, reveals if the animal has inflammation, crystals, or bacteriuria. However, the test's sensitivity to the presence of bacteria is only 75 %, although this can be improved to 83 % or higher with the use of staining techniques. The type of bacteria influences the ability to detect a given urinary infection. In general, if bacilli are present, just 10,000 CFU/ml is usually enough for detection, but if the infection is due to cocci, their identification requires up to 100,000 CFU/ml.

There are some other factors that affect urine cultures, such as the time between sample collection and analysis, whether the sample has been transported, and its storage conditions. Although it has limitations, the culture of urine samples obtained by cystocentesis is the recommended technique. When interpreted together with the sediment analysis, it can help identify samples with inflammatory processes (more than three inflammatory cells per oil-immersion field) and improve differentiation between clinical and subclinical bacterial infections.

HOW DO WE TREAT URINARY INFECTIONS?

Patients are generally treated according to whether they have a complicated or uncomplicated UTI.

UNCOMPLICATED URINARY TRACT INFECTIONS

Uncomplicated infections are those which occur no more than once every 6 months in healthy animals with an anatomically normal and correctly functioning urinary tract. Entire male cats and dogs are an exception that should always be considered complicated infections, since it may be accompanied by prostatitis in male dogs or a systemic disease in cats.

Most animals with uncomplicated UTIs manifest obvious clinical signs which often mean treatment should be initiated before receiving the results of the bacterial culture and antibiotic sensitivity test. Therapy should start with amoxicillin (11–15 mg/kg, PO, every 8 hours) or trimethoprim/sulphonamide (15 mg/kg, PO, every 12 hours) for 7–14 days. If the clinical signs improve, it is likely that no further measures are required. If the patient does not respond positively to the treatment, the vet must ensure they selected the correct antibiotic and check the sensitivity of the agent involved in the urinary infection.

Recent studies have shown that 3-day treatments with trimethoprim/sulphonamide or high doses of enrofloxacin are just as effective as treatments lasting 7–14 days.

COMPLICATED URINARY TRACT INFECTIONS

Complicated UTIs are those where the animal presents anatomical, functional, or metabolic alterations that make recurrences more likely or reduce the chances of eliminating the infection. In such situations, it is important to consider the presence of:

- Persistent or refractory infections: the urinary tract infection does not respond to antibiotics and it proves impossible to obtain a negative bacterial culture.
- Recurrent infections: less than 6 months after resolving a UTI, a new infection occurs with a different bacterium.
- Reinfections: following successful treatment, within 6 months the patient develops a new episode of UTI caused by a bacterium that was already identified in the previous infection.

In such instances it is important to identify the underlying cause of the new UTI, which means you should try to rule out anatomical, functional, and metabolic

causes. The origin cannot be determined in 25 % of cases. If the cause can be identified, it should be corrected insofar as possible.

Patients with complicated UTIs usually have to take antibiotics selected through cultures and antibiograms for 4–6 weeks. Shorter treatments of 7–14 days can be used in the case of systemic diseases that predispose urinary infections, such as Cushing's syndrome and diabetes. Furthermore, it is recommendable to repeat the urine culture 1 week after starting antibiotic therapy and 7–14 days after completing the treatment. In the case of pyelonephritis, quinolones can be used as the first-choice antibiotic and treatment tends to last for 6 weeks.

ARE THERE ANY ALTERNATIVES TO PREVENT INFECTIONS?

Although their effects have not yet been clearly demonstrated in cats and dogs, some adjuvant treatments have been administered in humans and reduced the incidence of urinary infections. A few examples are explained below.

CRANBERRY SUPPLEMENTS

The American cranberry (*Vaccinium macrocarpon*) contains a natural bioactive tannin (proanthocyanidin, PAC-A) that inhibits *E. coli* fimbriae from binding to the urothelium. This activity reduces the number of bacteria thanks to their elimination via urinary irrigation and a reduction in pathogenic colonisation and infection. Similar activity has been observed against *Enterococcus faecalis* .

Pharmaceutical-grade cranberry extract with PAC-A is available as a concentrated preparation for use in veterinary medicine. Recent in vitro and in vivo studies confirmed its efficacy and safety in dogs, while other field studies did not attest to these findings.

D-MANNOSE

D-mannose is a monosaccharide with antibacterial properties. When present in urine, it prevents bacteria from binding to urothelial cells. In vitro experiments have shown that D-mannose binds to and therefore blocks the FimH adhesin, which is found at the tip of type 1 fimbriae of enteric bacteria. During colonisation, bacteria use FimH adhesins to bind to carbohydrate-containing glycoprotein receptors found in the urinary tract epithelium. D-mannose has a similar structure to the urothelial glycoprotein receptor binding sites where bacterial adhesins attach,

so it acts as a competitive inhibitor of bacterial adherence. A sufficiently high urine concentration of D-mannose will saturate the FimH adhesins and prevent the bacteria from binding to the urothelial receptors. Studies have shown that *Escherichia coli* , *Pseudomonas aeruginosa* , and *Streptococcus zooepidemicus* are inhibited by D-mannose.

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METHENAMINE SALTS

Methenamine salts are used as an antimicrobial agent in the prophylaxis of recurrent urinary tract infections. Following oral administration, methenamine plasma concentrations are very low and its systemic antibacterial activity is insignificant. Some 70–90 % of each dose is excreted unchanged in the urine. In the acidic urine environment (pH <6.5), methenamine is transformed into formaldehyde. Formaldehyde is a nonspecific antibacterial agent with a bactericidal effect. Some bacteria such as *Proteus* and some strains of *Staphylococcus* , *Enterobacter* , and *Pseudomonas* can increase urine pH, which may require the addition of a urinary acidifier to improve the efficacy of the methenamine. This drug has also demonstrated activity against fungal infections.

It is not typically used in veterinary medicine and there is scant evidence available to confirm its efficacy in cats and dogs. Possible side effects are related to gastrointestinal problems such as nausea, vomiting, and anorexia.

ANTIBIOTICS AS PROPHYLAXIS

For prophylactic purposes, a third to one half of the normal antibiotic dose can be administered every night for 6 months. If there is no reinfection or recurrence by the end of this period, the antibiotic should be discontinued. However, note there is some controversy in veterinary practice regarding the success of this strategy.

RECOMMENDED READING

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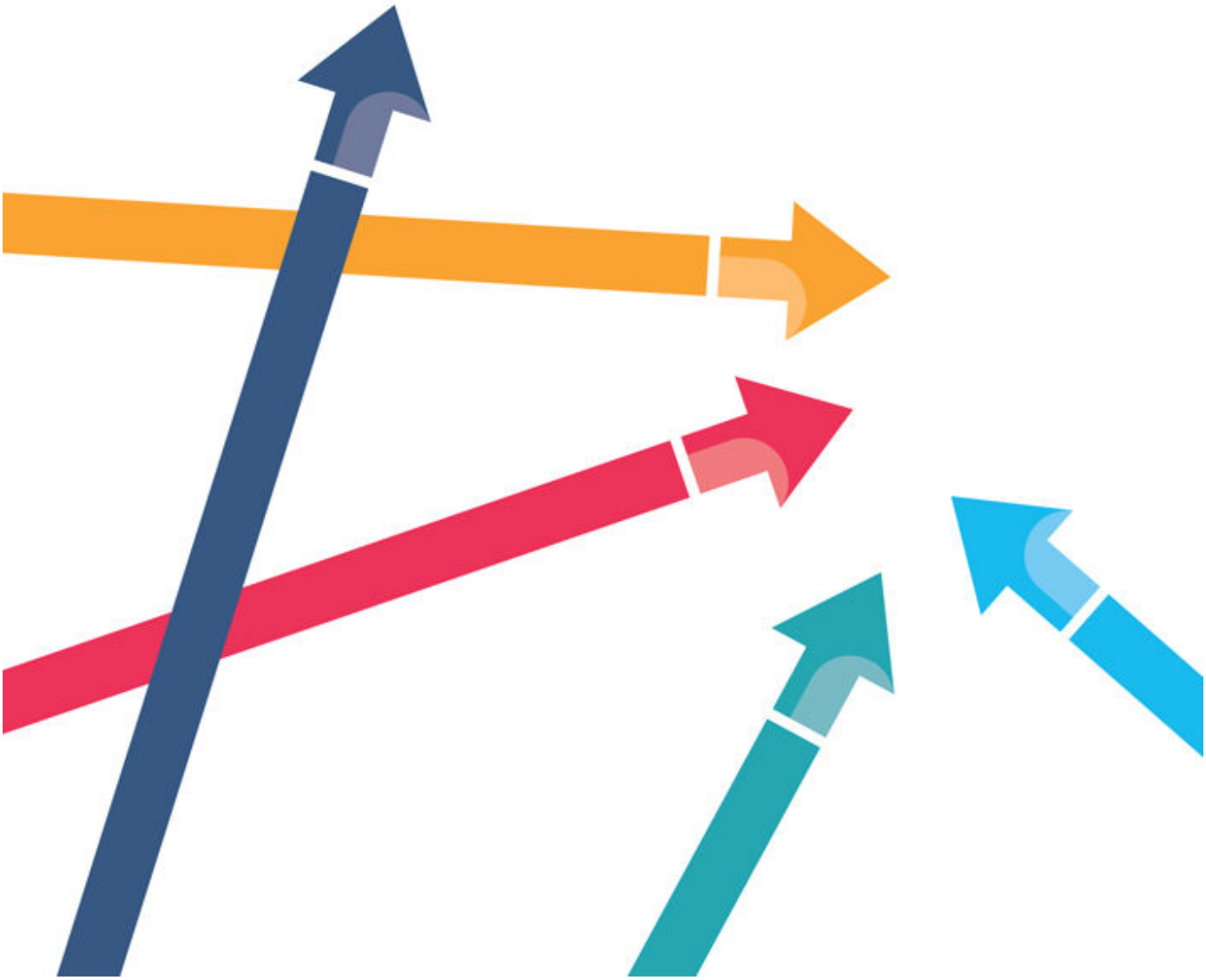
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3 CLINICAL REASONING IN A CASE OF POLYURIA/POLYDIPSIA



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3 CLINICAL REASONING IN A CASE OF POLYURIA/POLYDIPSIA

CLINICAL CASE
POLYURIA/POLYDIPSIA

***Z* is a 9-year-old, mixed-breed, sterilised female dog weighing 15 kg whose owners brought to the clinic due to a 3-month history of polyuria and polydipsia. She drank around 4 litres of water per day. They reported she had not manifested any other symptoms, her weight remained unchanged, and she ate normally. Physical examination did not reveal any alterations.**



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REASONING APPLIED TO THE CASE

Based on the available information, go through the first two steps of clinical reasoning:
1. Identify the animal's problems.
2. Prioritise the problems.





1. IDENTIFYING THE ANIMAL'S PROBLEMS

The patient has polyuria and polydipsia (PU/PD). These two problems are often hard to identify. A good anamnesis is important when it comes to distinguishing between polyuria, incontinence, nocturia, and increased urinary frequency. For example, many owners with a dog with increased urinary frequency will assume it produces more urine because it voids more often.

In this case, *Z* 's owners noted her daily water intake. This is a good method for determining if the animal has polydipsia. From previous experience, some owners know their vet often asks about the amount of water their pet drinks, so they have already estimated the volume. Measuring water intake during hospitalisation would give erroneous results, as many animals change their behaviour due to stress.

The normal water intake for dogs is, at most, 90 ml/kg/day and 45 ml/kg/day for cats.

In the case of *Z* , her water intake is much higher than normal, so we can conclude that both problems are present.

Alternatively, the presence of dilute urine is indicative of polyuria. Osmolality is the gold standard for measuring urine concentration, but it is not available in routine

clinical practice. Veterinarians normally measure urine specific gravity with a refractometer, as it generally correlates well with urine osmolality. More often than not, a urine specific gravity greater than 1.030 in dogs and 1.035 in cats is not indicative of polyuria, except in cases of marked glycosuria or intermittent polyuria (primary polydipsia or alterations in the regulation of antidiuretic hormone [ADH] secretion).

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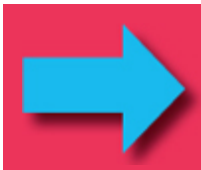


2. PRIORITISE THE PROBLEMS

Here, the patient's two problems are strongly interrelated: when receptors in the hypothalamus detect changes in plasma osmolality and blood volume, which control fluid balance, it alters both the regulation of thirst and urine output. Urine output is controlled by the secretion of ADH from the pituitary gland, which when released results in the insertion of channels in the renal tubules called aquaporins, hence water can move along these channels from the tubule lumen to the renal medulla where it is retained.

The only circumstances that can give rise to polydipsia without polyuria is when the animal loses water due to problems such as diarrhoea or excessive panting, rather than through its urine.

We know both problems are related, but we need to discover which is the primary issue.



KEY POINT

With the exception of primary polydipsia, polyuria is normally the main condition that leads to polydipsia. We can therefore focus on polyuria first.

Take these premises and proceed with the next two steps in the clinical reasoning procedure:

3. Structure and organise the animal's problem.

4. Individualise the diagnostic plan.



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3. STRUCTURING AND ORGANISING THE PROBLEM (DIFFERENTIAL DIAGNOSIS)

We have already explained the process that regulates fluid balance. With this in mind, we can define four mechanisms that can produce PU/PD (in some cases as a result of their combination).

CAUSAL MECHANISMS OF POLYURIA/POLYDIPSIA

1. **Insufficient ADH secretion**
   - Central diabetes insipidus (congenital or acquired).

2. **Insufficient ADH response**
   - Primary nephrogenic diabetes insipidus: congenital absence of ADH receptors.
   - Secondary nephrogenic diabetes insipidus: functional resistance to the effects of ADH in renal cells. Many of the causes of PU/PD are at least partly due to this mechanism, which can manifest throughout the course of various diseases and processes such as:
     - Hyperadrenocorticism
     - Hypoadrenocorticism
     - Hyperthyroidism
     - Hyperaldosteronism
     - Liver disease
     - Pyelonephritis
     - Pyometra/endotoxaemia caused by *Escherichia coli*
     - Hypokalaemia
     - Hypercalcaemia
     - Erythrocytosis
     - Leptospirosis
     - Acromegaly
     - Leiomyosarcoma
     - Medicines (glucocorticoids, phenobarbital, etc.)
3. **Osmotic diuresis**

- Particles excreted by the kidneys must be accompanied by water. When there is an excess of particles, it leads to polyuria. This mechanism occurs in processes such as:
  - Glycosuria: diabetes mellitus, primary renal glycosuria, Fanconi syndrome.
  - Postobstructive diuresis.
  - Iatrogenic causes: osmotic diuretics, sodium chloride.

4. **Primary polydipsia**
   - Psychogenic polydipsia.
   - This can develop in cases of hepatic encephalopathy, gastrointestinal disorders, and hyperthyroidism.

Besides classifying the diseases by action mechanisms, for everyday purposes, it may also help to know which is more typical in cats and dogs and therefore which condition is most likely to be affecting our patient (Table 1).



4. INDIVIDUALISE THE DIAGNOSTIC PLAN

What is the approach with such a patient?

As explained earlier, the first step when dealing with a patient manifesting polyuria and polydipsia is to confirm that the two problems are in fact present. In this case, although we shall later perform a complete urinalysis, we can assert that the patient has both problems because *Z* 's owners measured her daily water intake.

The next step consists of a complete anamnesis and physical exam. The animal's data will not provide a definitive diagnosis, but they will help us surmise the most likely differential diagnoses. For example, diabetes mellitus or pyometra are options in entire females that have recently been in oestrus, as are congenital diseases in young animals or hyperthyroidism in older cats. The breed can also provide clues: for instance, Basenjis are predisposed to Fanconi syndrome and Keeshonds and Norwegian Elkhounds are prone to primary renal glycosuria.

The clinical record can offer a lot of additional information. Besides verifying the presence of PU/PD, we should also try to discover if the patient presents clinical signs of lower urinary tract alterations, as urinary tract infections often appear alongside PU/PD. It is important to observe for any other clinical signs, since many of the diseases that cause PU/PD will also produce other manifestations that could help prioritise one differential diagnosis over another. As a case in point, if the patient also has polyphagia and weight loss, we can consider diabetes mellitus or hyperthyroidism. In this step we can also rule out the iatrogenic causes of PU/PD,

whether because the patient is being administered drugs such as diuretics, phenobarbital, or corticosteroids (which can also produce PU/PD when administered topically), or because of their diet such as those used to prevent urolithiasis which are supplemented with salt to dilute the urine.

The physical examination is extremely important as it helps prioritise the differential diagnoses. Cataracts can point to diabetes mellitus, jaundice is indicative of liver problems, or we might be able to palpate a swollen thyroid gland in the case of hyperthyroidism. The physical examination must be thorough; omitting a rectal palpation could mean we overlook an anal gland carcinoma that is causing hypercalcaemia and in turn PU/PD.

In *Z* 's case, the physical examination was completely normal, and her clinical record did not contain any information of use for the diagnosis, while diseases such as hyperadrenocorticism or diabetes would seem very unlikely.

Which diagnostic tests are required?

In this case a urinalysis is required. We should first measure the urine specific gravity. It helps to collect several urine samples on consecutive days at different times, particularly if primary polydipsia is suspected, as these patients tend to have concentrated urine intermittently. *Z* 's urine samples from three consecutive days had specific gravities of 1.003, 1.002, and 1.003. These values are considered hyposthenuric, that is, the specific gravity is lower than that of plasma. Our patient's specific gravity means we can rule out osmotic causes of polyuria or those related to kidney disease, since the observation of hyposthenuria means the distal renal tubules are absorbing solutes and therefore tubular function remains intact.

TABLE 1. Differential diagnosis of polyuria/polydipsia based on the probability of manifestation.

Species	Relevance	Causal processes
Dogs	Common causes	■ Chronic kidney disease ■ Pyometra ■ Diabetes mellitus ■ Hyperadrenocorticism ■ Hypercalcaemia ■ Pyelonephritis ■ Iatrogenic causes (drugs, diet, or fluid therapy)
	Uncommon causes	■ Liver disease ■ Hypoadrenocorticism ■ Primary polydipsia

	Rare causes	■ Central diabetes insipidus (CDI) ■ Primary nephrogenic diabetes insipidus (primary NDI) ■ Hyperviscosity syndrome ■ Primary glycosuria ■ Fanconi syndrome ■ Acromegaly ■ Hypokalaemia ■ Gastrointestinal disorders ■ Polycythaemia ■ Phaeochromocytoma ■ Primary hyperaldosteronism ■ Leiomyosarcoma ■ Sudden acquired retinal degeneration syndrome (SARDS)
Cats	Common causes	■ Chronic kidney disease ■ Hyperthyroidism ■ Diabetes mellitus ■ Postobstructive diuresis ■ Iatrogenic causes (drugs, diet, or fluid therapy)
	Uncommon causes	■ Liver disease ■ Pyometra ■ Pyelonephritis ■ Hypokalaemia (with kidney disease)
	Rare causes	■ Central diabetes insipidus ■ Hypercalcaemia ■ Acromegaly ■ Hyperadrenocorticism ■ Hypoadrenocorticism ■ Primary hyperaldosteronism

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KEY POINT

Urine is hyposthenuric in the case of central diabetes insipidus (CDI), primary nephrogenic diabetes insipidus (NDI), or primary polydipsia. Urine concentration in patients with secondary NDI is more variable and can be hyposthenuric, isosthenuric, or slightly concentrated.

Either way, a full urine analysis is required (which is totally normal in this case), as it can provide important clues such as the detection of glycosuria. Lower urinary tract infections are a very common complication in patients with PU/PD and a urine culture may be necessary to definitively rule them out. *Z* had normal urine sediment, but we cannot eliminate an infection because such a low urine specific gravity often results in false negatives as any cells or bacteria present in the sample would be highly diluted.

The diagnostic plan for *Z* also includes a blood test (blood count, blood chemistry with electrolytes), urine culture, and abdominal imaging tests such as ultrasound. An abdominal ultrasound should be carried out as routine practice in patients with PU/PD. It can often provide a definitive diagnosis, for example in the case of pyometra, splenic haemangiosarcoma, or intestinal leiomyosarcoma. Ultrasound can also help highlight any changes in the adrenal glands, liver, or kidneys.

Z 's results were (Tables 2 and 3):

- Urine culture: positive result for the presence of *Escherichia coli* . The patient was treated with an antibiotic taken from the antibiogram for its effectiveness against *E. coli* ; enrofloxacin at a dose of 5 mg/kg every 24 hours for 28 days.
- Blood tests: the parameters measured were all within normal ranges.
- Abdominal ultrasound: revealed bladder wall thickening consistent with cystitis (Fig. 1). The rest of the abdomen appeared to be within normal limits.

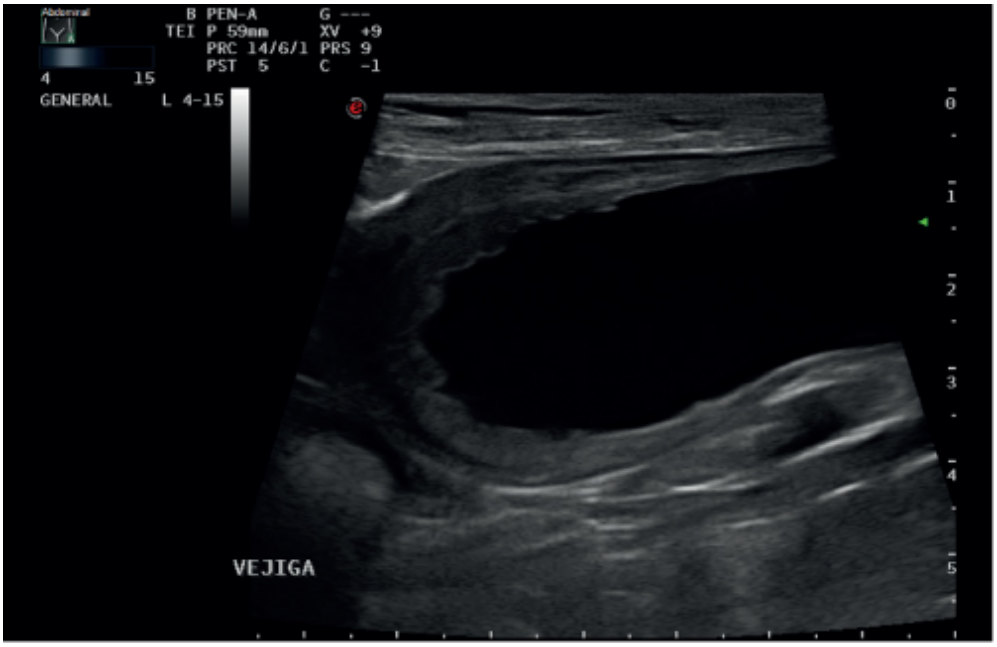


FIGURE 1. Abdominal ultrasound of the patient with evidence of bladder wall thickening.

5. ESTABLISH A DEFINITIVE DIAGNOSIS OR REASSESS THE DIFFERENTIAL DIAGNOSIS

Given there were no abnormal findings in the tests performed so far, and considering *Z* 's hyposthenuric urine sample, we can concentrate on CDI, primary NDI, and primary polydipsia. However, the first thing we should do is rule out hyperadrenocorticism. Some cases of pituitary-dependent hyperadrenocorticism secondary to macroadenoma cause compression of the posterior lobe of the pituitary gland, which may interrupt ADH secretion and trigger signs of CDI. The clinical signs of hyperadrenocorticism may not be evident from the outset, especially polyphagia, due to the behavioural change stimulated by the neoplasm.

Here, *Z* 's ultrasound did not reveal any changes in the adrenal glands. The adrenal glands in dogs with pituitary-dependent hyperadrenocorticism are characterised by symmetrical adrenomegaly and maintenance of a normal shape. These changes are not specific enough to rely on the use of ultrasound to rule out hyperadrenocorticism, as there is an overlap between normal and hyperplastic adrenal glands. Furthermore, ultrasound is a highly operator-dependent test. So, in this case it would be interesting, given the patient's age and the above information, to conduct a hormone test to exclude hyperadrenocorticism. To this end, we chose the low-dose dexamethasone suppression test over the ACTH stimulation test because it identifies 90–95 % of cases of pituitary-dependent hyperadrenocorticism compared to 85 % for the latter test.

The test results were normal (Table 4), as suppression was detected, so we could rule out hyperadrenocorticism. Therefore, the next step is to distinguish between CDI, primary NDI, and primary polydipsia. This requires a test to assess the patient's urine concentrating ability. Vets have traditionally used the water deprivation test, which involves denying supervised patients access to water and monitoring any changes in their urine specific gravity to determine if they can concentrate urine when required. The problem with this test is the risk of severe hypertonic dehydration, which is why the desmopressin (synthetic ADH) response test was developed. An animal with CDI will respond to the administration of exogenous ADH, as their problem relates to the lack of endogenous production, evidenced by an increase in their urine specific gravity. Dogs with hyperadrenocorticism can also respond to this test, as one of the mechanisms of polyuria in this disease is insufficient ADH production in response to an osmotic stimulus, so their urine becomes more concentrated after administering ADH. The difference lies in the fact that patients with hyperadrenocorticism no longer respond following several weeks of treatment.

A minimal improvement in urine specific gravity can be noted in patients with NDI; although the receptors do not work correctly, there is a lot more ADH available. A slight improvement may also be evident in cases of primary polydipsia, since a chronically low plasma osmolality tends to reduce endogenous ADH production.

For *Z* , the test was conducted with desmopressin acetate eyedrops, administering one drop in each eye twice a day for a week. We asked the owners to record her daily water intake.

KEY POINT

The effects of desmopressin administration should not be assessed in the first 5–7 days, as medullary solute washout can mean that animals with CDI do not concentrate urine for the first few days. Urine specific gravity should be measured after 7 days of treatment – an increase of 50 % or more supports the diagnosis of CDI, especially if it is greater than 1.030.

In this case, the owners noted a drop in PU/PD. On days 5, 6, and 7, the urine specific gravity was 1.028, 1.025, and 1.032, respectively, and the owners said they observed a significant improvement in *Z* 's symptoms and her water intake had diminished considerably.

The UTI detected could be secondary to the marked polyuria. UTIs rarely cause such a large reduction in urine specific gravity as the one observed in this case. The desmopressin response test was carried out several days after antibiotic treatment, which did not bring about any improvement in the animal's PU/PD.

FINAL TREATMENT PLAN AND EVOLUTION

Having reached this point, CDI was diagnosed, the patient was indicated to follow the same treatment, and a 1-month follow-up visit recommended to definitively rule out the possibility of undiagnosed hyperadrenocorticism (bearing in mind that the low-dose dexamethasone suppression test detects just 90–95 % of cases). After 1 month, *Z* had a urine specific gravity of 1.030 and normal water intake. We can therefore conclude that the patient has central diabetes insipidus.

The causes of central diabetes insipidus are:

- Idiopathic: this is the most common cause and it can develop at any age.
- Trauma: tends to be temporary and generally abates within 1–3 weeks.
- Anatomical: anatomical alterations in the pituitary gland, whether due to neoplasms, malformations, cysts, inflammation, parasites, and so on, although such cases are usually accompanied by behavioural changes or neurological clinical signs.

With respect to the present patient, an MRI scan would provide more detail about the problem, but as *Z* did not present any other neurological clinical signs, her owners decided against a scan, preferring to continue with the treatment and periodic check-ups.

TABLE 2. Blood count results.

Parameter	Value	Reference range
Erythrocytes (× 10^6 /µl)	8	5.5–8.5
Haemoglobin (g/dl)	17	12–18
Haematocrit (%)	50	37–55
MCV (fl)	62.5	62–77
MCHC (g/dl)	34	33–47
MCH (pg)	21.5	21.5–26.5
White blood cells (cells/µl)	7,500	6,000–17,000
Lymphocytes (cells/µl)	1,200	1,000–4,800
Monocytes (cells/µl)	250	150–1,350
Segmented neutrophils (cells/µl)	5,950	3,000–11,500
Band neutrophils (cells/µl)	0	0–300
Eosinophils (cells/µl)	100	100–1,500

Basophils (cells/µl)	0	0–200
Platelets (× 10^3/µl)	350	200–500
Reticulocytes (cells/µl)	**78,000**	0–60,000

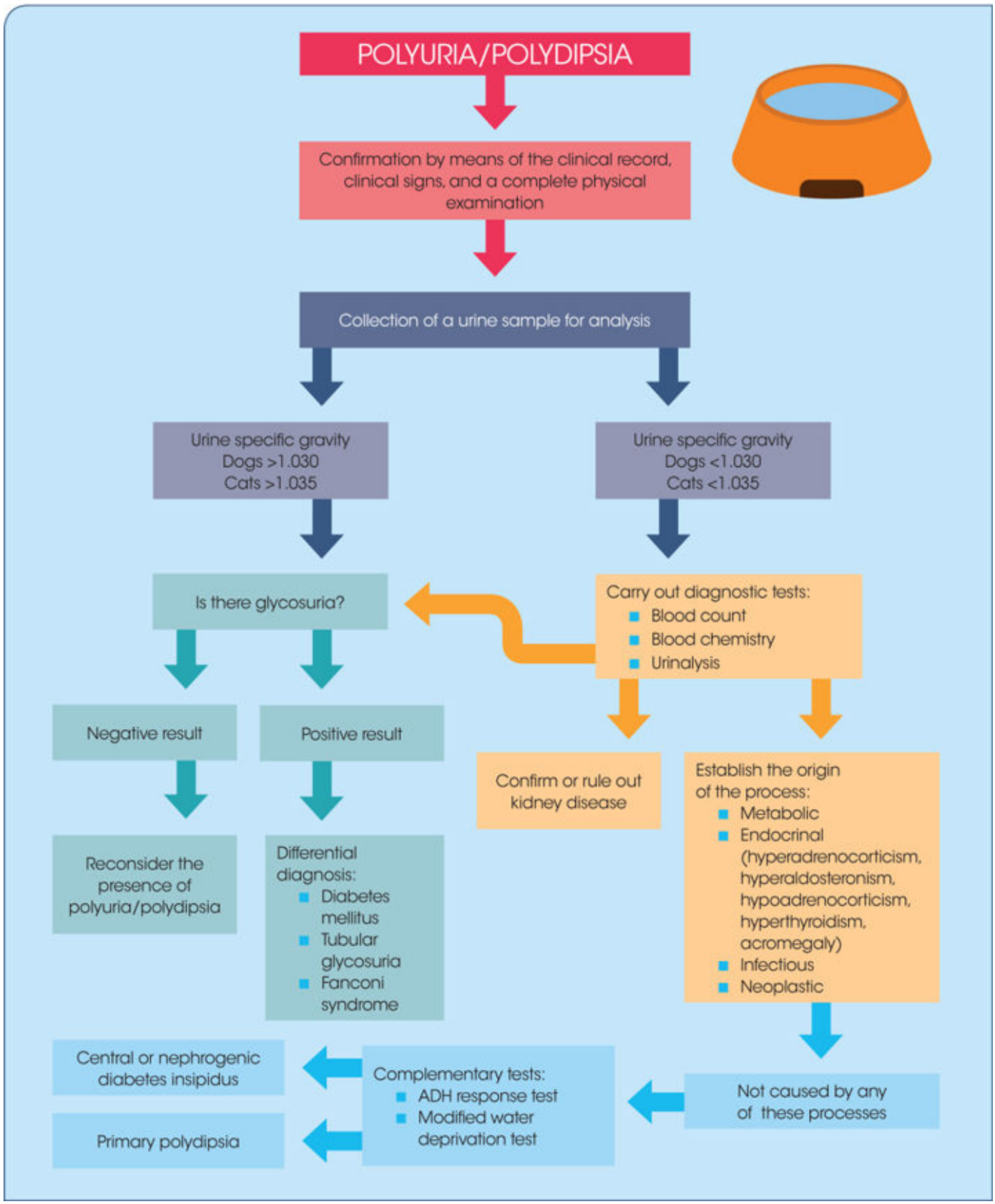
TABLE 3. Blood chemistry results.

Parameter	Value	Reference range
Creatinine (mg/dl)	1.2	0.5–1.5
Urea (mg/dl)	24	21.4–60.0
Cholesterol (mg/dl)	210	135–270
Glucose (mg/dl)	110	65–118
Total protein (g/dl)	6.5	6–8
Total bilirubin (mg/dl)	0.3	0.1–0.5
Alkaline phosphatase (IU/l)	150	20–156
GGT (IU/l)	5	1.2–6.4
ALT (IU/l)	85	21–102
CK-NAC (IU/l)	**160**	10–150
Calcium (mg/dl)	10	9.0–11.3
Phosphorus (mg/dl)	5.6	2.6–6.2
Potassium (mmol/l)	4.3	4.3–5.6
Sodium (mmol/l)	143	141–152
Chloride (mmol/l)	108	105–115

TABLE 4. Results of the low-dose dexamethasone suppression test.

Parameter	Value	Reference range
Basal cortisol (µg/dl)	5.5	0.5–6.0
Cortisol after dexamethasone administration (4 hours) (µg/dl)	<0.1	-
Cortisol after dexamethasone administration (8 hours) (µg/dl)	<0.1	-

DIAGNOSTIC ALGORITHM FOR POLYURIA/POLYDIPSIA



BRIEF REVIEW OF…

CENTRAL DIABETES INSIPIDUS (CDI)

WHAT IS CENTRAL DIABETES INSIPIDUS?

Central diabetes insipidus (CDI) is caused by the partial or complete absence of vasopressin (ADH or antidiuretic hormone). Animals with CDI have a low urine specific gravity, 1.008–1.020, and in the case of a total deficiency it can cause hyposthenuria with or without clinical signs of systemic dehydration and a urine specific gravity of less than 1.006.

Vasopressin is synthesised in the supraoptic and paraventricular nuclei of the hypothalamus, then it is stored in the posterior lobe of the pituitary gland. An increase in serum osmolality or decrease in blood volume stimulates the release of vasopressin into the bloodstream, so it may open water channels (aquaporins) in the apical membrane of the renal collecting ducts and prompt the reabsorption of water within the medullary interstitium.

WHAT CAUSES CENTRAL DIABETES INSIPIDUS?

CDI can be congenital or acquired. Congenital cases are uncommon, but they can be observed in patients with a hypothalamus or pituitary gland malformation. Acquired causes are usually secondary to cranial trauma, local infections, vascular accidents with ischaemia, pituitary gland surgery, neoplasms (lymphoma, infundibuloma, pituitary adenoma or carcinoma, meningioma), or of spontaneous, idiopathic origin.

CDI generally develops in isolation, but it is occasionally associated with panhypopituitarism, hypothyroidism, hyperadrenocorticism, and acromegaly.

WHICH CLINICAL SIGNS WARN ABOUT THIS PROCESS?

The clinical signs are predominantly polyuria/polydipsia, possibly accompanied by anorexia and weight loss, and result from the patient's inability to concentrate urine

(Fig. 1). If the CDI is caused by a pituitary neoplasm, clinical signs could include central nervous system compromise (disorientation, proprioceptive deficit, ataxia, tremors, convulsions) and behavioural changes.

No breeds or sexes are predisposed to CDI, but neoplasms tend to affect elderly animals.

Animals with central diabetes insipidus produce more than 50 ml/kg/day of urine and drink over 100 ml/kg/day of water.



FIGURE 1. Water intake increases to compensate for the inability to concentrate urine (Thka, Shutterstock.com).

WHAT ARE THE COMMON LABORATORY FINDINGS?

Some animals manifest dehydration or polycythaemia with hypernatraemia and isosthenuric or hyposthenuric urine. Nevertheless, blood chemistry tests generally reveal values within normal ranges, although there is sometimes evidence of prerenal azotaemia.

WHICH DIAGNOSTIC TESTS CAN BE USED TO CONFIRM A SUSPICION OF CDI?

The first step is to rule out other causes of polyuria/polydipsia, but animals with CDI often return negative urine cultures, normal results in the ACTH stimulation and low-dose dexamethasone suppression tests, normal levels of thyroid hormones (T_4 and TSH) and pre- and postprandial bile acids, and a normal abdominal ultrasound. However, some patients may manifest various pituitary gland alterations, which should always be taken into account.

The following diagnostic tests should be used whenever CDI is suspected.

MODIFIED WATER DEPRIVATION TEST

This test consists of reducing water intake to 60–80 ml/kg/day for 3–4 days. The animal is then deprived of water and its urine specific gravity measured in regular bladder voids until the specific gravity is greater than 1.030. If the animal develops dehydration, azotaemia, or falls ill, the test should be discontinued. This usually takes between 3 and 10 hours.

As for the results:

- If the specific gravity at the end of the test is <1.008, the result is compatible with CDI.
- If it is 1.010–1.020, it could be due to a partial deficiency or nephrogenic diabetes insipidus.
- If the value is >1.025, this is indicative of psychogenic polydipsia.

Due to the risks associated with the test, it is no longer recommended.

DESMOPRESSIN RESPONSE TEST

This test involves less risk for the animal and is currently the preferred option. It is conducted once the differential diagnosis has been reduced to central/nephrogenic diabetes insipidus or psychogenic polydipsia. This time the animal is given free access to water, their 24-hour intake is calculated by taking the average value over 2–3 days, and a urine sample is collected at the same time each day to determine the specific gravity. The patient is then administered desmopressin: 4 drops or 0.1 ml intranasally or as eyedrops, or 0.1 mg orally, every 12 hours for 5–7 days. The owners must calculate the animal's daily water intake and collect a urine sample at the same time each day, so the clinic can subsequently measure the urine specific gravity and osmolality, if possible.

The test results are interpreted as follows:

- If the reduction in water intake is greater than 50 %, the results are compatible with CDI.
- Animals with psychogenic polydipsia will present a partial improvement.
- Animals with nephrogenic diabetes insipidus do not usually respond favourably to the test.

If there is a suspicion of a neoplasm, a metastasis affecting the central nervous system, or a vascular accident, then this is an indication for advanced tests such as magnetic resonance imaging.

WHAT TREATMENT OPTIONS ARE AVAILABLE?

Treatment is not necessarily compulsory; if the owners can tolerate the clinical signs, patients can follow a normal life so long as they have unrestricted access to water and do not suffer from dehydration.

The most used treatments are desmopressin administered intranasally or as eye drops: 2–4 drops of solution (100 µg/ml) every 12–24 hours (Fig. 2). If the patient will not tolerate nasal or ocular administration due to irritation, other options are vaginal or preputial routes. Desmopressin can also be administered orally (0.1–0.2 mg tablets): 0.1 mg, PO, every 8–12 hours; or parenterally: 0.5–2 µg, SC, every 12–24 hours.

Other support treatments include thiazide diuretics or low-salt diets. Diuretics can increase urine osmolality and produce a proportional reduction in urine volume. Chlorothiazide has been administered, at an oral dose of 10–40 mg/kg every 12 hours, in conjunction with a low-salt diet. A low-salt diet diminishes urine production, since it increases the volume of filtrate reabsorbed by the kidneys.

WHAT'S THE CORRECT FOLLOW-UP FOR AN ANIMAL WITH CDI?

Having started treatment, it is important to control the clinical signs of overhydration and hyponatraemia. If signs of hyponatraemia develop, desmopressin treatment should be discontinued until the sodium concentration recovers, then restarted at a lower dose. If the owner calculates the animal's water intake, it will help the vet establish a more suitable desmopressin treatment regimen.

The prognosis for CDI is generally good, although it depends on the cause. Animals with pituitary neoplasms tend to deteriorate and have a shorter survival

time than those with idiopathic or vascular CDI.



FIGURE 2. If the patient tolerates it well, the treatment can be administered in the conjunctivae (Rodimov, Shutterstock.com).

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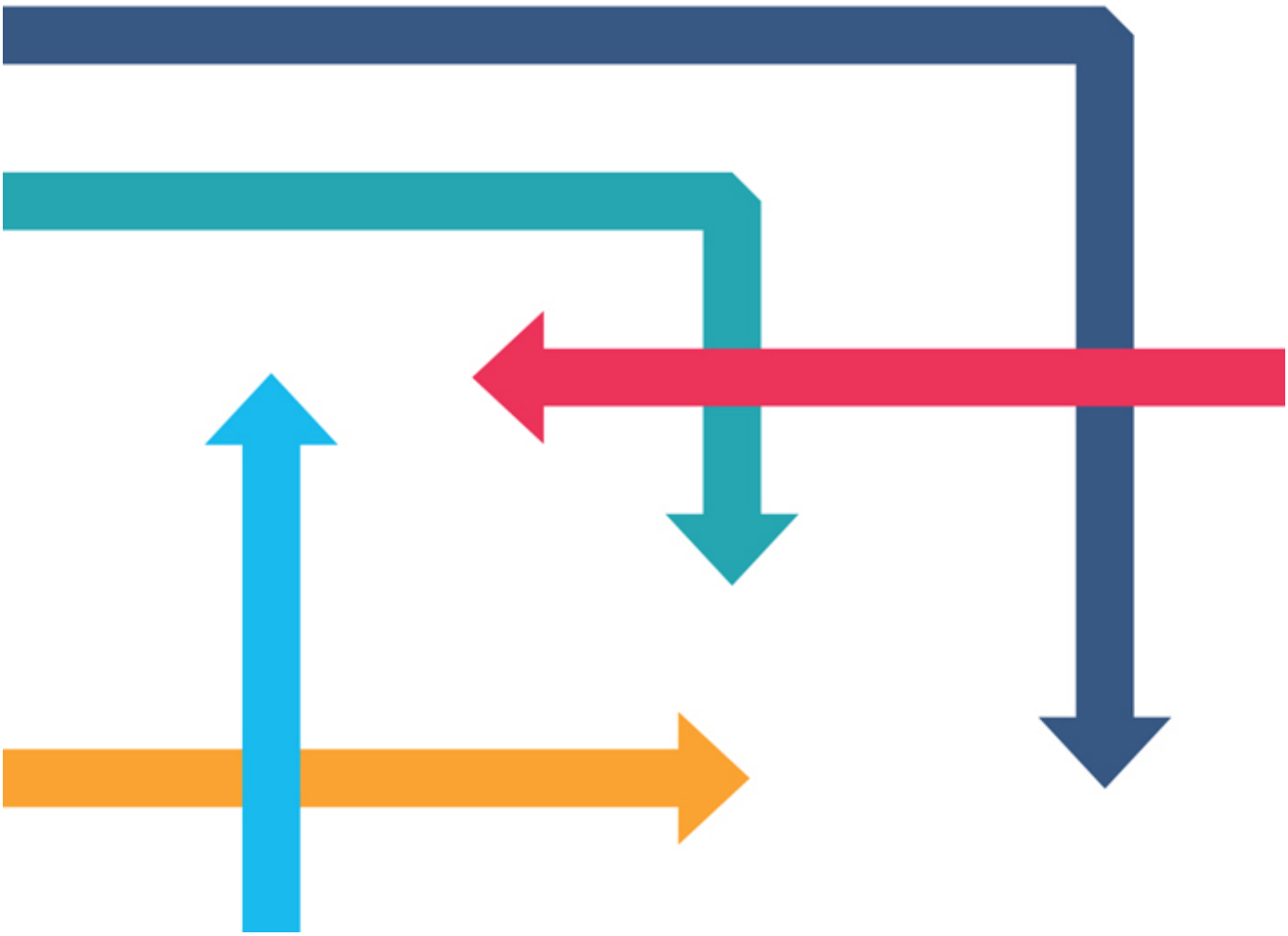
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4 CLINICAL REASONING IN A CASE OF URINARY DISORDER



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4 CLINICAL REASONING IN A CASE OF URINARY DISORDER

CLINICAL CASE
URINARY DISORDER

***X* is a 10-year-old, entire male Spanish Water Dog, brought to our clinic with a 3-day history of haematuria. The patient had suffered from urinary incontinence since the age of 5, along with recurrent episodes, approximately every 4 months, of reddish urine throughout the entire voiding, neither of which had ever been treated. He was not currently taking any medication, had never suffered any trauma, and had no known diseases. The physical examination did not reveal any alterations, although the prostate gland seemed large when palpated. A full neurological examination did not indicate any apparent lesions or deficits. Laboratory tests were performed at the patient's habitual veterinary clinic with normal results.**



Eric Isselee/Shutterstock.com

REASONING APPLIED TO THE CASE

Based on the available information, go through the first two steps of clinical reasoning:

1. **Identify the animal's problems.**
2. **Prioritise the problems.**

1. IDENTIFYING THE ANIMAL'S PROBLEMS

The patient has chronic urinary incontinence, reddish urine, and an enlarged prostate.

2. PRIORITISE THE PROBLEMS

In *X* 's case, the reddish urine could be due to the chronic urinary incontinence, since the owner reported during anamnesis that everything started with the incontinence at the age of 5 and the discoloured urine came later, although the colour change was not permanent.

The physical exam did not yield evidence of any systemic alterations related to haemorrhages (epistaxis, haematochezia, haematemesis) or red blood cell destruction (pale mucous membranes); nor was there a background of any physical activity to suggest myoglobinuria, hence the reddish colour in the urine appears to be caused by or related to the incontinence. While the three problems seem to be related, the causes of the incontinence and reddish urine are unclear at this point in the diagnostic process and one option would be to study these two issues together. The enlarged prostate seems to be an age-related finding and should be assessed separately, although it may be connected to the other two problems.

Take these premises and proceed with the next two steps in the clinical reasoning procedure:
3. Structure and organise the animal's problem.
4. Individualise the diagnostic plan.

3. STRUCTURING AND ORGANISING THE PROBLEM (DIFFERENTIAL DIAGNOSIS)

If we focus on the incontinence, it is a good idea to review the anatomy of the urinary system. From a simplified anatomical and physiological approach, we should consider the following: the upper urinary tract, with the kidneys (where urine is produced) and ureters (transfer urine to the bladder), and the lower urinary tract,

comprising the bladder (which stores urine at a low pressure and voids it a high pressure) and the urethra (including a valve that helps expel urine from the body).

A good clinical record, a physical examination, and a complete neurological exam are essential to help discover the cause of the incontinence.

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KEY POINT

We must remember that the objective is to pinpoint the problem to a specific anatomical region of the urinary tract.

The following questions should always be used in order to identify the causes of the condition.

QUESTIONS TO ASK THE OWNER OR WHICH THE VET SHOULD ADDRESS WHEN DEALING WITH AN ANIMAL WITH INCONTINENCE

- **In the clinical record and when observing the problem:**
  - Can the animal urinate normally? Does the urine flow normally?
  - Is the patient always incontinent or only when lying down or asleep? (If incontinence occurs while asleep, it is almost always because there is a large volume of urine in the bladder.)
  - Are the problems associated with a full or empty bladder? Or is there no relation?
  - Is the volume of urine output normal or greater than usual?
- **In the physical examination:**
  - Does the patient have a small or large bladder?
  - Does the bladder feel soft or tense when palpated?
  - After voiding, does the bladder feel empty or full?
  - Does (external and rectal) palpation of the urethra reveal any abnormalities? (It is important to palpate the prostate in males and perform a vaginal examination in females.)
  - Is the complete neurological examination normal?
  - Is it hard to compress and empty the bladder while the animal is awake?

From the information obtained, we can perform a differential diagnosis based on whether the bladder is large and distended or normal and empty or full. A distended bladder is usually due to a problem affecting the detrusor muscle or the urethra (Table 1).

With respect to the reddish urine, it is most likely due to haematuria, which must be confirmed through a urinalysis to detect the presence of red blood cells rather than pigment. Pinpointing the anatomical location of the problem is probably the first step to determine the cause, so we can consider a differential diagnosis like the one summarised in Table 2 . It also helps to know when haematuria occurs: haematuria at the end of urination is associated with kidney or ureteral problems, at the beginning with urethral problems, and blood throughout the entire voiding period is related to an issue located in the bladder.

TABLE 1. Differential diagnosis of urinary incontinence.

Appearance of the bladder	Cause	Causal processes
Distended bladder	Detrusor atony	■ Bladder overdistension ■ Dysautonomia ■ Lower or upper motor neuron lesion ■ Neoplastic/inflammatory infiltration of the bladder wall
	Functional obstruction	■ Reflex dyssynergia ■ Urethral inflammation ■ Urethral pain ■ Upper motor neuron lesion
	Partial obstruction	■ Urethritis ■ Neoplasm ■ Prostate conditions ■ Perineal hernia ■ Urolithiasis ■ Stenosis
Normal or small bladder	Bladder hypocontractility	■ Chronic partial obstruction ■ Inflammation ■ Neoplasm ■ Detrusor hyperreflexia
	Reduced bladder distension	■ Hypoplasia ■ Neoplasm
	Urethral sphincter incompetence	■ Congenital ■ Hormonal

		■ Prostate condition ■ Urethral inflammation ■ Neoplasm ■ Urinary tract infection
	Miscellaneous	■ Ectopic ureter ■ Secondary to polyuria ■ Polydipsia ■ Urolithiasis ■ Ureterocele

TABLE 2. Differential diagnosis of haematuria.

Origin/location	Causes or causal processes
Pseudohaematuria	■ Bilirubinuria ■ Haemoglobinuria ■ Myoglobinuria ■ Pigments (from blackberries, beetroot, drugs)
Extraurinary	■ Coagulopathies ■ Heatstroke ■ Thrombocytopaenia ■ Thrombocytopathy
Kidneys	■ Cysts ■ Glomerulonephritis ■ Pyelonephritis ■ Idiopathic ■ Neoplasm ■ Urolithiasis ■ Trauma
Ureters, bladder, or urethrae	■ Inflammation ■ Neoplasm ■ Polyps ■ Urolithiasis ■ Trauma
Prostate	■ Abscess ■ Hyperplasia

	■ Cysts ■ Neoplasm ■ Inflammation/infection
Uterus or vagina	■ Metritis ■ Pyometra ■ Neoplasm ■ Trauma
Penis	■ Neoplasm ■ Inflammation ■ Trauma

An enlarged prostate gland may be due to a range of causes, but the first point to address is whether the lesion is local, asymmetrical or symmetrical, or diffuse throughout the prostate. If the lesion is localised, the differential diagnosis should consider abscesses, cysts (prostatic and paraprostatic), and neoplasms. If the megaly is diffuse, it should include infections (prostatitis), hyperplasia, or neoplasms.



4. INDIVIDUALISE THE DIAGNOSTIC PLAN

In *X* 's case, there was no evidence of an overdistended bladder during the physical examination. Given the long-term nature of the incontinence in a male dog, if it were a prostate-related problem, it would be very unusual that it had not evolved in 5 years. The fact that the haematuria does not occur at the beginning of urination and the absence of any bloody drops unrelated to urination also imply there could be a different cause.

In patients with a normal/small bladder, we should consider two main anatomical causes:
1. Increase in detrusor contractility.
2. Decrease in the resistance to outflow.

The cases corresponding to the first group are associated with inflammation of the bladder or urethra that creates the urgency to urinate. These patients usually have other urinary signs (stranguria, increased urinary frequency, or dysuria) and urinalysis abnormalities.

On the other hand, in patients with reduced outflow resistance, the loss of urine is more pronounced when the animal is relaxed or asleep, and it is not usually accompanied by any other urinary alterations, unless there is a secondary ascending urinary tract infection.

Congenital alterations are more common in young and small-to-medium animals, manifesting as a constant loss of urine.

Given the above, we can arrange the possible causes for our patient into three functional groups and they will include incontinence and possibly haematuria:

- Detrusor hyperreflexia or instability:
  - Bladder inflammation
  - Urethral inflammation
  - Primary or idiopathic origin
- Urethral sphincter mechanism incompetence:
  - Abnormal bladder/urethra position (e.g. pelvic bladder, reduced response to α-adrenergic receptors, or obesity).
  - Hormonal origin – not very likely as the animal has not been castrated, but we should always include prostate-related problems.
- Congenital/acquired incontinence:
  - Ectopic ureter
  - Ureterocele
  - Intrapelvic bladder

The prostate has enlarged symmetrically and homogeneously, so we should consider hyperplasia, a neoplasm, or prostatitis.

To progress with the diagnosis, it would be recommendable to perform a urinalysis with bacterial culture, a blood count, and a general blood chemistry test to rule out systemic alterations or anything that could cause the reddish urine and, above all, diagnostic imaging tests to distinguish whether the origin is anatomical or functional and to assess the prostate.

The results of the blood count and blood chemistry were normal. Table 3 shows the results observed in the urine analysis.

TABLE 3. Urinalysis results (cystocentesis).

Parameter	Value
Specific gravity	1.020
pH	8
Proteins	3+
Blood	3+
Sediment	Presence of abundant red blood cells, neutrophils, and bacteria, and some struvite crystals.

Urine culture	Presence of *Escherichia coli* susceptible to the antibiotics studied.

The most relevant findings in the abdominal ultrasound were:

- Right kidney: severe hydroureter and hydronephrosis without any stones in the lumen (Figs. 1 and 2).
- Right extramural ectopic ureter, which possibly terminates in the proximal region of the prostate.
- Prostatomegaly with multiple mineralisations and cystic structures. Compatible with chronic, neoplastic prostatitis (Fig. 3).
- Two cystic structures in the caudal abdomen compatible with paraprostatic cysts (Fig. 4).
- A few bladder stones, measuring around 3 mm in diameter.

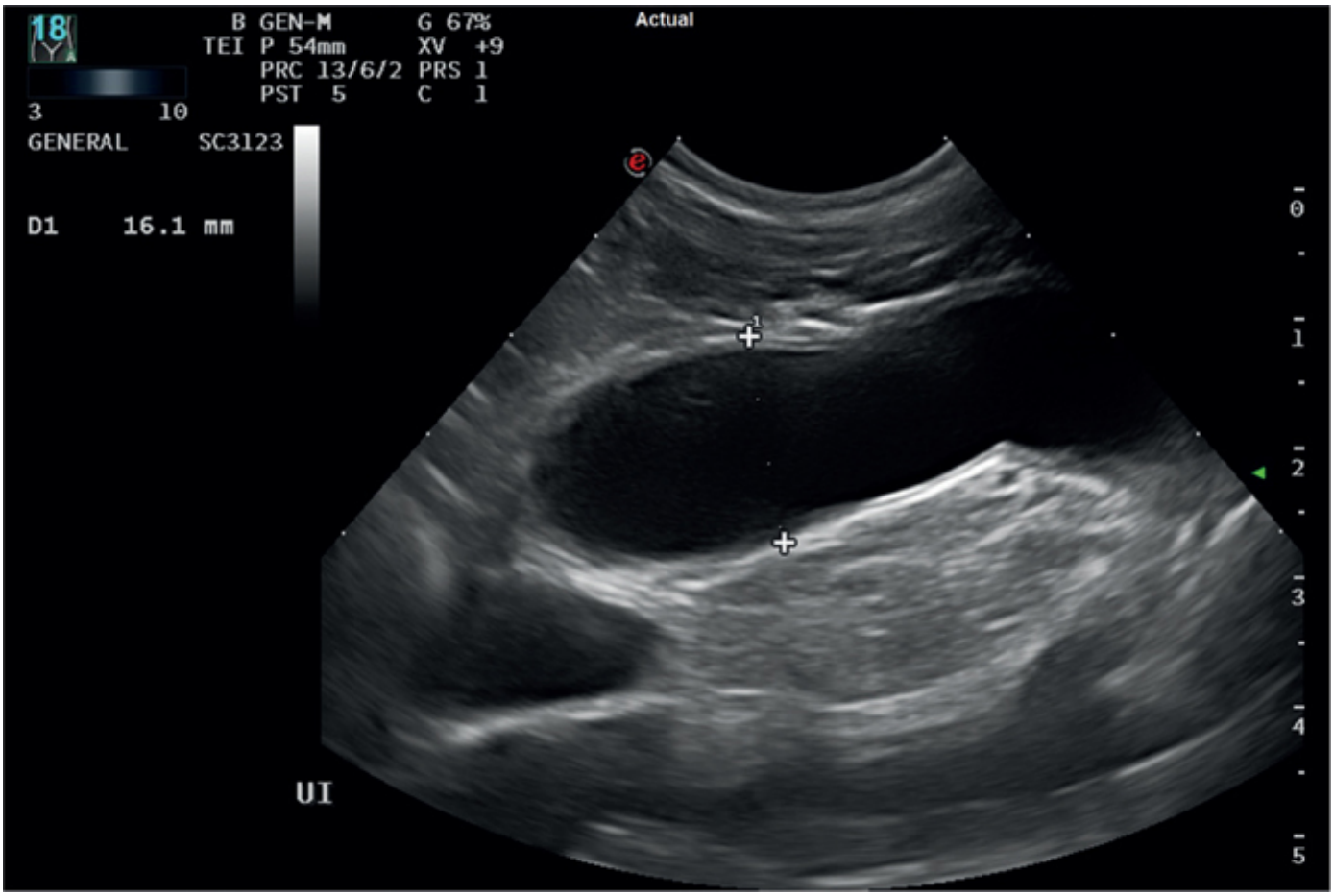


FIGURE 1. Abdominal ultrasound showing signs of hydroureter.

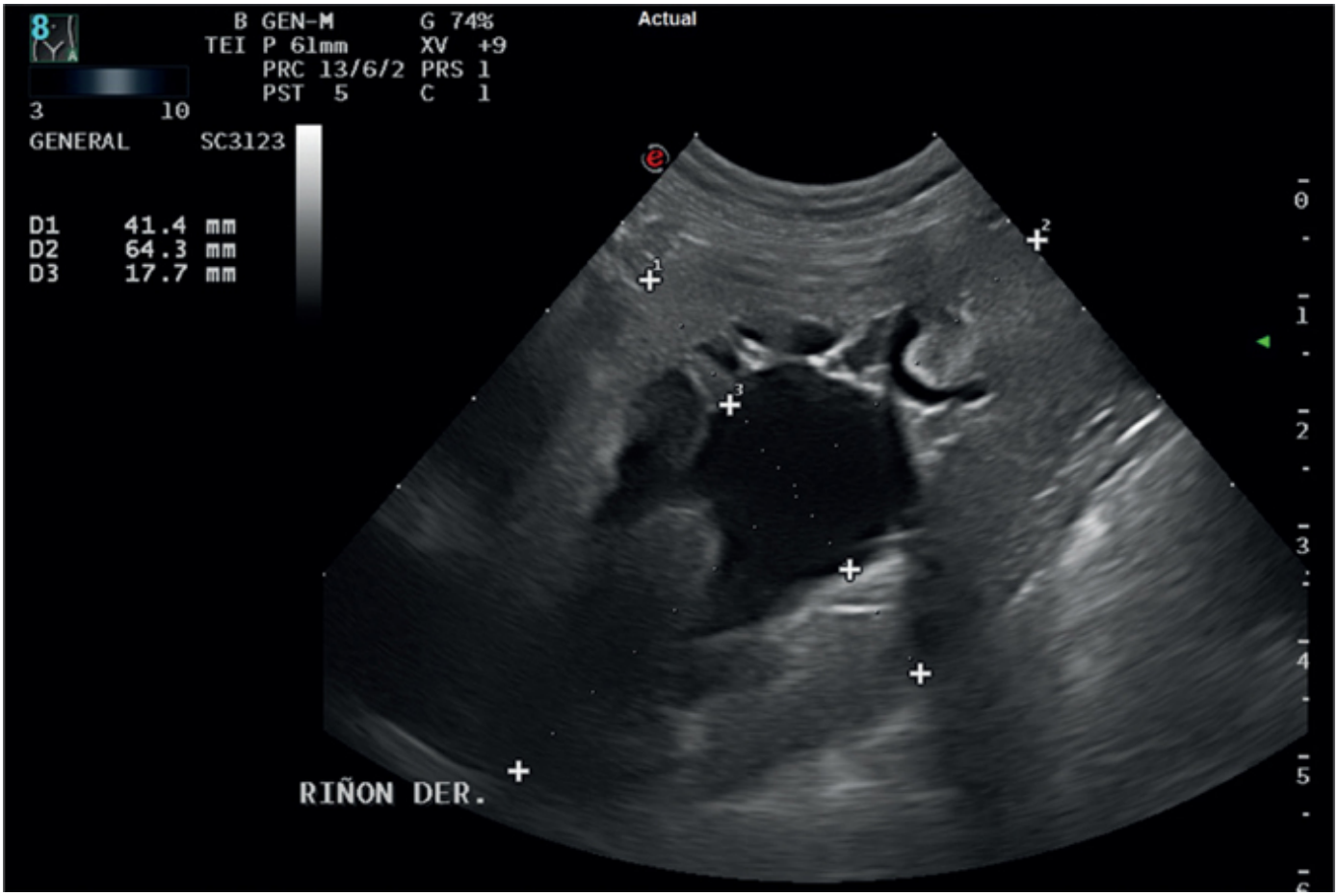


FIGURE 2. Abdominal ultrasound evidencing hydronephrosis in the right kidney.

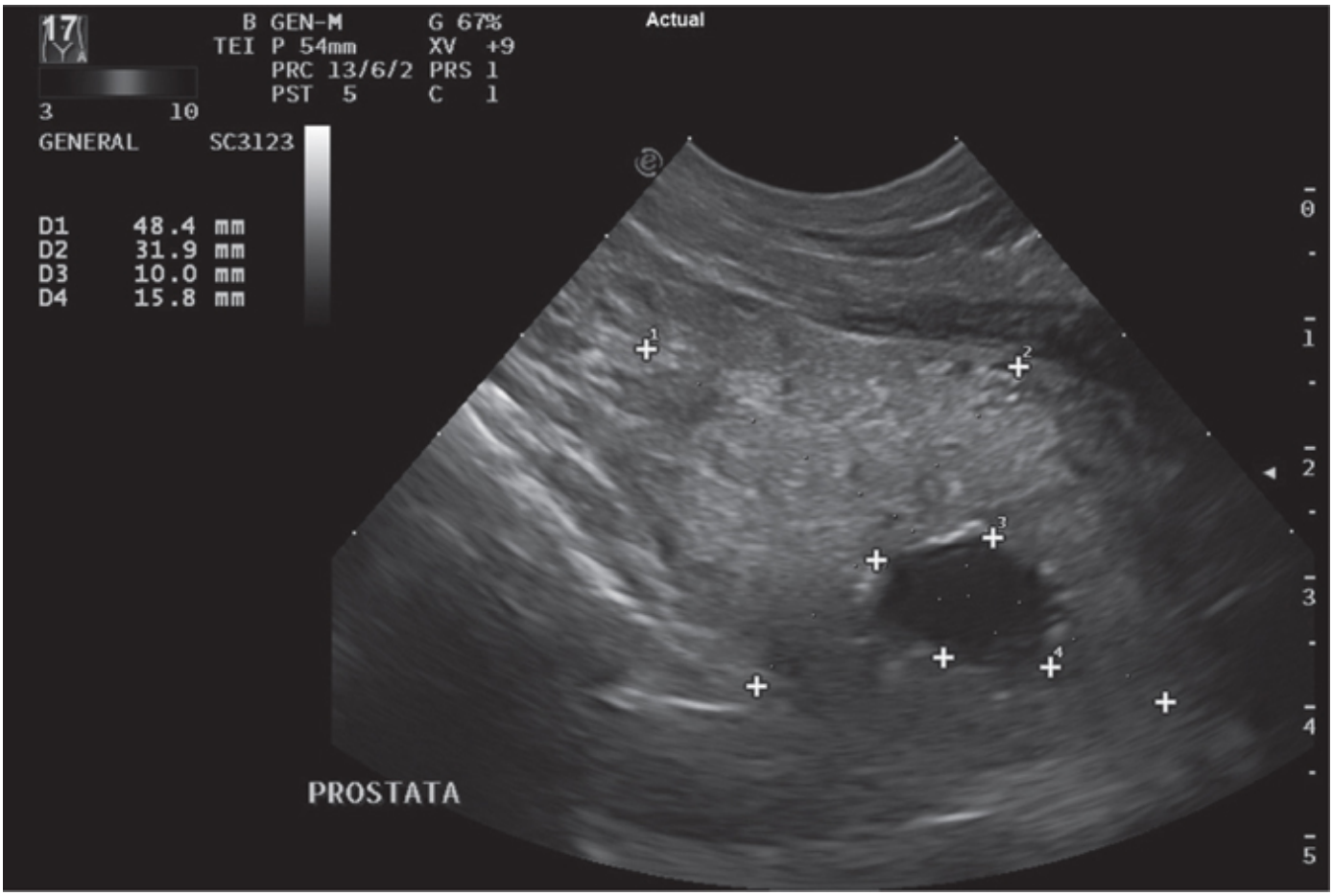


FIGURE 3. Ultrasound revealing an enlarged prostate with a central cystic area.

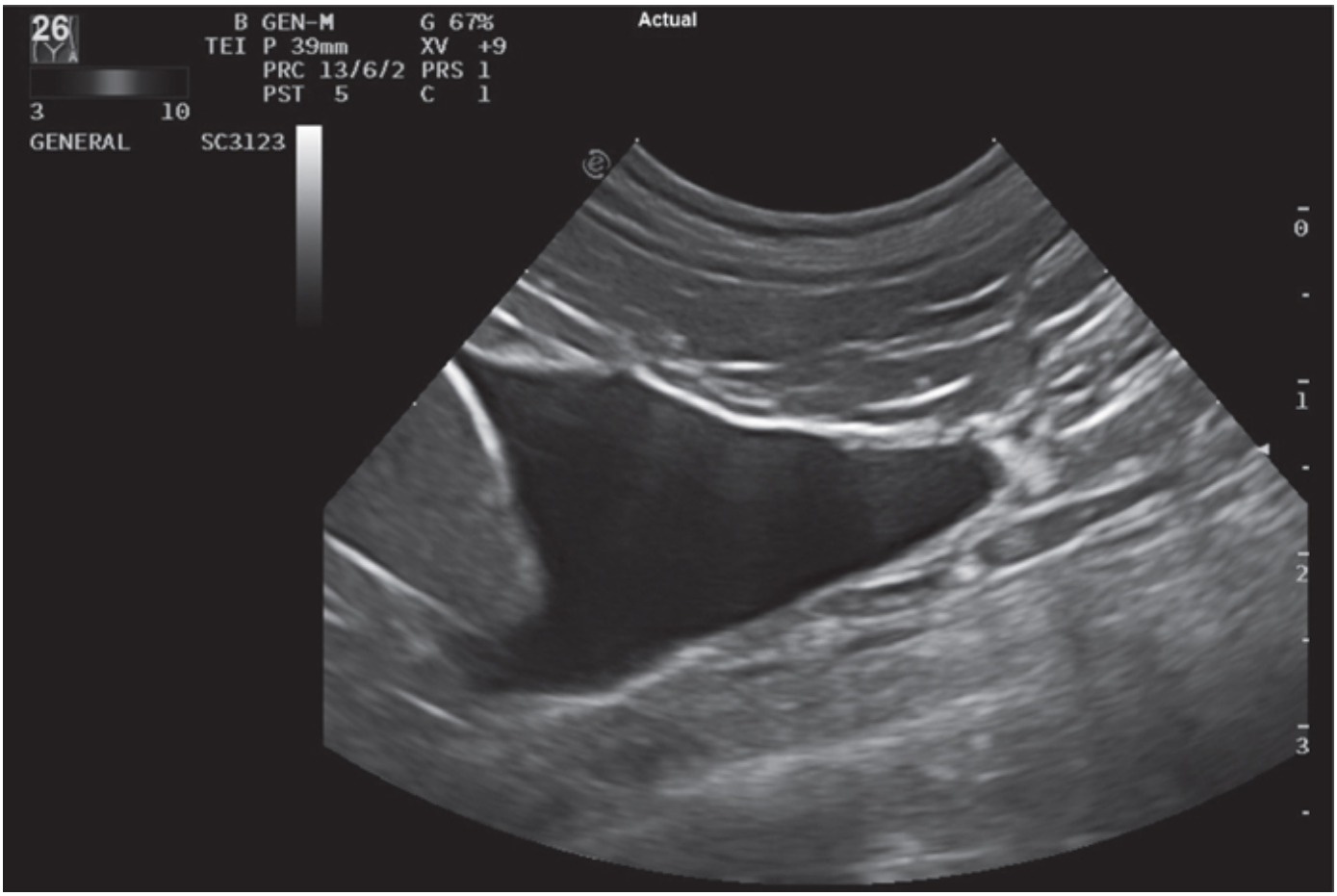


FIGURE 4. A cyst with hypoechoic content, compatible with paraprostatic cysts.

5. ESTABLISH A DEFINITIVE DIAGNOSIS OR REASSESS THE DIFFERENTIAL DIAGNOSIS

The patient's updated list of problems is:

- Confirmed haematuria
- Bacterial urinary tract infection
- Urolithiasis
- Enlarged prostate with possible paraprostatic cysts
- Hydronephrosis and hydroureter
- Ectopic ureter

Although at this age ectopic ureter is not the main suspicion, it should not be eliminated from the differential diagnosis because it explains *X* 's long-term clinical signs; the incontinence would be justified by this finding. Other changes derive from

the patient's age (enlarged prostate) or are inherent to the incontinence such as the urinary tract infection and urinary stones, which are possibly associated with the infection, as the urine pH and the crystals are indicative of struvite stones. A computed tomography (CT) scan would be a useful complementary test to confirm the diagnosis and to assess the need for surgery.

The enlarged prostate gland could be due to hyperplasia, an infection, or a neoplasm, so a cytology test should be carried out to shed more light on the changes indicated by the ultrasound.

The abdominal CT was conducted with excretory urography, revealing a right extramural ectopic ureter with right hydroureter and mild hydronephrosis, but with signs of adequate kidney function (Fig. 5). Prostate cytology evidenced a bacterial infection (possibly chronic prostatitis), which was the origin of the multiple mineralisations and cystic structures. Two cystic structures were also noted in the caudal abdomen, compatible with paraprostatic cysts, although we could not obtain a view of their connection with the prostate.

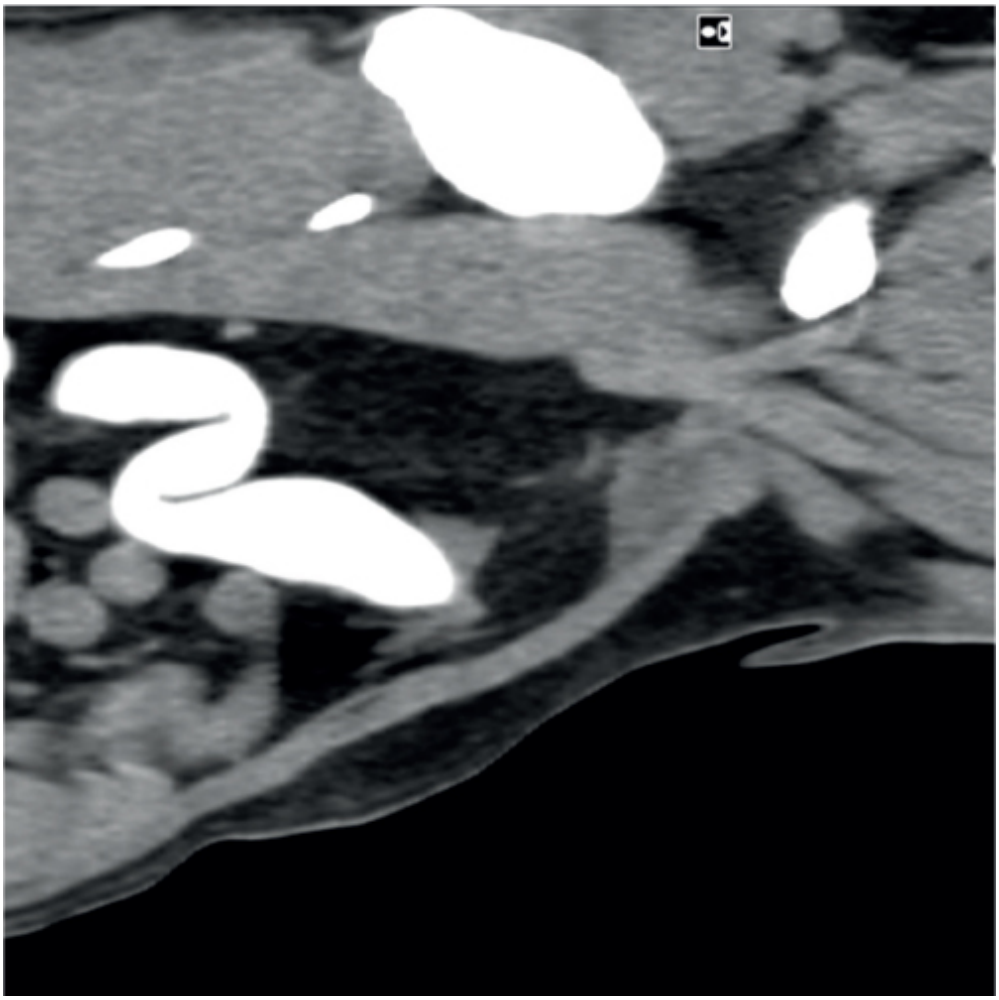


FIGURE 5. Contrast computed tomography (CT) scan of the ureter showing that its point of insertion is caudal to the neck of the bladder.

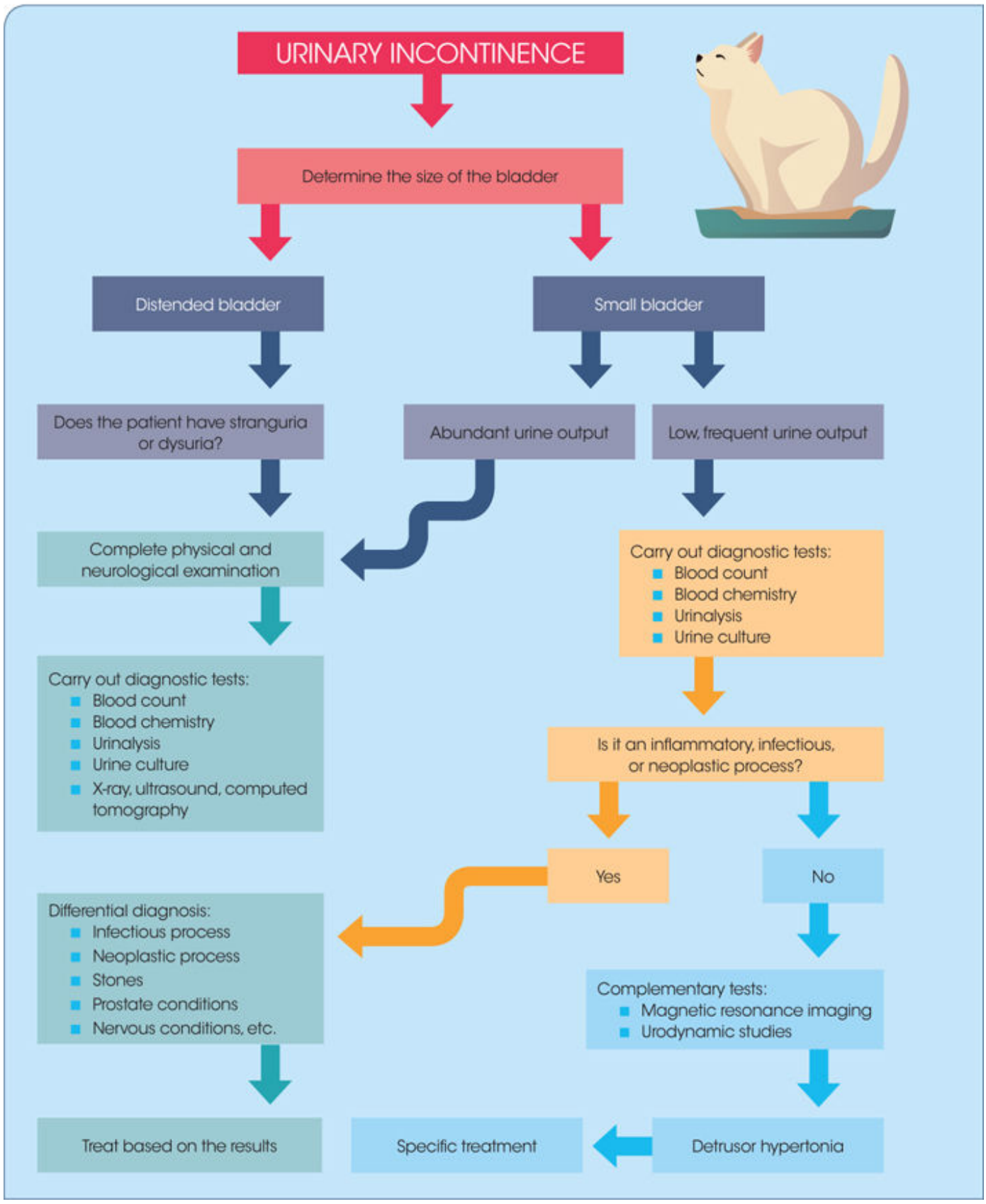
FINAL TREATMENT PLAN AND EVOLUTION

Recommendations for the definitive treatment plan were surgery to resolve the ectopic ureter, omentalisation, prostate biopsy (to confirm the cytological findings by repeating the bacterial culture), elimination and analysis of the stones, and castration.

Following the surgical resolution and a favourable response to the antibiotics, the clinical signs subsided completely and there were no signs of haematuria or urinary incontinence in subsequent check-ups. The extracted stones were confirmed to be struvite.

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DIAGNOSTIC ALGORITHM FOR URINARY INCONTINENCE



BRIEF REVIEW OF…

ECTOPIC URETER

WHAT CAUSES ECTOPIC URETER?

Ectopic ureter is a congenital anomaly wherein the embryonic metanephric duct, which is what develops into the ureters, forms in the wrong position or migrates by mistake. The outcome is that one or both ureters terminate in an abnormal location, generally caudal to the trigone of the bladder. They are classified according to their path:

- Extramural or extravesical: when the ureter does not terminate in the bladder wall, rather it is inserted in the urethra, vagina, etc.
- Intramural or intravesical: when the ureter terminates in the bladder, but its opening is caudal to the trigone.

The incidence of ectopic ureter in dogs is low, estimated to be 0.016 %, while unilateral ectopic ureters are most common, although males tend to have a greater incidence for bilateral compromise. The condition is diagnosed more frequently in females than in males. Studies have found that certain breeds seem to be more prone: Labrador Retriever, Golden Retriever, Siberian Husky, West Highland White Terrier, Poodle, and short-haired terriers.

Some animals may suffer from other, associated urinary alterations such as urethral sphincter incompetence, renal agenesis, renal dysplasia, hydroureter, hydronephrosis, intrapelvic bladder, and vestibulovaginal malformations which can contribute to their clinical signs.

WHAT IS THE MOST SIGNIFICANT CLINICAL SIGN IN ECTOPIC URETER?

Owners usually complain of urinary incontinence, but its importance depends on the location of the ectopic ureter or ureters. Animals may sometimes go through periods of normal bladder voiding or only develop incontinence as an adult, which hinders its identification at an early age. Males tend to manifest fewer clinical signs of incontinence than females due to the mechanisms of the external urethral sphincter and the length of the urethra.

Another common complaint made by owners relates to the symptoms of bacterial infections of the lower urinary tract. It has been reported that 64 % of animals with ectopic ureter have urinary infections at the time of diagnosis.

WHAT IS THE BEST METHOD FOR RULING OUT OR CONFIRMING A CLINICAL SUSPICION OF ECTOPIC URETER?

The presence of an ectopic ureter cannot always be identified through abdominal X-rays and ultrasound. However, there is generally evidence of related alterations such as nephromegaly or hydronephrosis. Ultrasound is the better of the two techniques, but even so the test still has a low sensitivity for ectopic ureter. The use of a contrast agent improves the sensitivity of X-rays, particularly with excretory urography, but helpful information can also be obtained from a retrograde urethrogram. Cystoscopy is another technique that can be used to identify ectopic ureters.

Contrast computed tomography is considered the most sensitive method for identifying ectopic ureters.

WHAT IS THE TREATMENT OF CHOICE FOR ECTOPIC URETERS?

Of all the treatments, surgery offers the best long-term results. There are several techniques, from traditional surgery to transection and laser ablation in females. A unilateral nephrectomy may be required in certain cases, after checking the contralateral kidney functions correctly. With respect to complications of surgery, some animals may develop hydroureter or obstructive hydronephrosis, normally transitory, due to inflammation, oedema, or clot formation in the postoperative period. In such cases, the obstruction usually resolves itself within 4 to 6 weeks, but the patient may have permanent stenosis with hydroureter and hydronephrosis requiring follow-ups with excretory urography.

In some patients, between 30 and 60 % according to different studies, surgery alone may not be enough to resolve incontinence and phenylpropanolamine should be used or ureteral reimplantation surgery combined with colposuspension to increase urethral pressure, the administration of collagen in the submucosa to increase urine outflow resistance, or even the placement of an adjustable hydraulic artificial urethral sphincter.

Urinary tract infections should be treated based on the results of the urine culture and antibiogram.

RECOMMENDED READING

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5 CLINICAL REASONING IN A CASE OF REGURGITATION/ DYSPHAGIA



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5 CLINICAL REASONING IN A CASE OF REGURGITATION/DYSPHAGIA

CLINICAL CASE
REGURGITATION/DYSPHAGIA

***B* is an 8-year-old, castrated male Maltese referred to our clinic with a 2-month history of chronic regurgitation, polyphagia, and weight loss. He would not tolerate food or water taken orally, experienced constant swallowing, and regurgitated food, sometimes via the nose. He was being treated with metoclopramide at the time of referral, but with no apparent improvement.**
The general physical examination did not reveal any significant alterations. His previous veterinarian had conducted various tests (chest and abdominal X-rays, contrast oesophageal and abdominal X-rays, thoracic CT, and gastrointestinal endoscopy) without reaching a definitive diagnosis.



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REASONING APPLIED TO THE CASE

Based on the available information, go through the first two steps of clinical reasoning:
1. Identify the animal's problems.
2. Prioritise the problems.



1. IDENTIFYING THE ANIMAL'S PROBLEMS

The patient has polyphagia, weight loss, chronic regurgitation, and constant swallowing.

2. PRIORITISE THE PROBLEMS

In the present case it seems reasonable to presume that the polyphagia and weight loss are secondary to a reduced nutritional intake because of the patient's chronic regurgitation. Therefore, we can consider that *B* 's main problem is regurgitation, although difficulty swallowing cannot be ruled out at this point. To establish the correct diagnosis, we need to define these two problems in more detail and confirm what is happening with the patient.

Take these premises and proceed with the next two steps in the clinical reasoning procedure:

3. Structure and organise the animal's problem.

4. Individualise the diagnostic plan.





3. STRUCTURING AND ORGANISING THE PROBLEM (DIFFERENTIAL DIAGNOSIS)

Regurgitation is defined as the passive, retrograde expulsion of food or fluid from the oesophagus due to a mechanical condition, obstruction, or functional anomalies (motility). It can occur immediately, minutes, or hours after eating, and the regurgitated substance could be digested or undigested food or fluid. So, the initial question should be: **does the patient suffer with vomiting, regurgitation, or dysphagia?**

The first important clinical distinction is to discern between regurgitation and vomiting. This can be achieved through a detailed anamnesis, clinical observation of the patient, or from a recording of the event made by the owner. Regurgitation differs from vomiting because there is no forced abdominal contractions and the regurgitated substance will not contain any bile. Other systemic signs of regurgitation are weight loss, polyphagia, weakness, and other neurological abnormalities. If the patient has incurred aspiration pneumonia, they may manifest signs of dyspnoea, fever, and cough.

Dysphagia is defined as difficulty swallowing food.

If we focus on the fact that the patient has a regurgitation problem, we should consider a broad differential diagnosis (Table 1), which has probably been studied and ruled out previously in this case.

Vomiting can sometimes be confused with regurgitation; on the other hand, regurgitation can also be confused with dysphagia. In our case, the exact problem is unclear given the clinical history and physical examination. In such circumstances the veterinarian must carry out a swallowing test or the owners should record their pet to obtain a clear example of the problem.

Swallowing is a reflex action consisting of four stages: oral preparatory, oral, pharyngeal, and oesophageal. Pharyngeal and oesophageal dysphagia are very hard to diagnose.

KEY POINT

Findings in the physical examination or a description in the clinical record of constant swallowing, nausea, and repeated gagging associated with food, nasal regurgitation when eating, cough related to swallowing, food falling from the mouth when swallowing, or recurrent pneumonia are all indicative of dysphagia, possibly pharyngeal.

An assessment of dysphagia almost always implies a review of the patient's medication or anaesthetic history, a complete physical exam together with a meticulous and thorough neurological exam, and observation of the animal eating and swallowing.

B 's clinical record showed he had difficulties with prehension of food, particularly fluids. When trying to drink, he would cough, with water falling from his mouth, and normally regurgitate the food or water he was ingesting at the time.

Observing how *B* ingests some food or water is very important and should help define in which stage of swallowing lies the problem:

- Dogs with **abnormal swallowing during the oral stage** find it hard to pick up food and push it towards the base of the tongue, which focuses our attention on problems in the oral cavity that will require a rigorous examination, sometimes under sedation or anaesthesia.
- **When the dysphagia affects the pharyngeal phase** it is harder to diagnose and often manifests with nonspecific signs such as nausea, gagging, and several attempts at swallowing before the food bolus passes successfully to the proximal oesophagus. These patients suffer with abnormal food bolus transport from the oropharynx to the hypopharynx or from the hypopharynx to the proximal oesophagus.
- Dogs with **oesophageal stenosis or oesophagitis** can show signs of odynophagia (painful swallowing) and regurgitation seconds or minutes after bolus ingestion. *B* more than likely suffers from a swallowing disorder.

The differential diagnosis for an animal with pharyngeal or oesophageal dysphagia is summarised in Table 2 .

TABLE 1. Differential diagnosis of regurgitation.

Cause	Causal processes

Oesophageal disorder	■ Megaoesophagus (primary or secondary) ■ Obstruction (stenosis, foreign body, vascular ring anomaly) ■ Oesophageal diverticulum ■ Oropharyngeal or oesophageal neoplasm ■ Gastroesophageal reflux
Digestive alterations	■ Pyloric obstruction ■ Hiatal hernia ■ Gastric dilatation or volvulus
Neuropathy/myopathy	■ Peripheral neuropathies ■ Inflammatory myopathies (infectious, immune-mediated, preneoplastic) ■ Dermatomyositis ■ Muscle dystrophies ■ Myasthenia gravis
Inflammation/infection	■ Oesophagitis ■ Botulism ■ Tetanus ■ Rabies ■ Spirocercosis ■ Neosporosis ■ Abscess ■ Organophosphate poisoning
Metabolic origin	■ Hypothyroidism ■ Hypoadrenocorticism

TABLE 2. Differential diagnosis of dysphagia.

Location	Causal processes
Pharyngeal dysphagia	■ Foreign body ■ Neoplasm ■ Neuromuscular conditions (idiopathic, myasthenia gravis, endocrinopathies, etc.)
Oesophageal dysphagia	■ Foreign body ■ Neoplasm ■ Megaoesophagus

	■ Stenosis ■ Vascular ring anomalies ■ Neuromuscular conditions (idiopathic, myasthenia gravis, endocrinopathies, etc.)

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4. INDIVIDUALISE THE DIAGNOSTIC PLAN

For *B* , the diagnostic plan for dysphagia should be far-reaching and include a repetition of the blood count and general blood chemistry, together with a hormone and electrolyte analysis (Tables 3 , 4 , and 5) and a urinalysis. The stages of swallowing must also be recorded in more detail, which requires a videofluoroscopic swallowing study to localise the problem. The results of the urinalysis were normal.

How do we interpret the results?

The blood count did not reveal any significant alterations (for example, there would be signs of inflammation in the case of aspiration pneumonia). However, the blood chemistry highlighted a slight change in phosphorus, probably associated with the digestive signs, and creatine kinase (CK-NAC), which is more marked (four times the reference value) and could be indicative of myositis.

Generalised inflammatory myopathies normally present moderate increases in CK activity (2,000–20,000 IU/l), whereas focal inflammatory myopathies, such as masticatory muscle myositis (MMM), endocrine myopathies, neuropathies, and other congenital muscular diseases, produce no or only a slight increase (0–2,000 IU/l) in CK activity.

Diagnostic imaging tests confirmed cricopharyngeal dysphagia (Fig. 1).

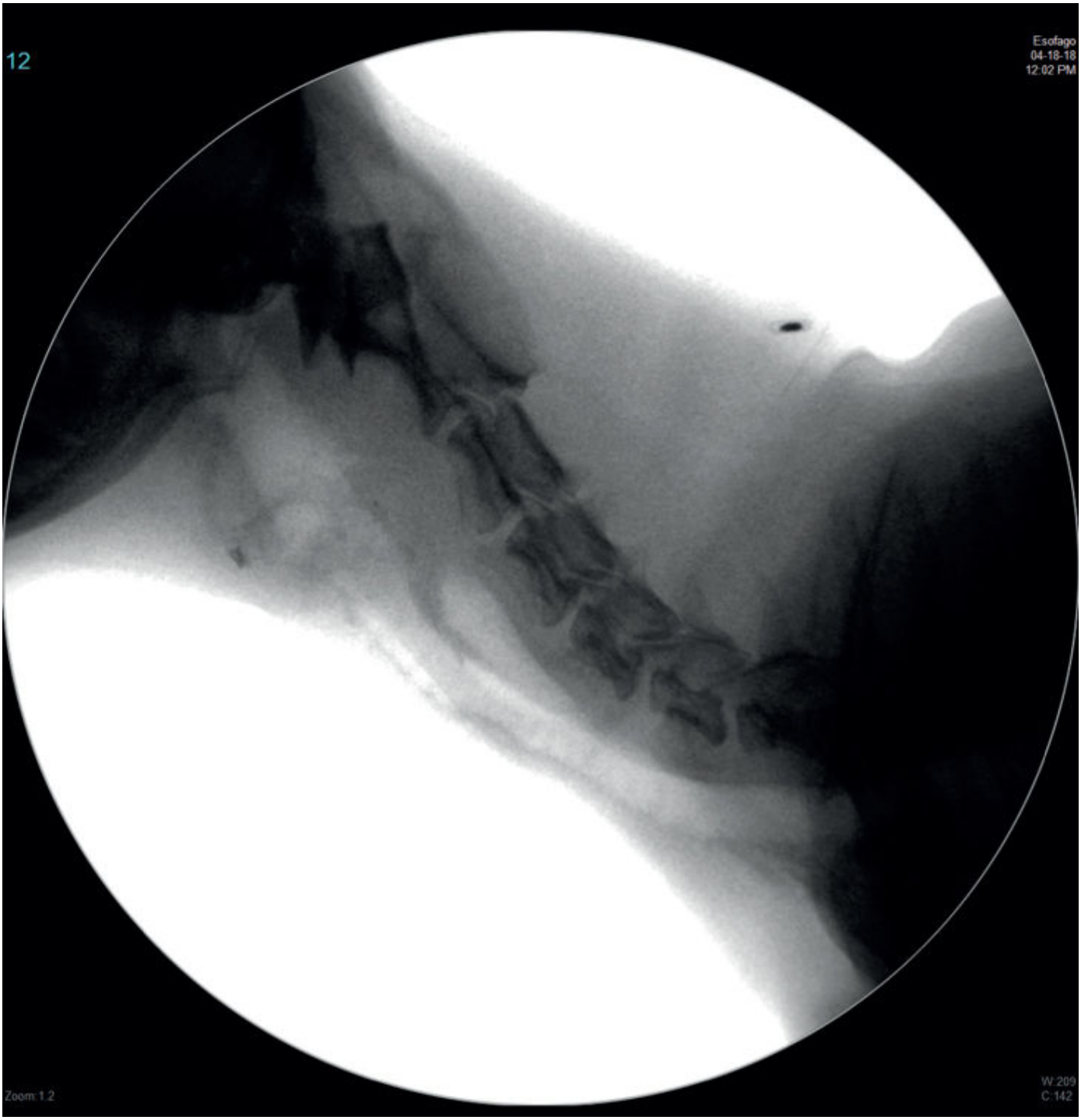


FIGURE 1. Videofluoroscopy image of the patient swallowing that confirmed the diagnosis of cricopharyngeal dysphagia.

TABLE 3. Blood count results.

Parameter	Value	Reference range
Erythrocytes ($\times 10^6$ /µl)	7.2	5.5–8.5
Haemoglobin (g/dl)	17.3	12–18
Haematocrit (%)	47	37–55
MCV (fl)	65	60–77

MCHC (g/dl)	35.8	32–36
MCH (pg)	23.9	19.5–24.5
Platelets (× 10^3 /µl)	258	200–500
White blood cells (cells/µl)	12,100	6,000–17,000
Lymphocytes (%)	16.9	12–30
Eosinophils (%)	9.5	2–10
Monocytes (%)	3	3–10
Neutrophils (%)	70.5	50–80

TABLE 4. Blood chemistry results.

Parameter	Value	Reference range
Albumin (g/dl)	3.3	2.3–4.5
Total protein (g/dl)	6.1	5.2–7.6
Globulins (g/dl)	2.8	2.1–4.4
Total calcium (mg/dl)	11.2	8.7–12.1
Glucose (mg/dl)	**121**	60–120
BUN (mg/dl)	17	7–25
Phosphorus (mg/dl)	**2.25**	2.9–6.5
Amylase (IU/l)	711	360–1,580
Cholesterol (mg/dl)	140	125–280
ALT (IU/l)	**105**	0–100
Total bilirubin (mg/dl)	0.2	0.0–0.6
Alkaline phosphatase (IU/l)	28	0–180
Creatinine (mg/dl)	0.94	0.5–1.9
CK-NAC (IU/l)	**774**	24–190

TABLE 5. Other test results.

Parameter	Value	Reference range
Total T_4 (µg/dl)	2.1	1.0–4.0
Free T_4 (ng/dl)	1.52	0.6–3.0
TSH (ng/ml)	0.23	0.03–0.6

5. ESTABLISH A DEFINITIVE DIAGNOSIS OR REASSESS THE DIFFERENTIAL DIAGNOSIS

By this point we have developed a better profile of the problem, but **which complementary tests would be appropriate given the information obtained so far? Have we definitively pinpointed the location of the patient's problem?**

Further tests could include:

- An acetylcholine receptor antibody test (myasthenia gravis).
- New imaging tests on the pharyngeal area while under anaesthesia.
- Electromyography to determine if the problem is neuromuscular.
- Muscle and nerve biopsy samples could be collected to help better define the problem.

Regarding whether we have localised the problem, cricopharyngeal dysphagia is essentially due to two conditions: cricopharyngeal dyssynchrony and cricopharyngeal achalasia.

In cricopharyngeal dyssynchrony the pharyngeal muscles cannot push the food bolus through the upper oesophageal sphincter. The videofluoroscopy evidenced a lack of coordination between the contraction of the pharyngeal constrictor and dorsal cranial muscles (oropharyngeal, pterygopharyngeal, and palatopharyngeal muscles) and the opening of the cricopharyngeal and thyropharyngeal muscles. Dogs with cricopharyngeal dyssynchrony have a less favourable prognosis than those with cricopharyngeal achalasia.

Cricopharyngeal achalasia occurs when the cricopharyngeal muscle does not open adequately during the cricopharyngeal stage of swallowing. The exact underlying cause remains unknown in most cases. It is diagnosed by means of contrast videofluoroscopy. Animals present marked hypertrophy of the cricopharyngeal muscle which causes severe obstruction to the food bolus being pushed through the upper oesophageal sphincter.

Based on the imaging test results, cricopharyngeal achalasia is the most likely diagnosis for *B* . The acetylcholine receptor antibody test was negative, so we were unable to determine the origin of the cricopharyngeal achalasia.

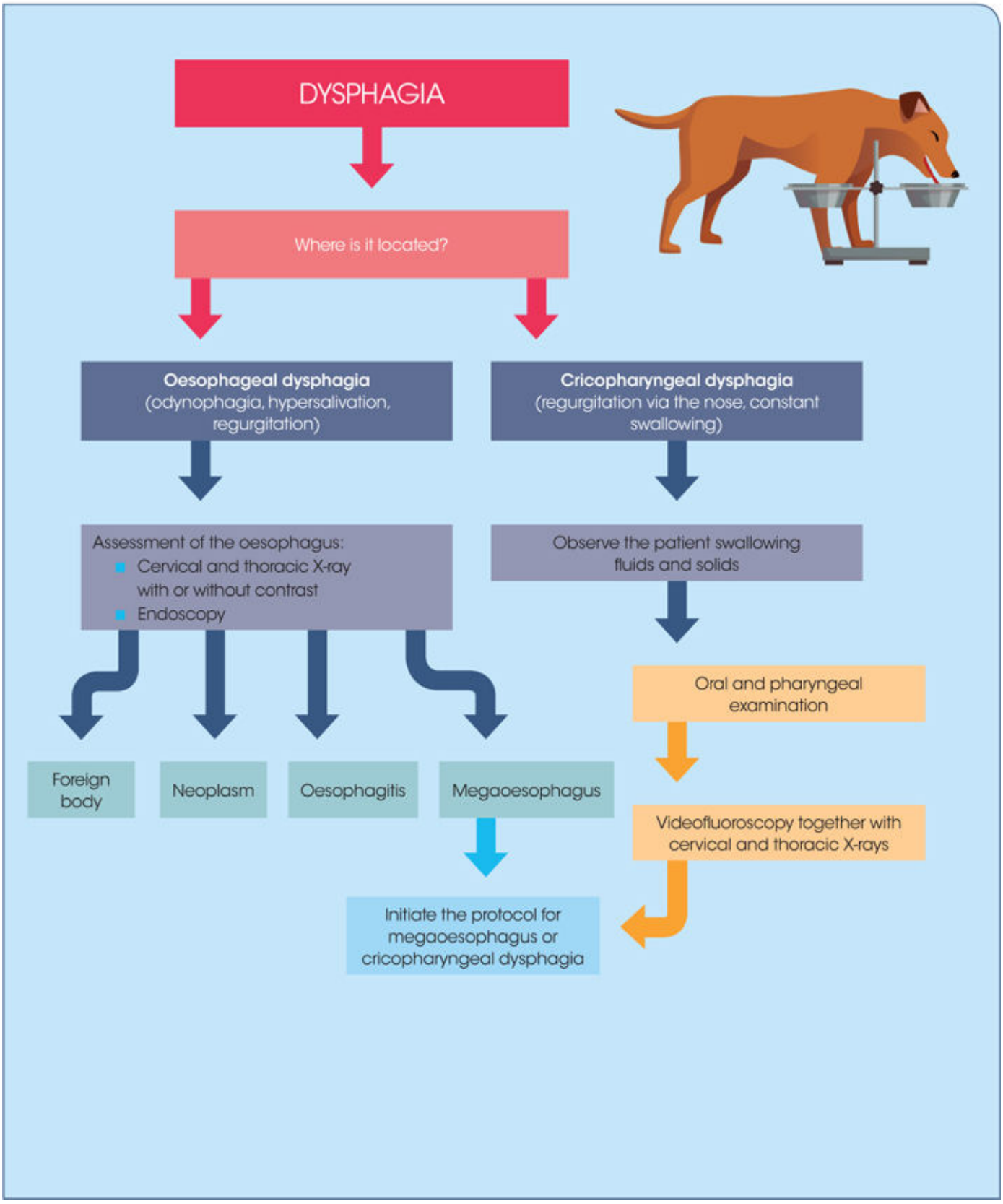
FINAL TREATMENT PLAN AND EVOLUTION

We recommended more tests such as botulinum toxin injections in the cricopharyngeal muscles. However, *B* improved with the introduction of water and food (semisolid) thickening techniques, so the owners decided to continue with conservative treatment (Fig. 2).



FIGURE 2. Given the improvement after changing the texture of *B* 's food, the owners decided against more therapeutic tests (Monika Wisniewska, Shutterstock.com).

DIAGNOSTIC ALGORITHM FOR DYSPHAGIA



BRIEF REVIEW OF…

CRICOPHARYNGEAL DYSPHAGIA

WHAT IS CRICOPHARYNGEAL DYSPHAGIA?

Cricopharyngeal dysphagia is a neuromuscular disorder of the upper oesophageal sphincter characterised by a failure to relax (achalasia) or lack of coordination between upper oesophageal sphincter relaxation and pharyngeal contraction (asynchrony).

WHAT ARE THE CLINICAL SIGNS OF CRICOPHARYNGEAL DYSPHAGIA?

Affected animals manifest progressive dysphagia, which is generally worse when swallowing water. Subjects will try to swallow several times, coupled with nausea and regurgitation, sometimes through the nasal cavity. The physical examination tends to be irrelevant, apart from the occasional presence of aspiration pneumonia, with crackling, dyspnoea, and fever.

From a clinical perspective, it is impossible to differentiate between asynchrony and cricopharyngeal achalasia based on a physical examination.

WHAT CAUSES THIS DISORDER?

Cricopharyngeal dysphagia can be the result of congenital or acquired causes. In most cases it is due to a focal neuropathy or myopathy; therefore, these conditions, primarily myasthenia gravis, should be ruled out during the differential diagnosis. By the same token, it is important to eliminate morphological abnormalities (such as foreign bodies), soft palate and dental injuries, morphological alterations of the glottis, and oropharyngeal neoplasms during the initial differential diagnosis.

Some breeds have a genetic predisposition to these alterations:

- Golden Retriever (pharyngeal weakness) (Fig. 1)
- Cocker and Springer Spaniel (cricopharyngeal dysphagia)

- Bouvier des Flanders and Cavalier King Charles Spaniel (muscular dystrophy)
- Boxer (inflammatory myopathy)

With respect to myasthenia gravis, the acetylcholine receptor antibody test can give dubious or negative results in the early stages of the disease, so it is generally a good idea to repeat it 2–4 weeks later in negative cases or even carry out a tensilon test.

Although animals with myasthenia gravis tend to have another systemic alteration, focal myasthenia gravis cannot be ruled out.



FIGURE 1. Golden Retrievers have a genetic predisposition to pharyngeal weakness (Christian Mueller, Shutterstock.com).

HOW IS CRICOPHARYNGEAL DYSPHAGIA DIAGNOSED?

A videofluoroscopic (radioscopy) swallowing study is the only technique that can be used to diagnose the problem and discern between achalasia and asynchrony, which is an important point as they should be treated differently.

The study generally involves recording the subject while they swallow a series of five foods with different textures, including a liquid barium contrast agent, followed by canned food with barium, and finally barium-laced food with a mixed consistency.

This technique can be used to study the pharyngeal constriction ratio, calculated by dividing the area of maximum constriction by the area when at rest; as pharyngeal contractility decreases, the ratio approaches 1, providing a measurement of pharyngeal force of contraction.

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ARE ELECTROMYOGRAMS AND BIOPSIES ESSENTIAL FOR THE DIAGNOSTIC PROCESS?

Electromyography does not usually produce a definitive diagnosis, but it can be used to study the local involvement of the pharynx and tongue muscles, and the systemic involvement of the condition, as well as its severity. It also helps correctly identify which muscles or nerves have suffered the most damage, which is where biopsy samples should be taken. The realisation of these tests must take into account the animal's overall health and their tolerance to general anaesthesia; if the procedure poses a high risk of adverse effects for the animal, maybe these techniques will not provide enough information to justify their execution. If a biopsy can be performed, it will help guide the veterinarian concerning the possible causes and different therapeutic options.

WHAT IS THE BEST TREATMENT FOR CRICOPHARYNGEAL ACHALASIA?

The definitive treatment for cricopharyngeal achalasia is to section the cricopharyngeal muscle (myotomy). Closed endoscopic cricopharyngeal myotomy using a CO_2 laser has given better results than transcervical cricopharyngeal myotomy.

While one article has reported that a bilateral myectomy is useful in the treatment of cricopharyngeal asynchrony, there is controversy regarding the benefit of surgery for this disorder and it cannot be recommended due to insufficient evidence, which is why animals with asynchrony have a worse prognosis.

As surgery does not always provide clear improvements for patients, the use of botulinum toxin injections in the cricopharyngeal muscles has been proposed in both human and veterinary medicine. The treatment usually lasts just 3–4 months, but it can be used to assess the improvements expected from surgery. Botulinum toxin is normally resuspended in a saline solution at a concentration of 25 IU/ml, then 10 IU are injected in three different areas of the cricopharyngeal muscle using a transbronchial needle.

Furthermore, it is helpful to determine the optimum consistency at which the patient can swallow food. Water thickeners are often used to facilitate swallowing, as animals with cricopharyngeal dysphagia initially have difficulty swallowing fluids effectively. In extreme situations patients can be fed using an oesophageal tube.

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CLINICAL REASONING IN A CASE OF DIARRHOEA 6



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6 CLINICAL REASONING IN A CASE OF DIARRHOEA

CLINICAL CASE
DIARRHOEA

_A_ is a 3-year-old, entire female Sphynx cat that lives strictly indoors and cohabits with other cats that also have no outdoor access. All the animals were negative for feline leukaemia virus and feline immunodeficiency virus. The owner visited our clinic because _A_ had been suffering chronic weight loss and intermittent episodes of diarrhoea for more than 2 months. They dewormed all their animals regularly but did not observe any improvement.
During the episodes of diarrhoea, the faeces had a completely liquid consistency with no signs of mucus or blood. There were periods in which the faeces had a pasty consistency, but they were rarely completely normal. In the general physical examination, the patient had a low body condition and abdominal palpation revealed a distended, and possibly rigid, stomach. All other findings were normal.



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REASONING APPLIED TO THE CASE

Based on the available information, go through the first two steps of clinical reasoning:
1. **Identify the animal's problems.**
2. **Prioritise the problems** .





1. IDENTIFYING THE ANIMAL'S PROBLEMS

The patient has (chronic) diarrhoea, weight loss, and rigidity/distension of the bowel loops.



2. PRIORITISE THE PROBLEMS

In this case it seems logical to presume the diarrhoea is the patient's main problem, while the weight loss is very likely secondary to this. Any change in body weight over time is a balance between nutrient intake, their absorption, and their use by the body. Unintentional weight loss is clinically significant when the patient loses more than 5 % of their body weight. In *A* 's case we did not how much weight she had lost, but we assumed it was over 5 % because the owners indicated this to be the case. She lives strictly indoors, does not have anorexia, and her diet and lifestyle have not changed in recent years, so we can assume the weight loss is secondary to the main problem (diarrhoea). The finding of rigid bowel loops upon palpation is uncommon and could

definitely be a cause of the diarrhoea. When this is noted during the physical exam, it is usually related to small intestine diarrhoea and often associated with a primary gastrointestinal process, so it would make sense to treat diarrhoea as the main problem.

Take these premises and proceed with the next two steps in the clinical reasoning procedure:
3. Structure and organise the animal's problem.
4. Individualise the diagnostic plan.





3. STRUCTURING AND ORGANISING THE PROBLEM (DIFFERENTIAL DIAGNOSIS)

Intestinal health is the result of the interaction between microbiota or bacterial flora, the intestinal mucosa, and the immune system. If we greatly simplify intestinal pathophysiology, diarrhoea occurs when there is an excess of aqueous content in the faeces, whether due to an increase in intestinal secretion or because the large intestine is unable to reabsorb the excess aqueous content from the faeces. There is a very long list of conditions that can destabilise one or more of the three elements mentioned above, and it also involves a lot of complicated pathophysiological mechanisms. In clinical terms, there is no advantage in structuring the problem of diarrhoea according to its causal mechanisms because some diseases induce diarrhoea via various different mechanisms simultaneously. Therefore, an alternative means of going about the differential diagnosis is to organise it into two large groups according to the origin of the diarrhoea: gastrointestinal and nongastrointestinal, with an indication as to whether it is acute or chronic. These two groups can also be referred to as primary and secondary gastrointestinal, respectively. Applying this general classification ensures that we not only focus on the most obvious factors, which are the diarrhoea and the gastrointestinal tract, but also on other possible systemic causes of diarrhoea.



- Most cases of diarrhoea in small animals have a gastrointestinal origin, especially in the large intestine.
- Nongastrointestinal causes should always be considered whenever there is systemic involvement in an animal with diarrhoea.

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When dealing with diarrhoea it is important to address the following questions during the anamnesis and physical examination.

Is the breed prone to any gastrointestinal diseases?

It is always important to consider the species and breed, as certain breeds are predisposed to gastrointestinal diseases. For example, Siamese cats suffer a higher incidence of intestinal adenocarcinomas and, along with other Asian breeds, chronic intestinal inflammatory processes. In dogs, German Shepherds are predisposed to local immunoglobulin A (IgA) deficiencies and diarrhoea due to bacterial overgrowth or in response to antibiotics. Brachycephalic breeds are predisposed to granulomatous colitis caused by infiltrating *Escherichia coli* bacteria, English Setters are susceptible to gluten, and Shar Pei are prone to a cobalamin deficiency with a recessive autosomal genetic basis (chromosome 13).

Is it acute or chronic diarrhoea?

Acute diarrhoea is defined as having an evolution of less than 14 days. While chronic diarrhoea refers to intermittent or episodic spells lasting more than 2 weeks, cases with a 14-day history and no clear signs of improvement, or even animals with sporadic diarrhoea over the course of several months.

Classification into acute or chronic cases means we can decide which tests should be conducted, since most cases of acute diarrhoea respond to symptomatic treatment and do not require an in-depth diagnostic study. The exception being systemically ill, febrile, or young patients when there is a suspicion of viral diarrhoea that could require hospitalisation, treatment, and further investigation of the cause and whether it is primary or secondary diarrhoea.

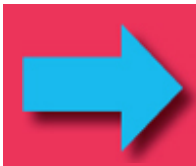
Chronic situations tend to require a better definition of the clinical problem and identification of which tests should be carried out next. This means the origin of the diarrhoea must be located to a specific area of the gastrointestinal tract.

Is it large intestine or small intestine diarrhoea?

Table 1 summarises the clinical characteristics of diarrhoea depending on whether its origins are in the small or large intestine. The clinical signs are not pathognomonic, although the presence of mucous, fresh blood, and a reduced volume of faeces tends to point towards large intestine diarrhoea. It is worth remembering that small intestine diarrhoea can in turn affect the large intestine and therefore it manifests as mixed diarrhoea. On the other hand, there are cases of severe colitis that course with weight loss, or mild cases that course without the presence of mucous or blood. Another consideration are diseases that can affect both sections of the intestine, producing clinical signs of both types of diarrhoea. What is more, with respect to conditions affecting the small intestine, the colon may be able to reabsorb the excess aqueous content that accumulates in the ileum and therefore the intestinal problem courses without causing diarrhoea.

TABLE 1. General characteristics of small and large intestine diarrhoea.

Clinical signs	Small intestine	Large intestine
Related to the faeces		
Volume	Large	Small
Presence of mucous	Rare	Common
Blood (if present)	Melaena	Fresh blood
Steatorrhoea	Sometimes	Never
Colour	Variable	Normal
Undigested food	Sometimes	Never
Tenesmus	Rare	Common
Stool frequency	2–3 times a day	More than 3 times
Urge to defecate	Rare	Common
Other clinical signs		
Vomiting	Sometimes	Rarely
Gas	Sometimes	Never
Weight loss	Generally	Rarely
Ascites or peripheral oedema	Sometimes	Rarely
Dehydration	If the diarrhoea is severe	Does not usually affect fluid balance
Thickened or rigid bowel loops	Sometimes present	Absent



KEY POINT

Bowel disease may be present without diarrhoea.

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Having identified the type of diarrhoea, and paying special attention to the signalment, clinical record, and physical exam, we can now approach the differential diagnosis.

Do we need more diagnostic tests? Which ones?

Whenever the animal has systemic signs, significant weight loss, hypoproteinaemia, or dehydration, it is always worth performing more diagnostic tests or considering the following steps:

1. The clinical record should note whether the animal has been dewormed and how often. If in doubt, a broad-spectrum deworming product such as fenbendazole is recommendable to cover most helminths and *Giardia* . A stool test should also be performed where possible, as some parasites such as *Strongyloides* or *Trichuris* can be very persistent in the environment and the patient may suffer frequent reinfections. Some species of *Giardia* and *Tritrichomonas foetus* can also be very resistant to treatment. In all of these cases the vet must always confirm the animal has responded adequately to the treatment and does not become reinfected, hence a series of stool analyses are essential.
2. In the event of acute diarrhoea, a low-residue diet can be tried for a few days. If it is chronic, it is estimated that up to 50 % of patients will respond to dietary modifications, particularly compositional changes; hypoallergenic, easy to digest, with a higher fibre content, etc.
3. If the animal does not respond to the dietary changes or deworming, try to resolve the diarrhoea with antibiotics such as metronidazole (10–20 mg/kg, every 12 hours) or, if dysbacteriosis is suspected, tylosin. At this point, and in the initial stages of the diarrhoea, it is worth considering the use of probiotics to help recover normal gut microbiota and improve the diarrhoea. This is also known to displace the pathogenic flora and replace it with normal flora. Either way, if the new diet works, improvements are usually noted within 2 weeks of the dietary change.
4. If at any point it is considered to be a case of small intestine diarrhoea or the animal is unwell, attempts should be made to rule out nongastrointestinal causes such as hyperthyroidism (in cats), liver disease, hypoadrenocorticism (using the ACTH or basal cortisol tests), pancreatitis, or exocrine pancreatic insufficiency (EPI). Systemic alterations derived from a chronic gastrointestinal problem should also be assessed by determining cobalamin and folic acid levels and through protein electrophoresis. Occasionally, due to the intermittent nature of diarrhoea or because the patient lives in a shelter, it might be worth carrying out molecular tests (PCR

assays for *Campylobacter* , *Salmonella* , *Escherichia coli* or toxins produced by *Clostridium*) or even a stool culture. If chronic inflammatory processes, foreign bodies, or neoplasms are prominent in the differential diagnosis, an abdominal imaging study (ultrasound) is recommendable.

5. Whenever the animal does not show a sufficient response to the previous strategies, it is usually a good idea to collect a biopsy sample from the gastrointestinal tract, as the next step involves administering immunosuppressants and we need to confirm there is intestinal inflammation with evidence from a biopsy.

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KEY POINTS

- A gastrointestinal biopsy is rational once a parasitic process has been ruled out, the patient has been treated with metronidazole or antibiotics, probiotic/antibiotic-responsive diarrhoea has been dismissed, and there is no response to suitable dietary changes.
- A gastrointestinal biopsy is recommendable if there are indications of an infiltrative gastrointestinal disease such as weight loss, hypoproteinaemia, palpation of abnormal bowel loops, or ultrasound evidence of a gastrointestinal disease.

With the above information and depending on the breed, age of presentation, and clinical signs, the most reasonable decision in this case would be that it is a significant gastrointestinal problem. We are dealing with chronic diarrhoea, because the clinical picture started approximately 2 months ago, that is possibly located in the small intestine. Furthermore, the presence of systemic clinical signs such as weight loss and a low body condition alert us to the importance of the process. The physical examination revealed abnormal bowel loops, which is again indicative of the seriousness of the problem and places the process primarily in the small intestine; therefore, in this patient, it would be very interesting from the outset to include diagnostic imaging, blood, and stool tests, although *A* 's lifestyle means parasites or infections are unlikely. Hence, the main problem is located in the small intestine and with systemic involvement.

An appropriate differential diagnosis to consider for this animal is summarised in Table 2 . After determining the location of the problem, we can use the VITAMIN D mnemonic to facilitate the differential diagnosis or classify the options into two large aetiological groups, similar to the steps performed in the diagnostic process described on page 13 .

Based on the above and individualising the initial differential diagnosis to our case of chronic, small intestine diarrhoea in a 3-year-old, neutered female cat with a strictly indoor lifestyle, the leading diagnoses in order of likelihood would be those shown below.

If the patient were elderly or had outdoor access, other conditions such as hyperthyroidism or infectious/parasitic processes, respectively, would feature higher on the list of differential diagnoses.

DIFFERENTIAL DIAGNOSIS OF THE PATIENT

- Inflammatory bowel disease (IBD), food allergy, intestinal neoplasm (lymphoma, mast cell tumour)
- Pancreatic disease (EPI, chronic pancreatitis)
- Liver disease (hepatitis, cholangiohepatitis, or chronic cholangitis)
- Infectious origin (very unlikely): toxoplasmosis, feline infectious peritonitis, bacteria (*Salmonella* , *Campylobacter*)



4. INDIVIDUALISE THE DIAGNOSTIC PLAN

In view of the patient's clinical record and general physical examination (dehydration, low body condition, etc.), we already have an indication that it appears to be a severe process associated with the diarrhoea. What is more, it does not seem logical to follow the diagnostic steps used to rule out a parasitic (unlikely in this case) or infectious process (bacterial or viral), or anything related to a dietary change or the use of antibiotics. In an attempt to reach a diagnosis and finish assessing the patient's clinical condition, we decided upon the following diagnostic tests: a blood count (Table 3), a routine blood chemistry test with the addition of some specific parameters (Table 4), a urinalysis (Table 5), and an abdominal ultrasound (Box 1).

How do we interpret the results?



The blood count indicated the presence of moderate neutrophilic leukocytosis without a left shift, compatible with an infectious, inflammatory, or neoplastic process.

There was also mild lymphocytosis, suggestive of antigenic stimulation, although a lymphoproliferative process cannot be ruled out.

The blood chemistry revealed: mild hypokalaemia (3.36 mmol/l), possibly secondary to the excessive loss and poor absorption of potassium; hypocholesterolaemia (80.4 mg/dl), probably due to a problem with intestinal absorption; and severe hypocobalaminaemia (< 150 ng/l), whether due to poor absorption (EPI, ileal disease, liver disease), increased bacterial consumption (dysbiosis), or both mechanisms together. Although there was no hypoproteinaemia, total protein and albumin were at the lower limits, which is suggestive of an alteration in absorption.

With regard to the urinalysis, a specific gravity of 1.020 means there could be an emerging case of kidney disease that is currently coursing without azotaemia. However, it cannot be diagnosed from just one analysis. In the present case there are no clinical signs of kidney disease such as polyuria/polydipsia, but if we wanted to investigate further, we could measure symmetric dimethylarginine (SDMA).

TABLE 2. Causes of diarrhoea in cats and dogs.

Causes	Examples
Related to diet	■ Dietary changes ■ Deviations in the feeding regime or accidents (foreign bodies, etc.) ■ Food intolerances/allergies
Parasites	■ *Ascaris* (*Toxocara* , *Ancylostoma* , *Uncinaria* , *Strongyloides* , etc.) ■ Protozoa (*Giardia* , *Cystoisospora* , *Cryptosporidium* , etc.)
Infections	■ Bacteria (*Campylobacter* , *Salmonella* , *E. coli* , *Clostridium* , etc.) ■ Viruses (parvovirus, coronavirus, distemper, norovirus, etc.)
Antibiotic-responsive diarrhoea	■ Idiopathic antibiotic-responsive diarrhoea ■ Bacterial overgrowth
Infiltrative	■ Idiopathic inflammations (inflammatory bowel disease [IBD], sclerosis) ■ Neoplasms (lymphoma, carcinoma, mast cell tumour)
Miscellaneous	■ Idiopathic haemorrhagic gastroenteritis

	■ Lymphangiectasia ■ Brush border enzyme defects ■ Exocrine pancreatic insufficiency ■ Selective cobalamin deficiency ■ Toxic agents
Nongastrointestinal	■ Pancreatitis ■ Motility alterations (hyperthyroidism, dysautonomia, lead poisoning) ■ Hypoadrenocorticism ■ Liver disease ■ Systemic disease (renal, metabolic, etc.)

TABLE 3. Blood count results.

Parameter	Value	Reference range
Erythrocytes (× 10^6 /µl)	8.18	6–10.2
Haemoglobin (g/dl)	11.1	9–15
Haematocrit (%)	34	29–48
MCV (fl)	44.5	41–53
MCHC (g/dl)	32.1	30–34
MCH (pg)	13.6	13–17
White blood cells (cells/µl)	**28,130**	5,000–15,000
Lymphocytes (cells/µl)	**7,876**	1,400–6,100
Monocytes (cells/µl)	**1,407**	100–600
Segmented neutrophils (cells/µl)	**18,285**	2,500–11,300
Eosinophils (cells/µl)	563	0–1,500
Platelets (× 10^3/µl)	551	200–600

TABLE 4. Blood chemistry results.

Parameter	Value	Reference range
Routine blood chemistry		
Creatinine (mg/dl)	0.65	0.5–1.5
Urea (mg/dl)	44.1	21.4–60.0
Cholesterol (mg/dl)	**80.4**	135–270

Glucose (mg/dl)	**149.6**	65–118
Total protein (g/dl)	5.73	5.6–7.5
Total bilirubin (mg/dl)	0.12	0.1–0.5
Alkaline phosphatase (IU/l)	**17.84**	20–156
GGT (IU/l)	**1.0**	1.2–6.4
ALT (IU/l)	21	21–102
CK-NAC (IU/l)	129.6	10–150
Calcium (mg/dl)	9.0	9.0–11.3
Phosphorus (mg/dl)	2.95	2.6–6.2
Potassium (mmol/l)	**3.36**	4.4–5.4
Sodium (mmol/l)	150.7	141–152
Chloride (mmol/l)	**120.7**	105–115
Protein electrophoresis		
Albumin (g/dl)	2.77 (48.26 %)	2.6–3.3
α_1 globulin (g/dl)	0.31 (5.38 %)	0.2–0.5
α_2 globulin (g/dl)	**1.21 (21.16 %)**	0.3–1.1
β globulin (g/dl)	**0.77 (13.44 %)**	0.9–1.6
Gamma globulin (g/dl)	0.67 (11.76 %)	0.3–0.8
Albumin/globulin (g/dl)	0.93	-
Special blood chemistry		
Folic acid (ng/ml)	18.6	9.5–20.2
Cobalamin/vitamin B_{12} (ng/ml)	**< 150**	270–1,000

TABLE 5. Urinalysis results (cystocentesis).

Parameter	Value
Specific gravity	1.020
pH	6
Blood	3+
Sediment	No evidence of cells or bacteria
Urine protein:creatinine ratio (UPC)	0.2

The data obtained so far mean we require more information about the gastrointestinal tract and need to rule out infiltrative or neoplastic processes, although given the cat's age the former is more likely. To this end, an abdominal ultrasound would be very helpful.

DESCRIPTION OF THE ABDOMINAL ULTRASOUND STUDY

- Small amount of peritoneal effusion.
- Jejunum: bowel wall thickening (5.8 mm) is notable in some of the loops. Diffuse and marked thickening of the muscularis, visible as a very hypoechoic area, as well as hyperechoic spots in some bowel loops. There are also hyperechoic spots on the mucosa of some jejunal loops.
- Jejunal lymph nodes: enlarged and hypoechoic. Visible pancreatic lymph node measuring 3.7 mm.
- Common bile duct: dilated (4.2 mm) and tortuous. No signs of obstruction.

The ultrasound evidenced a jejunum with a severe, diffuse infiltrative process mainly affecting the muscularis (Fig. 1) As such, the list of differential diagnoses will include a neoplastic process and a severe, chronic inflammatory process (IBD). The hyperechoic spots in the jejunal mucosa indicate material being digested, lymphangiectasia (rare or undiagnosed in cats), or ulcers. The mild, anechoic peritoneal effusion could be due to hypoalbuminaemia (not evidenced in the blood chemistry analysis and therefore less probable) or a reactive/inflammatory process, as could the jejunal, colonic, and pancreatic lymphadenopathy. A neoplastic process cannot be ruled out at this point.



5. ESTABLISH A DEFINITIVE DIAGNOSIS OR REASSESS THE DIFFERENTIAL DIAGNOSIS

We still do not have a definitive diagnosis, but *A* 's list of problems has grown: moderate neutrophilic leukocytosis, mild lymphocytosis, hypocholesterolaemia, low urine specific gravity, hypocobalaminaemia, severe diffuse jejunal infiltration with jejunal, pancreatic, and colonic lymphadenopathy, and mild abdominal effusion.

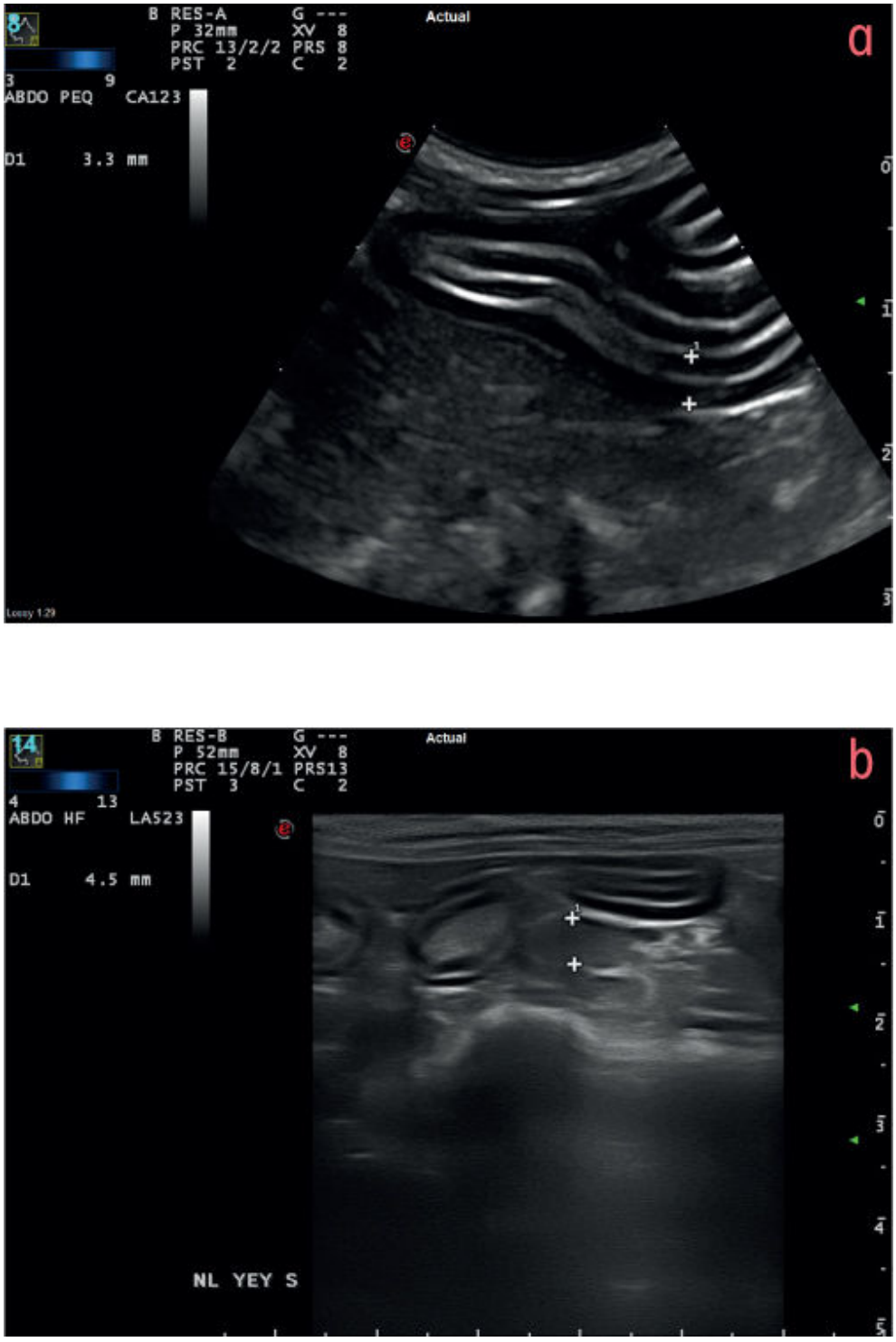


FIGURE 1. Ultrasound images of the patient evidencing diffuse and marked thickening of the muscularis (a), visible as a very hypoechoic area, as well as hyperechoic spots in some bowel loops (b).

Hypocobalaminaemia has been established as a negative prognostic factor in chronic, idiopathic gastrointestinal disorders (IBD). In addition, cats with hypocobalaminaemia and chronic diarrhoea (regardless of the cause) respond better to treatment when they are administered cobalamin. So, the prognosis and treatment plan change depending on whether or not the patient has hypocobalaminaemia (and its intensity) and hypoproteinaemia or hypoalbuminaemia.

With all this information, it seems *A* has a severe, mainly infiltrative process localised principally in the region of the jejunum. Hence a biopsy sample should be collected from this area to obtain a more definitive diagnosis and differentiate between a neoplastic and infiltrative process. Lymph node cytology or a gastrointestinal tract biopsy are two viable choices amongst the different options. The owners agreed to an exploratory laparotomy with biopsy sample collection (Box 1).

BOX 1. Surgery and biopsy reports.

Surgery report (laparotomy)

- The jejunal wall is very enlarged and the loops are rigid when palpated. Two punch biopsy samples were collected. During the procedure, the mucosal layer separated from the muscularis. Mucosal and lymph node samples were sent to the laboratory.

Biopsy report

- Microscopic lesions to the jejunum: no alterations observed in the epithelial layer. Moderate thickening of the intestinal villi and discrete dilatation of the crypts of Lieberkühn. Abundant oedema observed in the lamina propria with discrete fibrosis and lymphoplasmacytic inflammatory infiltrate. Some isolated eosinophils. **Diagnosis: lymphoplasmacytic enteritis** .
- Microscopic lesions in the lymph node: normal architecture is preserved. Marked activation of the lymphatic tissue. **Diagnosis: reactive lymph node** .

FINAL TREATMENT PLAN AND EVOLUTION

Pending the surgical procedure, and to avoid interfering with the biopsy, we initiated treatment solely to address the hypocobalaminaemia by administering a gastrointestinal diet. After the intervention, we started treatment with methylprednisolone (1.5 mg/kg, PO, every 12 hours).

Based on the results of the biopsy and all the other tests, the patient was diagnosed with inflammatory bowel disease (IBD). The following treatment was inaugurated:

- Methylprednisolone: 1.5 mg/kg, PO, every 12 hours.
- Cyanocobalamin: 250 µg in total, SC, at least once a week for 1 month.
- Gastrointestinal prescription diet, although a hypoallergenic diet would also be indicated at this point.
- Check-up in 1 month.

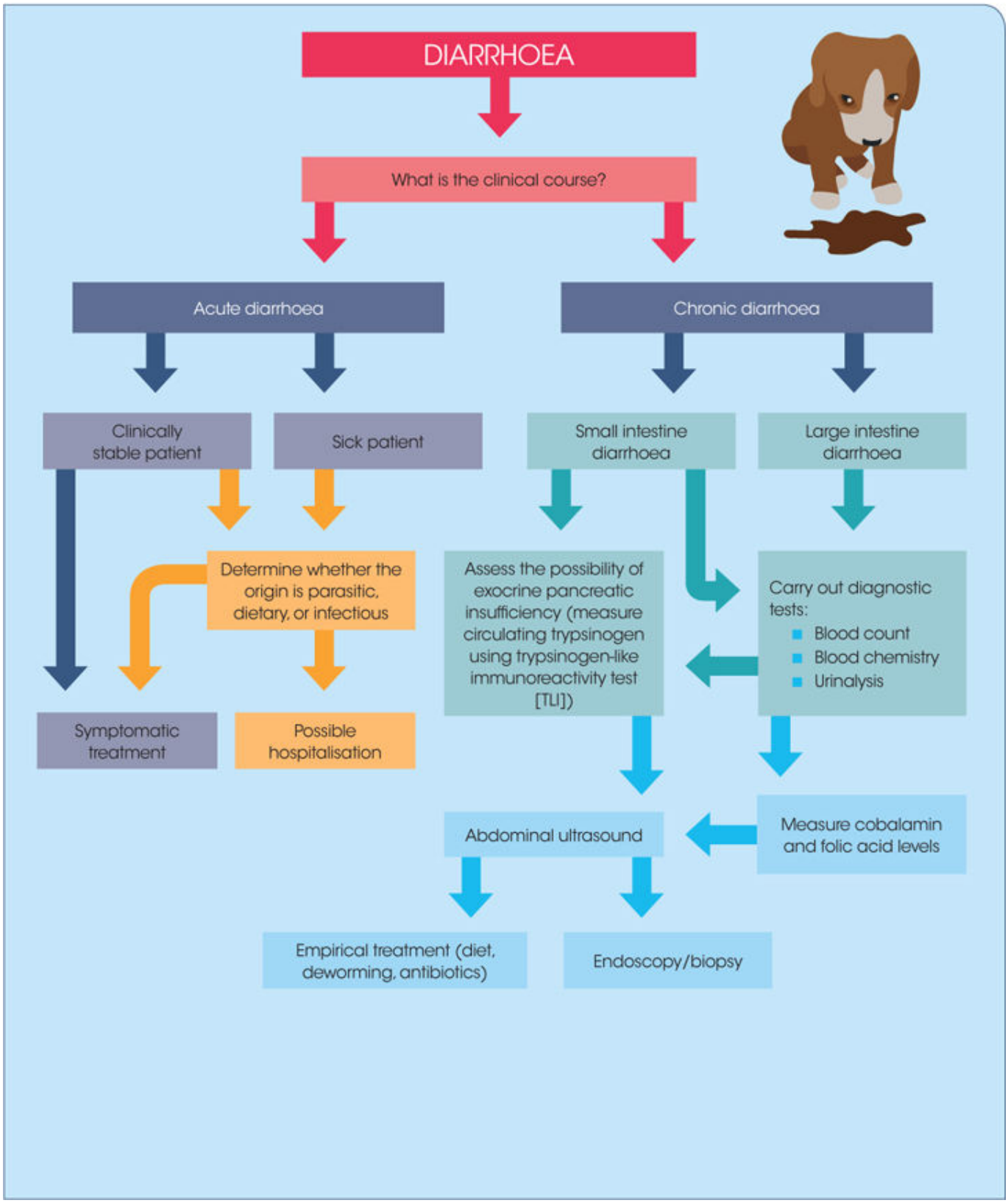
The biopsy report confirmed lymphoplasmacytic IBD with reactive lymph nodes, ruling out intestinal lymphoma or another neoplasm or an intestinal infiltrative process.

The patient progressed very favourably and in the last check-up (4 months after diagnosis) the diarrhoea had remitted completely, she did not suffer vomiting, and had a normal appetite. The general physical exam was normal, and the animal had gained weight (800 g). A follow-up ultrasound revealed the jejunal muscularis was still thickened, but there was no loss of stratification or mesenteric lymphadenopathy. The owners rejected any follow-up blood tests. Of their own accord, the owners had discontinued the methylprednisolone treatment 10 days earlier and the patient had remained stable.

The next step was to propose moving forwards without corticosteroids, changing to a hypoallergenic diet, continuing with cobalamin administration every 2 months, and another follow-up visit in 6–12 months.

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DIAGNOSTIC ALGORITHM FOR DIARRHOEA



BRIEF REVIEW OF…

FELINE INFLAMMATORY BOWEL DISEASE

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WHAT IS CHRONIC INFLAMMATORY BOWEL DISEASE (IBD)?

IBD (inflammatory bowel disease) is a group of immune- mediated gastrointestinal tract disorders characterised by persistent or recurrent inflammatory histological changes and clinical signs. It has a multifactorial aetiology involving interactions between genetic factors, the mucosal immune system, and local environments. Enteric microbiota and components of food may be recognised as antigens leading to an abnormal, inappropriate, and uncontrolled inflammatory response, which is in turn responsible for chronic inflammation in the gastrointestinal tract. It is thought there could be genetic defects in processes that play an important role in recognising pathogenic bacteria from commensal bacteria.

HOW ARE INTESTINAL MICROBIOTA INVOLVED IN IBD?

The presence of certain intestinal microbiota can trigger an abnormal inflammatory response in animals with IBD. There is very little information available regarding the microorganisms attached to the mucosa in cats with IBD. One study has reported an increase in enterobacteria (family *Enterobacteriaceae*) in duodenal biopsies from cats with IBD, while another described the presence of *Campylobacter coli* associated with neutrophilic IBD. A change in the intestinal microbiota has also been noted in cats with treatment-responsive IBD. In conclusion, microbiota apparently fulfil a significant role in IBD, but further research is necessary to learn which microorganisms are involved and how to use this information for therapeutic purposes.

IS IBD ASSOCIATED WITH OTHER DISEASES?

Dermatological signs are observed in 10–15 % of cats with diet-responsive enteritis. Triaditis, which involves inflammation of the intestine, pancreas, and liver, can be

encountered in some animals. A recent study found cholangitis in 22.2 % and pancreatitis in 7.4 % of cats with IBD, while 29.65 % manifested an inflammatory response in two or all three of the aforementioned organs, although other studies reported a greater incidence of triaditis – in up to 60 % of cases. However, the latest studies seem to suggest a lack of any association between IBD and inflammation in other organs.

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IS IT POSSIBLE TO MEASURE THE DEGREE OF IBD INVOLVEMENT?

A feline chronic enteropathy activity index (FCEAI) has been published for this purpose. The index comprises clinical signs (vomiting, diarrhoea, anorexia, weight loss, and apathy), laboratory variables (total protein, phosphorus, alanine aminotransferase [ALT], and alkaline phosphatase), and endoscopic lesions (granularity, friability, ulcers, or erosions); each parameter is given a score (Table 1). The FCEAI is used to make an objective assessment of the treatment response by comparing pre- and posttreatment scores. If the endoscopy cannot be repeated, the points for this parameter are not included in the overall score.

The FCEAI includes the most relevant biopathological changes observed in cats with IBD such as hypo- or hyperproteinaemia, hypophosphataemia, increased ALT, or increased alkaline phosphatase. Total protein may be increased or decreased depending on the severity and cause of the process. ALT and alkaline phosphatase enzymes are altered if there is liver compromise and possibly triaditis. Hypophosphataemia could be secondary to malnutrition, intestinal malabsorption, or chronic vomiting. These points are defined as factors with a prognostic value in cats with IBD, which is why they are included in the FCEAI. Other common analytical changes are anaemia and neutrophilia.

TABLE 1. Parameters and scoring for the feline chronic enteropathy activity index (FCEAI).

Parameter		Score				Subtotal
		0	1	2	3	
Gastrointestinal signs	Attitude/activity	Normal	Slight decrease	Moderate decrease	Severe decrease	
	Appetite	Normal	Slight decrease	Moderate decrease	Severe decrease	
	Vomiting	None	Mild (1 time/week)	Moderate (2–3 times/week)	Severe (> 3 times/week)	
	Diarrhoea	None	Soft faeces, with mucus or blood, or slight increase in frequency (2–3 times/day)	Very soft faeces or moderate increase in frequency (4–5 times/day)	Watery faeces or severe increase in frequency (> 5 times/day)	
	Weight loss	None	Mild (< 5 %)	Moderate (5–10 %)	Severe (> 10 %)	
		0		1		
Laboratory variables	Total protein	Normal		Increased/decreased		
	ALT/alkaline phosphatase	Normal		Increased		
	Phosphorus	Normal		Decreased		
Endoscopic lesions		No		Yes		
						Total score

ALT: alanine aminotransferase.

WHICH TESTS ARE RECOMMENDED FOR A CAT WITH SUSPECTED IBD?

The correct diagnosis of IBD may require various diagnostic tests. The most typical tests are given below.

DIAGNOSTIC TESTS IN CATS WITH CHRONIC INFLAMMATORY BOWEL DISEASE

Blood tests:
- Blood count
- General blood chemistry with protein electrophoresis
- Total T_4
- Feline pancreas-specific lipase
- Cobalamin and folic acid
- FIV and FeLV antibody status

Urine analysis.

Faeces tests:
- Small intestine diarrhoea:

- Stool test (faecal flotation)
- PCR: *Giardia* spp., *Cryptosporidium* spp., *Campylobacter* spp., bacterial enteropathogenic toxins

- Large intestine diarrhoea:
  - Stool test
  - PCR: *Tritrichomonas foetus*
- Bloody diarrhoea, with fever and general clinical signs:
  - Culture or PCR for: *Salmonella* spp., *Clostridium* spp., *Campylobacter* spp.

Diagnostic imaging tests:

- Abdominal ultrasound
- Thoracic X-rays

Treatment response:

- Fenbendazole (50 mg/kg, PO, every 24 hours, for 5 days)
- Dietary changes
- Hypoallergenic diet

WHICH IMAGING TESTS PROVIDE THE MOST INFORMATION IN CATS WITH IBD?

Abdominal ultrasound has a greater diagnostic capacity than X-rays in cases of IBD, although the results may be within normal ranges in some animals. In IBD, as with feline intestinal lymphoma, diffuse or localised gastrointestinal changes can be observed. Ultrasound tends to reveal thickening of the intestinal wall, generally due to an increase in the muscularis and preservation of the other intestinal layers. A recent study defined a muscularis to submucosa thickness ratio of less than 1 as physiologically normal, whereas cats with intestinal involvement usually present higher values. The increased thickness of the muscularis may be due to infiltration of neoplastic cells (generally lymphoma) or secondary to IBD, although a previous study suggested that the probability of an intestinal lymphoma was greater in cases of enlarged intestinal muscularis. Mesenteric lymphadenopathy can be associated with IBD or intestinal lymphoma; however, the likelihood of lymphoma increases if the lymphadenopathy is colonic and there is a diffuse increase in the thickness of the small intestine muscularis. In addition, ultrasound can be used to assess liver and pancreas involvement, which can occur in animals with triaditis. When comparing ultrasound and histological findings, ultrasound detected 50–80 % of cases with pancreatic changes and only 20–25 % of those with hepatic involvement in animals with intestinal disorders, although the observation of pancreatic lesions had a very low specificity.

IS INTESTINAL LYMPH NODE CYTOLOGY HELPFUL IN THE DIAGNOSIS OF IBD?

Animals with IBD manifest signs of thickened bowel loops and regional lymphadenopathy. Cytology does not usually provide a definitive diagnosis in these cases, but often establishes that it involves (occasionally neutrophilic) lymphoplasmacytic infiltration and reactive lymph nodes. Nevertheless, cytology is helpful when trying to rule out intestinal lymphomas, especially for intermediate- or high-grade lymphomas, but it is slightly less effective when dealing with small cell lymphomas.

Whenever there is doubt about the presence of reactive or neoplastic lymphadenopathy, molecular tests (PCR for antigen receptor rearrangement [PARR], flow cytometry) or biopsies and histopathological studies can be conducted to better define the pathology.

WHAT IS THE BEST TYPE OF BIOPSY IN ANIMALS WITH SUSPECTED IBD?

There is some debate about which type of biopsy should be used to diagnose feline IBD and it sometimes depends on the veterinarian's preferences. The techniques employed are laparotomy, laparoscopy, or endoscopy, each with their own advantages and disadvantages (Table 2). Table 3 indicates the number of biopsy samples that should be obtained for a correct analysis of IBD.

TABLE 2. Comparison of biopsy techniques in the diagnosis of feline chronic enteropathy.

Characteristics	Full biopsies		Partial biopsies
	Laparotomy	Laparoscopy	Endoscopy
Sample obtained	Mucosa, submucosa, muscularis, and serosa		Mucosa and submucosa
Assessment of other organs	Visual inspection of the gastrointestinal tract serosa and other abdominal organs		Visualisation of the mucosal surface of the intestinal tract
Invasiveness	High, plus days of hospitalisation	Intermediate	Low
Access to intestinal segments	All segments	All segments, but generally a sample is only taken from the ileum	■ Gastroduodenoscopy: gastric and duodenal mucosa ■ Colonoscopy: colon and ileum
Postoperative	Tissues must be allowed to heal		No postoperative period required
Surgical skill	High	High, with certain amount of specialisation	High, with certain amount of specialisation
Pathological interpretation of the samples	From a histopathological perspective, these samples are easier to align for study and interpretation		Of variable quality, histopathological interpretation is harder

TABLE 3. Number of endoscopy biopsy samples required for the correct study of IBD.

Gastrointestinal segment	Recommended number of samples
Stomach	6
Duodenum	6
Ileum	3–5, blind biopsies are feasible if the intestinal segment is not visible
Colon	9–12, 3–4 samples from each segment of colon

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RECOMMENDED READING

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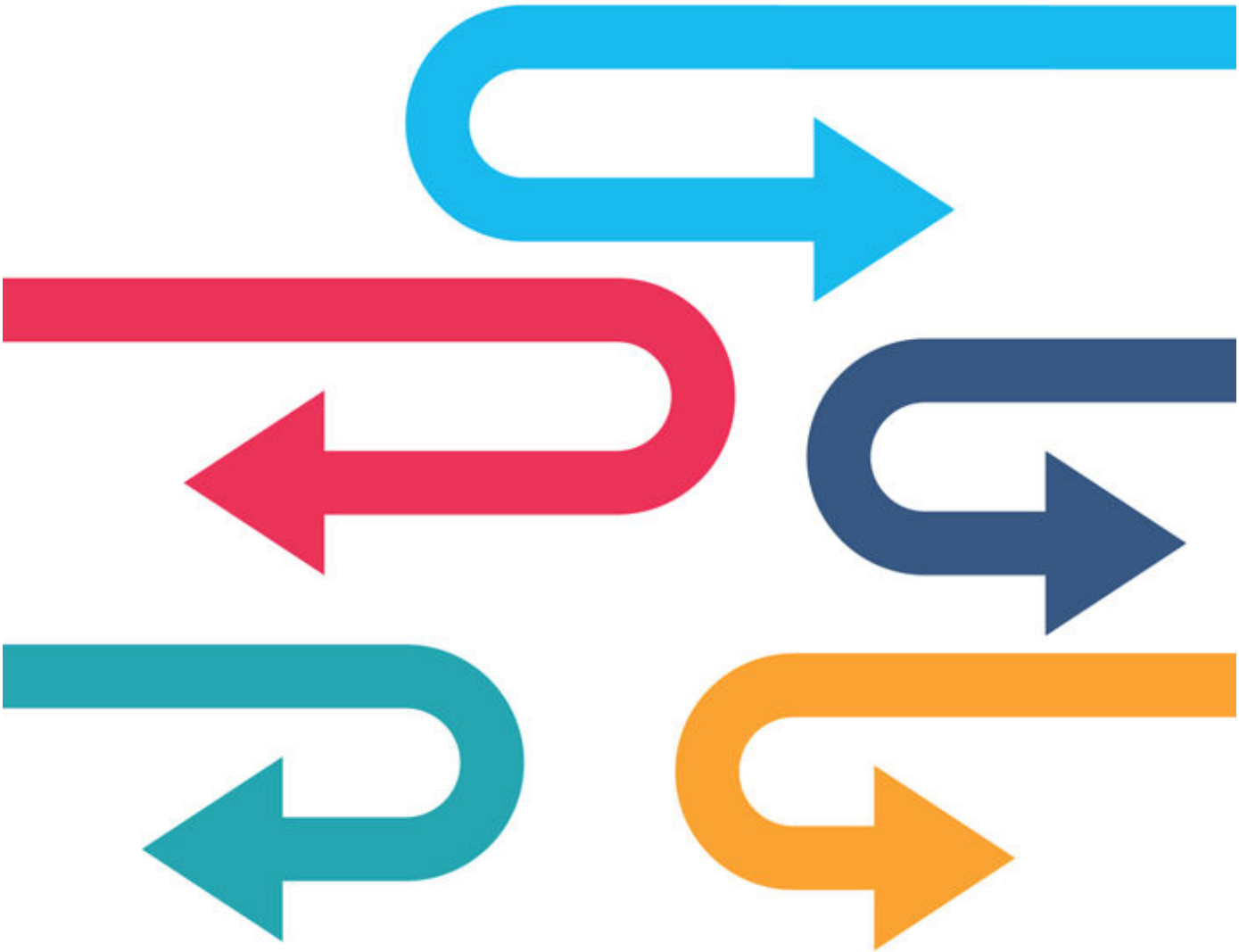
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CLINICAL REASONING IN A CASE OF JAUNDICE

7



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7 CLINICAL REASONING IN A CASE OF JAUNDICE

CLINICAL CASE
JAUNDICE

V **is a 4-year-old, castrated male French Bulldog brought to the clinic with a 7-day history of apathy, anorexia, and vomiting, and jaundice for the last 24 hours. His owners also mentioned progressive loss of weight and appetite over the last 6 months. They confirmed no current medications, recent vaccinations (although the animal is vaccinated regularly), or access to toxic substances. The patient has no history of contact with ticks or recent trips outside his normal surroundings.**
The physical examination did not reveal any relevant alterations, apart from pinkish, slightly jaundiced mucous membranes.



Svetography/Shutterstock.com

REASONING APPLIED TO THE CASE

Based on the available information, go through the first two steps of clinical reasoning:
1. **Identify the animal's problems.**
2. **Prioritise the problems** .





1. IDENTIFYING THE ANIMAL'S PROBLEMS

The patient has suffered anorexia, apathy, and vomiting for the past 7 days, and jaundice and chronic weight loss.



2. PRIORITISE THE PROBLEMS

It seems logical to consider a clinical picture with a chronic progression, wherein the patient started with hyporexia/anorexia, progressive weight loss, and apathy, subsequently developing vomiting and finally the onset of jaundice. Therefore, the most significant clinical sign or finding upon which we should focus for the differential diagnosis is probably jaundice. The vomiting is also important, but it is often secondary or related to the jaundice, so we can leave it on the back burner for the time being.

Take these premises and proceed with the next two steps in the clinical reasoning procedure:
3. Structure and organise the animal's problem.
4. Individualise the diagnostic plan.





3. STRUCTURING AND ORGANISING THE PROBLEM (DIFFERENTIAL DIAGNOSIS)

Jaundice is defined as yellowing of the skin, mucous membranes, and sclerae due to the accumulation of bilirubin resulting from hyperbilirubinaemia, which corresponds to high bilirubin blood levels. As a general rule, bilirubin blood levels are only clinically detectable above 2 mg/dl, which mean some patients may have hyperbilirubinaemia without jaundice, although the differential diagnosis is carried out in a similar manner.

BILIRUBIN METABOLISM

Bilirubin is the end product of haeme catabolism, which is mainly found in the haemoglobin of red blood cells, although it can also come from myoglobin or liver enzymes containing the haeme group. Old or damaged red blood cells are eliminated from circulation by the mononuclear phagocyte system (spleen, liver, and bone marrow), which breaks down haemoglobin into iron and the haeme group within macrophage cells. The macrophages store the iron for reuse and the haeme group is transformed into biliverdin and subsequently unconjugated bilirubin. Unconjugated bilirubin is insoluble in water and is neither filtered in the kidneys nor eliminated by the renal tubules.

Dogs have renal enzymes that can conjugate part of the bilirubin, so that it can be eliminated in urine and therefore a low level of bilirubinuria is normal in dogs. But this is not true for cats and the presence of bilirubinuria is always a sign of disease.

Unconjugated bilirubin in the bloodstream is reversibly bound to albumin and is taken up by hepatocytes, conjugated, and excreted into the intestine via the bile ducts.

Following biliary excretion and storage in the gallbladder, conjugated bilirubin is released into the duodenum where it is metabolised by intestinal bacteria into a series of faecal pigments, including stercobilin, which gives faeces its normal brown colour. At the same time, it may be reabsorbed by the enterohepatic circulation or transferred to the blood for subsequent renal elimination. The biliary excretion stage is the rate limiting step in bilirubin catabolism and the first to become overloaded when there is an excessive demand for bilirubin excretion (Fig. 1).

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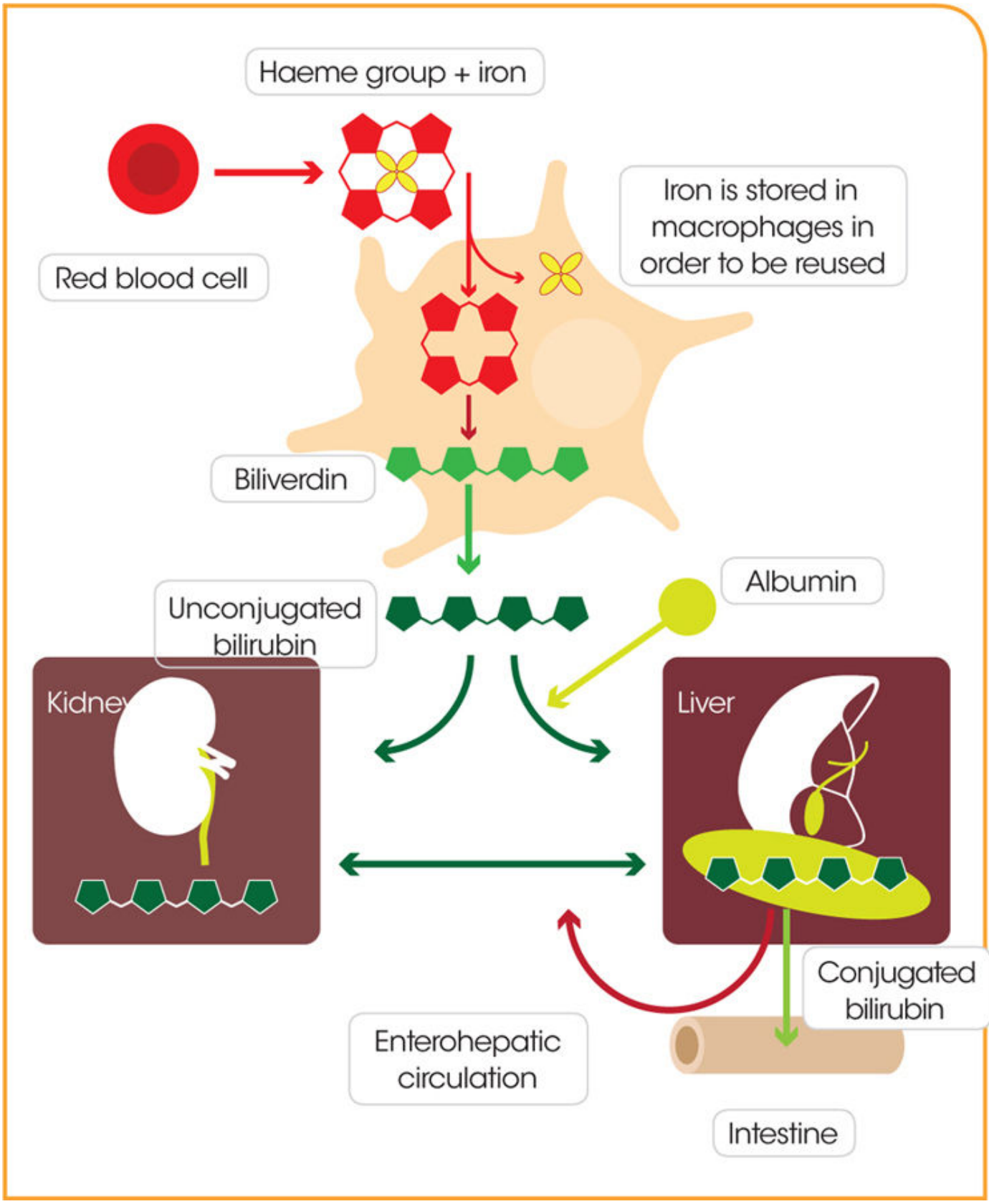


FIGURE 1. Diagram of bilirubin catabolism.

Jaundice is a clinical sign that stems from an underlying cause, rather than a disease in itself; therefore, we need to be familiar with bilirubin metabolism (explained above) in order to perform a logical clinical and diagnostic approach.

As explained earlier, hyperbilirubinaemia, and consequently jaundice, can result from three basic mechanisms:

- An increase in bilirubin production that surpasses the liver's capacity to metabolise the excess. This is known as **prehepatic jaundice** . It is associated with moderate or severe haemolysis.
- Hepatocytes are unable to metabolise, conjugate, or excrete bilirubin, a situation known as **hepatic jaundice** .
- The biliary system is unable to eliminate conjugated bilirubin into the digestive system due to an obstruction (intra- or extraluminal) or rupture. This is known as **posthepatic jaundice** .

So, when dealing with a patient with jaundice, it is very important to locate the origin of the problem and ask ourselves: **does the animal have marked haemolysis or is it a case of hepatic or posthepatic jaundice?**

The first step in answering this question is to collect a blood sample, principally so we can scrutinise the blood count, and a urine sample. Moderate to severe anaemia with signs of regeneration (increased reticulocyte count, polychromasia, spherocytes, anisocytosis) or agglutination will help situate the problem at the prehepatic level. In this situation, the jaundice may be secondary to haemolytic anaemia, whether primary (immune-mediated) or secondary, but we must also consider other causes of haemolysis (babesiosis, onion poisoning, congenital enzymatic alterations, microangiopathies, etc.).

Animals with prehepatic jaundice also tend to manifest pale mucous membranes and clinical signs of associated anaemia such as tiredness, tachycardia, tachypnoea, and depressed mental status. These signs will depend on the degree of anaemia.

Cases of hepatic and posthepatic jaundice are the hardest to diagnose. Nevertheless, jaundice of a hepatic origin tends to occur in the final stages of liver disease and patients have previously exhibited systemic clinical signs compatible with liver failure, although this depends on the speed with which the failure develops. However, animals with posthepatic jaundice usually display very few clinical signs until obstruction has occurred.

The most common causes of hepatic jaundice are:

- Cholangiohepatitis
- Infections (leishmaniasis, leptospirosis, etc.)
- Neoplasms (particularly lymphoma)

In *V* 's case, in view of the evolution, it is surely a chronic process as indicated by the animal's weight loss. The absence of signs caused by anaemia such as tachycardia, tachypnoea, or pale mucosae (our patient's mucosae are pink and slightly jaundiced), imply that a prehepatic origin is unlikely. What is more, the patient's clinical record rules out the involvement of drugs, recent vaccinations, toxins, and, to a lesser degree, infectious agents, especially those related to haemolysis. The appearance of vomiting and progressive weight loss also suggest that the origin of *V*

's jaundice is hepatic, posthepatic, or both. Table 1 shows the initial differential diagnosis.

4. INDIVIDUALISE THE DIAGNOSTIC PLAN

In this patient, we need to confirm the clinical suspicion that the jaundice is not prehepatic, so we need to request a complete blood count (Table 2). We need more information about the liver from a general but comprehensive blood chemistry analysis (Table 3). An increase in bile acids is observed in all cases of jaundice, so this parameter does not provide any extra information in the initial stages of the assessment. Other recommendable tests include: *Leishmania* and *Leptospira* serology, coagulation tests, and diagnostic imaging tests.

At this point, we have not ruled out the possibility of neoplasms and therefore a chest X-ray could be considered, although this can wait until we have performed abdominal ultrasound.

How do we interpret the results?



The blood count presented signs of mild polycythaemia, possibly relative, due to haemoconcentration. There were no alterations in the white blood count, but there was marked thrombocytopaenia (45 × 10^3/µl). The smear revealed aggregated platelets, which indicates that this parameter was lower than the true value; however, the coagulation times suggested the platelets were being consumed and the patient was in a compensated stage of disseminated intravascular coagulation.

TABLE 1. Differential diagnosis of hepatic and posthepatic jaundice.

Jaundice	Origin	Causal processes
Hepatic	Infectious	■ Leishmaniasis ■ Leptospirosis ■ Canine adenovirus

	Inflammatory/immune-mediated	■ Chronic active hepatitis
	Toxic	■ Copper hepatopathy
	Neoplastic	■ Lymphoma ■ Carcinoma ■ Metastasis
Posthepatic	Intraluminal obstruction	■ Mucocele ■ Cholelithiasis ■ Cholangitis ■ Neoplasm
	Extraluminal obstruction	■ Duodenal foreign body ■ Regional lymphadenopathy ■ Pancreatitis ■ Intestinal neoplasm

TABLE 2. Blood count results.

Parameter	Value	Reference range
Erythrocytes (× 10^6 /µl)	**8.86**	5.4–8.7
Haemoglobin (g/dl)	**20.8**	13.4–20.7
Haematocrit (%)	**58.8**	38.3–56.5
MCV (fl)	66.4	59–76
MCHC (g/dl)	35.4	32.6–39.2
MCH (pg)	23.5	21.9–26.1
Reticulocytes (cells/µl)	41,642	10,000–110,000
White blood cells (cells/µl)	10,620	6,000–17,000
Lymphocytes (cells/µl)	2,500	1,000–4,800
Monocytes (cells/µl)	850	150–1,350
Segmented neutrophils (cells/µl)	7,170	3,000–11,500
Band neutrophils (cells/µl)	0	0–300
Eosinophils (cells/µl)	100	100–1,500

Basophils (cells/µl)	0	0–200
Platelets (× 10^3/µl)	**45**	143–448
Prothrombin time (PT) (s)	**> 100**	11–17
Partial thromboplastin time (PTT) (s)	**> 300**	72–102

TABLE 3. Blood chemistry results.

Parameter	Value	Reference range
Creatinine (mg/dl)	0.5	0.5–1.8
Urea (mg/dl)	11	7–27
Cholesterol (mg/dl)	**69**	110–320
Glucose (mg/dl)	112	70–143
Total protein (g/dl)	5.6	5.2–8.2
Total bilirubin (mg/dl)	**15.1**	0.0–0.9
Alkaline phosphatase (IU/l)	**1,292**	23–212
GGT (IU/l)	**49**	0–11
ALT (IU/l)	**237**	10–125
Calcium (mg/dl)	9.1	7.9–12.0
Phosphorus (mg/dl)	6.1	2.5–6.8
Potassium (mmol/l)	4.1	3.5–5.8
Sodium (mmol/l)	**138**	144–160
Chloride (mmol/l)	**106**	109–122

The blood chemistry evidenced a very marked increase in bilirubin and liver enzymes, while markers of liver damage (ALT) and cholestasis (alkaline phosphatase and GGT) were also high. The notable augment in alkaline phosphatase and GGT and slight increase in ALT raise suspicions of a problem primarily involving bile duct obstruction. ALT rises when there is liver damage and the discrepancy between these enzymes may suggest very chronic changes in the liver, with the destruction of hepatocytes and cirrhosis, or alternatively an infiltrative process such as lymphoma or mastocytoma. The hypocholesterolaemia is probably due to the liver's inability to produce cholesterol. The slight changes in sodium and chloride are related to the patient's hydration status and the secondary gastrointestinal signs. All other parameters were within normal ranges. The results of the serological tests for *Leishmania* and *Leptospira* were negative.

The abdominal ultrasound presented signs of hepatomegaly with no apparent changes in the liver's echogenicity, biliary sediment with gallbladder wall oedema/inflammation, slightly distended bile ducts, and perihepatic lymphadenopathy. The rest of the abdomen appeared normal. The ultrasound findings are compatible with possible cholangiohepatitis (Fig. 2). There was no evidence to indicate an obstruction, but it is still too early to rule out a potential inflammatory/infectious process affecting the bile ducts and causing cholestasis. Chest X-rays did not provide any relevant findings.

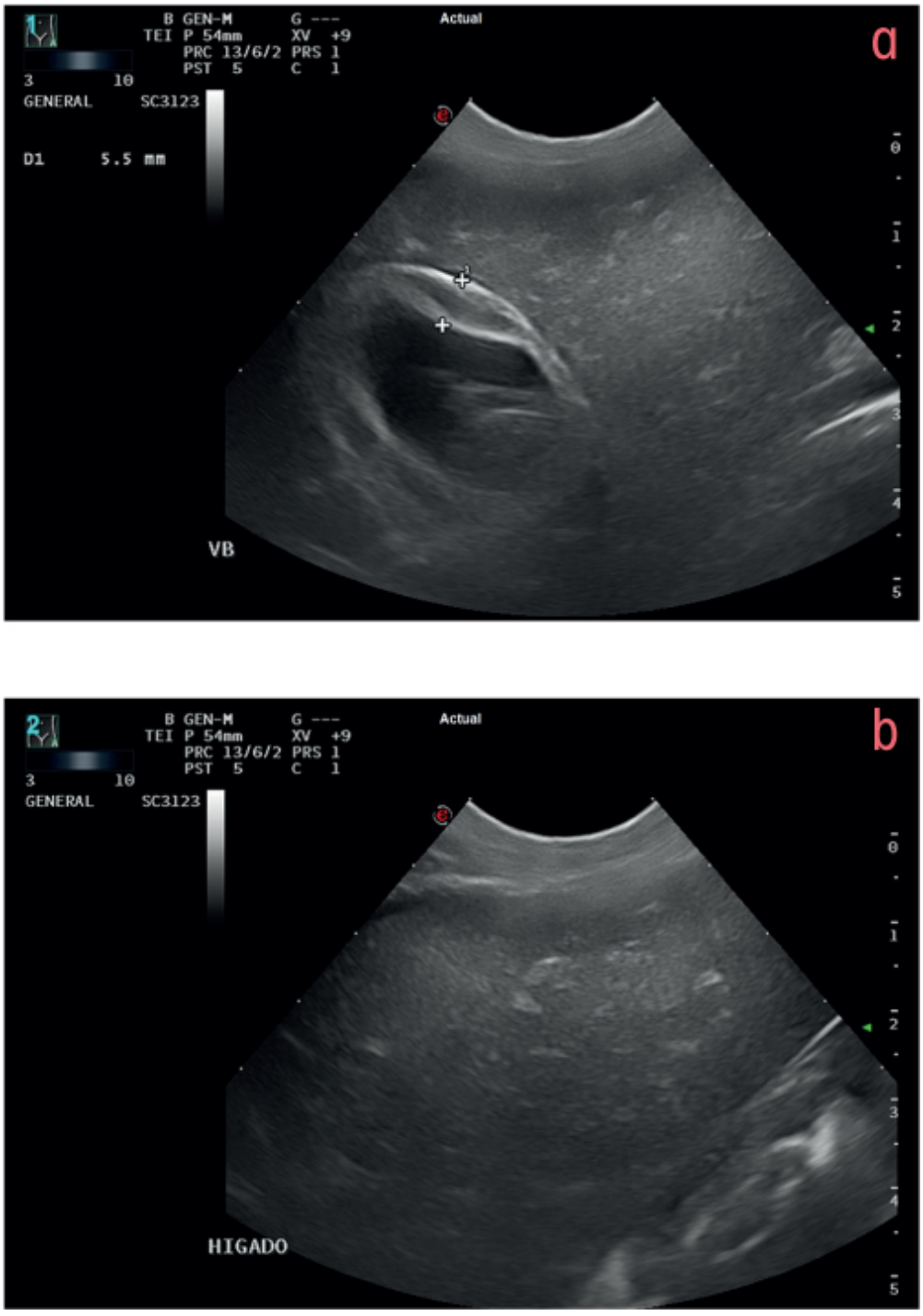


FIGURE 2. Ultrasound image revealing a distended gallbladder with an enlarged wall and biliary sludge (a). The liver presents a slight increase in echogenicity (b).

5. ESTABLISH A DEFINITIVE DIAGNOSIS OR REASSESS THE DIFFERENTIAL DIAGNOSIS

V 's list of problems has grown with the results of the tests carried out so far. Our patient possibly has disseminated intravascular coagulation, which is an extremely serious situation, with diffuse hepatobiliary involvement that cannot be better defined in the ultrasound and regional lymphadenopathy. All of which makes us believe that the jaundice has a hepatic origin and is more serious than we first thought after the initial assessment.

Based on the patient's new list of problems, and having identified the hepatic origin, the next step is to obtain a liver sample by means of an ultrasound-guided fine-needle aspiration or normal biopsy and collect bile for cytology and culture. Given the alteration in the coagulation times, the only safe means of conducting these tests would be after a fresh plasma transfusion and vitamin K supplementation, as levels are often diminished in animals with liver problems. The owners initially agreed to stabilise *V* , carry out the transfusions, and try to obtain samples for cytology.

The cytological analysis revealed nonlipid degenerative changes in the hepatocytes, mild cholestasis, and the presence of abundant lymphoblasts (Fig. 3). The cytological picture was compatible with a hepatic lymphoma.

In this patient, and in most hepatic cases, it is impossible to reach a definitive diagnosis without a liver biopsy or cytology sample. Sometimes the cytological study only represents an initial approach and an ultrasound-guided or laparoscopic biopsy or even an exploratory laparotomy is required.

FINAL TREATMENT PLAN AND EVOLUTION

Hepatic lymphomas imply a poor prognosis and in *V* 's case there is a suspicion of disseminated intravascular coagulation, which makes this a very difficult case to treat. Our advice to the owners was to continue stabilising the patient and initiate a CHOP chemotherapy protocol (Madison–Wisconsin protocol), but *V* worsened rapidly and they opted for euthanasia. The necropsy confirmed the cytological findings of a hepatic T-cell lymphoma.

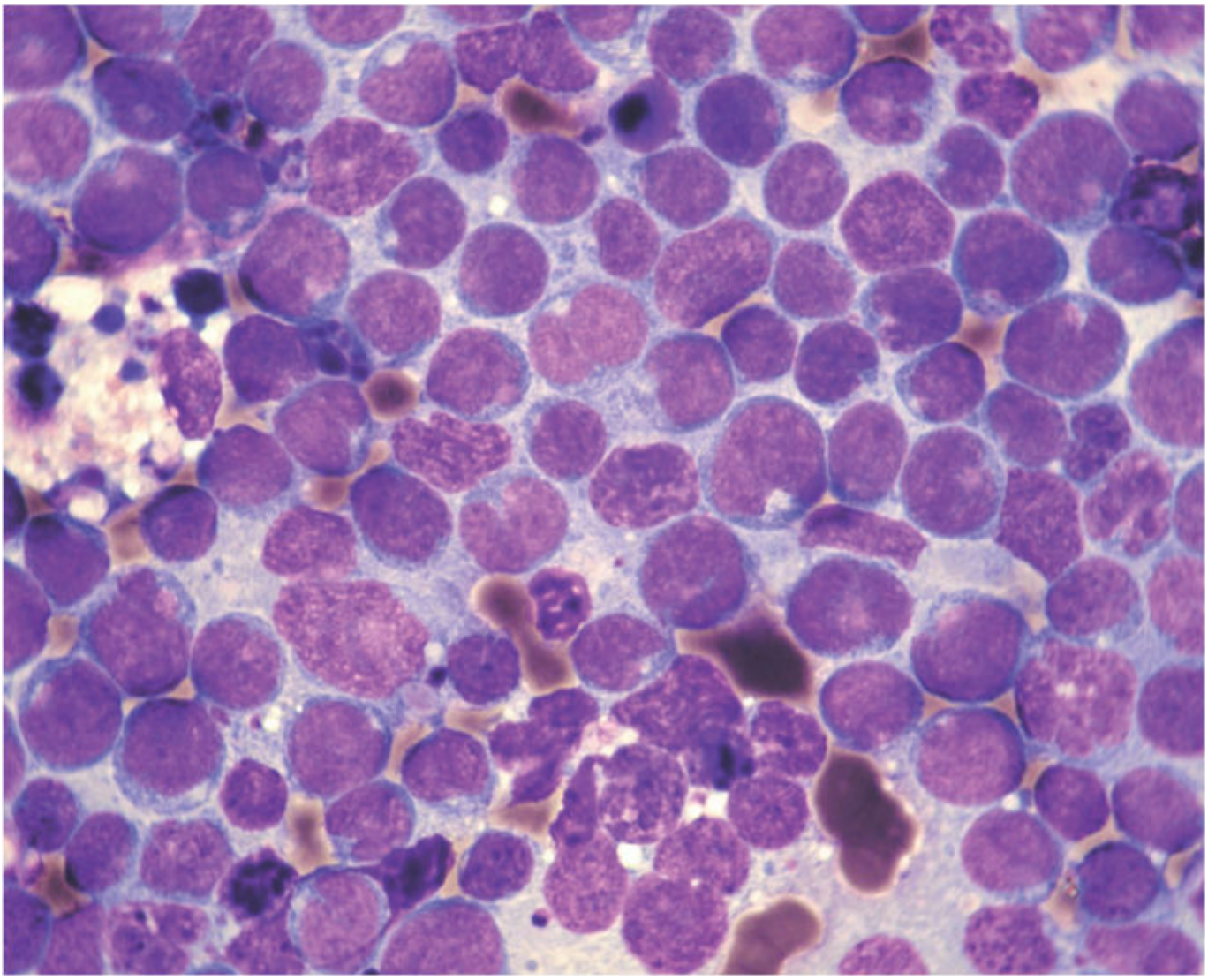
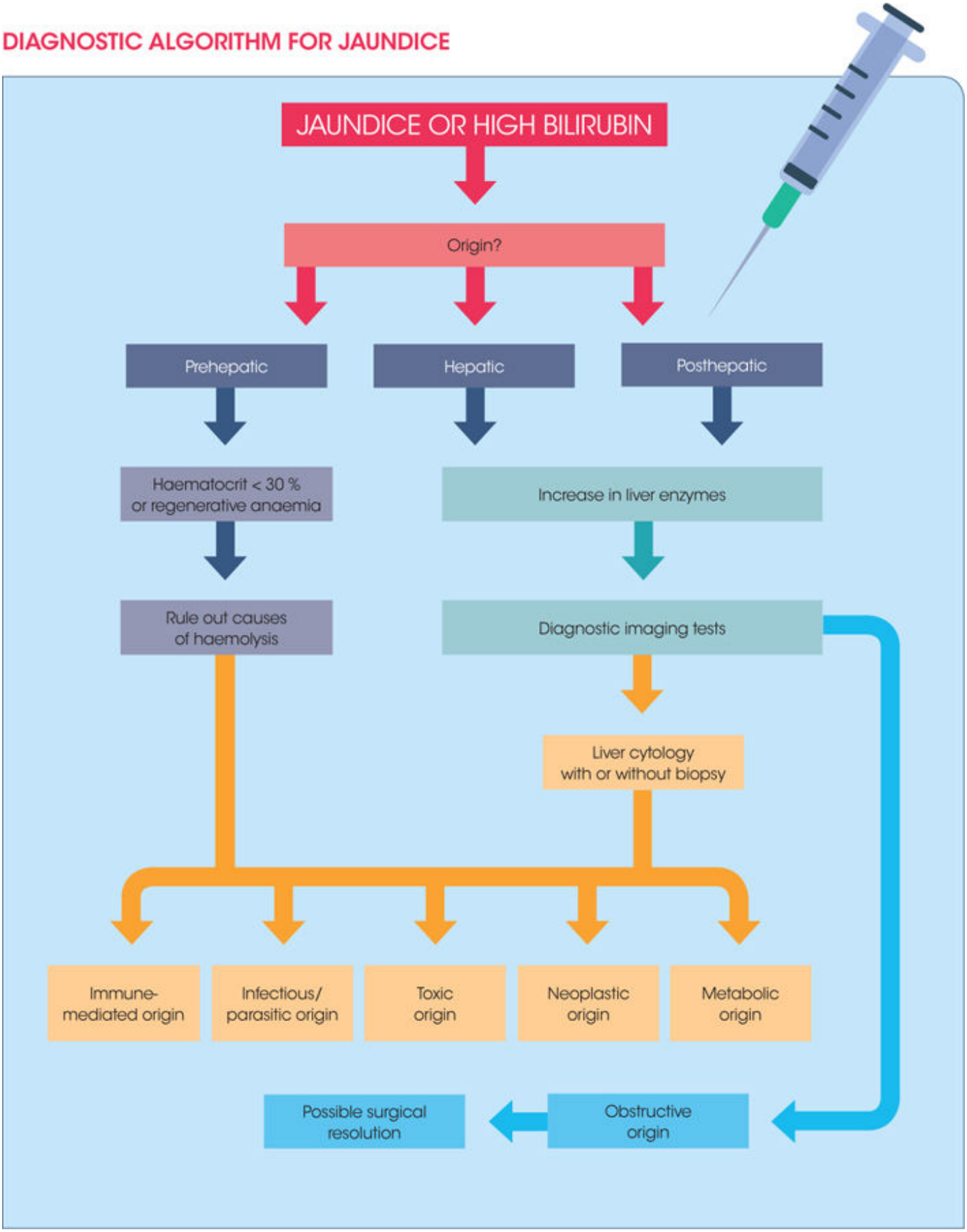


FIGURE 3. A fine-needle aspiration biopsy of the liver showed the presence of abundant medium/large lymphoblasts.

DIAGNOSTIC ALGORITHM FOR JAUNDICE



BRIEF REVIEW OF…

CANINE HEPATIC LYMPHOMA

CAN THERE BE AN EXCLUSIVELY HEPATIC LYMPHOMA?

Lymphomas correspond to 24 % of all tumours in dogs. Multicentric lymphomas are the most common, constituting 80 % of all lymphomas. This type can affect one or several peripheral lymph nodes, as well as the liver, spleen, or bone marrow. However, lymphoma can appear in isolated locations such as the nasal cavity, urinary tract, or liver, as in the present case. There is little information about isolated lymphomas.

IF A MULTICENTRIC LYMPHOMA CAN AFFECT THE LIVER, HOW CAN IT BE DISTINGUISHED FROM A PRIMARY HEPATIC LYMPHOMA?

Most multicentric lymphomas involve one or more peripheral lymph nodes and, subsequently or concurrently, the liver or spleen. Sometimes there is no evidence of peripheral lymphadenopathy and in such cases the primary origin is believed to be in the affected organ. The liver, as a haematopoietic organ, may give rise to leukaemia because it possesses pluripotent cells.

WHICH PHENOTYPE USUALLY AFFECTS THE LIVER IN DOGS?

T-cell lymphomas are the most common phenotype to affect the liver and tend to present atypical markers. The World Health Organization currently recognises two forms of hepatic lymphoma: hepatocytotropic and hepatosplenic T-cell lymphomas. They are believed to follow different clinical courses. Hepatosplenic lymphomas feature lymphocytes on the hepatic and splenic sinusoids, whereas in the hepatocytotropic form, the lymphocytes usually invade the hepatic cords as well.

IS IT EASY TO IDENTIFY HEPATIC LYMPHOMA WITH DIAGNOSTIC IMAGING?

Several ultrasound and tomography studies have reported that splenic lymphoma tends to produce ultrasound changes suggestive of an alteration in the organ, while it is often hard to observe any significant changes in the case of hepatic lymphoma and a cytological analysis is always required to rule out or confirm lymphoma.

DO MULTICENTRIC LYMPHOMAS AND HEPATIC LYMPHOMAS HAVE THE SAME PROGNOSIS?

One study assessed the response to chemotherapy in patients with primary hepatic lymphomas and found that survival was worse in multicentric cases, with an average survival time of 63 days. The authors identified hypoalbuminaemia or hyperbilirubinaemia and an incomplete response to the treatment as factors for a worse prognosis. Animals with the hepatosplenic form were liable to a poorer prognosis.

RECOMMENDED READING

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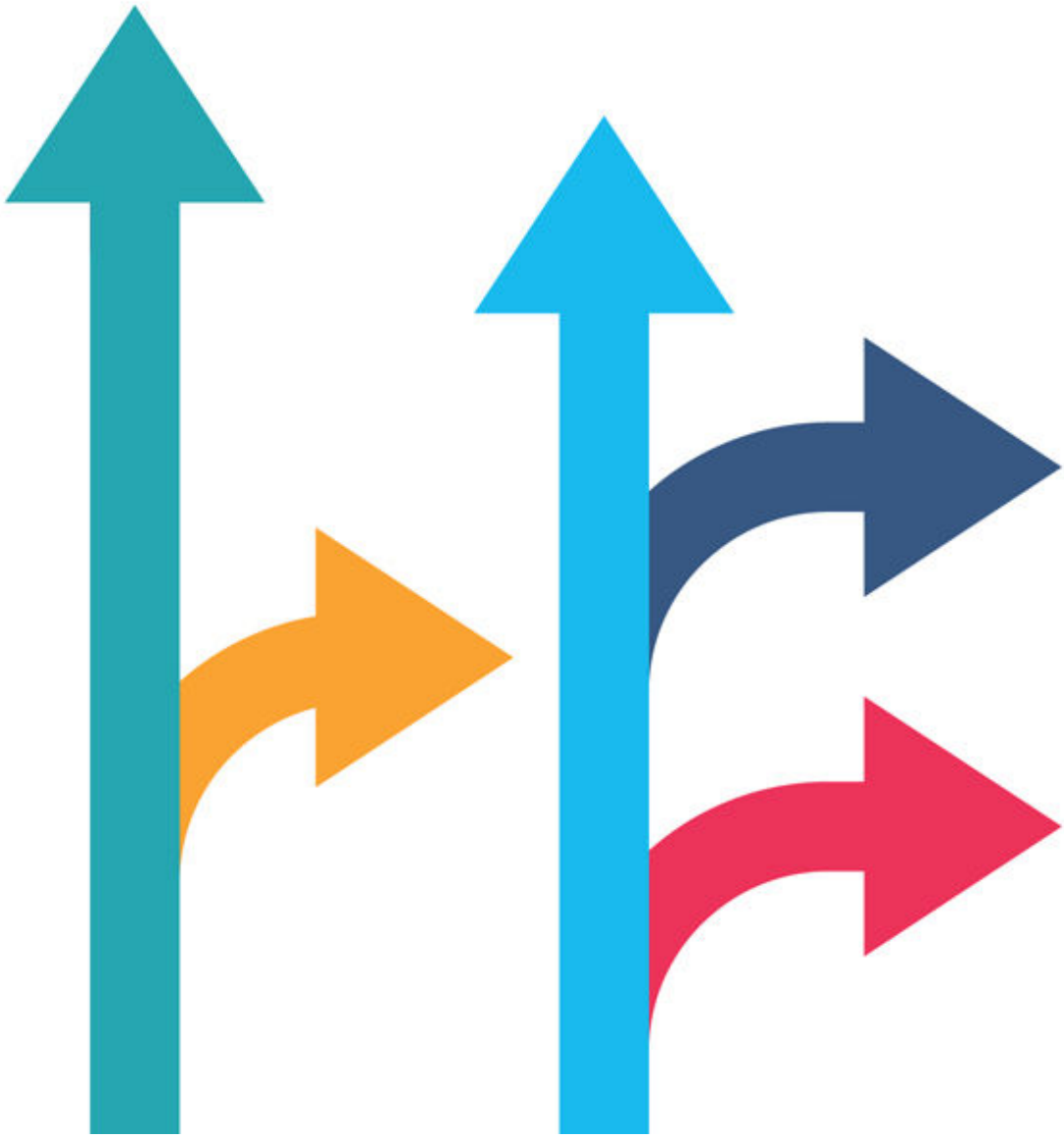
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CLINICAL REASONING IN A CASE OF RESPIRATORY DISTRESS

8



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8 CLINICAL REASONING IN A CASE OF RESPIRATORY DISTRESS

CLINICAL CASE
RESPIRATORY DISTRESS

S **, an entire female common European kitten around 3 months old, was brought to our clinic having suffered from tachypnoea for 3 days and anorexia over the last 24 hours. The patient was taken in from the street 1 month before the consultation in apparently healthy condition. The veterinarian completed deworming and external antiparasitic treatment then administered the first dose of trivalent vaccine.**

In the physical examination, *S* had respiratory distress (inspiratory and expiratory) accompanied by severe tachypnoea (140 bpm) and slight generalised crackling noted upon pulmonary auscultation. No other relevant findings were observed in the rest of the exam.



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REASONING APPLIED TO THE CASE

Based on the available information, go through the first two steps of clinical reasoning:
1. Identify the animal's problems.
1. Prioritise the problems .



1. IDENTIFYING THE ANIMAL'S PROBLEMS

The patient has the following problems:
- Respiratory distress
- Tachypnoea
- Pulmonary crackles
- Anorexia

2. PRIORITISE THE PROBLEMS

In this case, it seems reasonable to assume that the respiratory distress, tachypnoea, and pulmonary crackles are related and correspond to the patient's main problems. The anorexia is probably secondary to the respiratory process.

Take these premises and proceed with the next two steps in the clinical reasoning procedure:
3. Structure and organise the animal's problem.
4. Individualise the diagnostic plan.





3. STRUCTURING AND ORGANISING THE PROBLEM (DIFFERENTIAL DIAGNOSIS)

The initial approach to a patient with respiratory distress includes locating the affected regions and creating a list of preliminary differential diagnoses based on the anamnesis and findings from the physical examination. Determining the location is essential for the best possible management of the problem.

So, when dealing with a patient such as *S* , we need to answer the following questions.

How can we detect the presence of respiratory distress?

Respiratory distress and tachypnoea (increase in respiration frequency) are closely related, as frequency and the effort required to breath increase as compensatory mechanisms to cope with respiratory failure. A patient with these signs may also exhibit mouth breathing (an indication of severe respiratory failure in cats), cyanotic mucosae, increased breath sounds, anxiety, distressed facial expression, orthopnoeic position (extension of the head and neck in dogs, sphinx position in cats), and paradoxical respiration (the abdomen and chest move in opposite directions with each breath).

What causes respiratory distress?

We know that breathing is the process in which carbon dioxide is exchanged for oxygen. This requires coordination between the regulatory (receptors at both a central and peripheral level that are sensitive to changes in CO_2 , O_2 , and temperature) and anatomical elements (airways and respiratory muscles), followed by adequate oxygen transport to the tissues.

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Based on the origin, that is, which element is affected, respiratory distress can be classified as:

1. **Upper respiratory diseases:** oral cavity, pharynx, larynx, and extrathoracic trachea. These cases are often characterised by inspiratory dyspnoea and rales, stridor, or cough. Some examples include laryngeal paralysis, brachycephalic syndrome, hypothyroid patients, upper respiratory tract neoplasms, trauma, and inflammation, etc. Patients with these problems cannot dissipate heat, so close attention must be paid to the possibility of hyperthermia.
2. **Lower respiratory diseases:** intrathoracic trachea and bronchi. Typical signs of these problems are expiratory effort and wheezing upon auscultation; patients may have a cough. For example: feline asthma or chronic bronchitis in dogs.
3. **Parenchymal lung diseases:** involving the bronchi, interstitium, alveoli, and vasculature. There is a notable increase in breath sounds and crackling can be detected upon auscultation. This classification includes cases of pulmonary oedema, pneumonia (bacterial, viral, parasitic, haematogenous), neoplasms, etc.
4. **Pulmonary thromboembolism (PTE):** in the case of PTE, it is essential to identify and treat the underlying cause and reduce the risk of its recurrence. Any process involving systemic inflammation can result in a procoagulant state that predisposes patients to PTE.
5. **Pleural cavity diseases:** these patients exhibit a restrictive respiratory pattern, in other words, short, shallow breathing cycles and paradoxical respiration. It may be impossible to auscultate heart and lung sounds during the physical examination. Some examples are pneumothorax, haemothorax, chylothorax, pyothorax, diaphragmatic hernia, etc.
6. **Rib cage alterations:** respiratory distress in these patients is due to the destabilisation of ribcage structures and courses with a lot of pain as well as concurrent alterations such as pulmonary contusion or pneumothorax. Examples include flail chest or penetrating wounds.
7. **Abdominal distension:** the pressure the abdomen exerts on the chest prevents the lungs from expanding during inspiration. These patients normally have tachypnoea rather than dyspnoea and the abdominal distension is evident.
8. **Respiratory distress-like syndromes:** although known by this expression, they do not originate within the respiratory system. For example, behavioural changes such as fear or excitation, or metabolic disorders such as respiratory acidosis, anaemia, hypotension, and hyperthermia.

Another means of classifying dyspnoea, and which can be carried out rapidly in the physical examination, is observing the **respiratory pattern** . As we have already seen, there are diseases with characteristic respiratory patterns, although there is a lot of variation and each case may present more than one pattern. The main respiratory patterns are:

1. **Inspiratory effort:** characterised by inspiratory sounds (rales, stridor, cough), mouth breathing, dilated nostrils, and the corner of the mouth withdrawn caudally. This pattern is seen in animals with obstructive diseases of the upper airways or lung parenchyma, heart diseases, neuromuscular disorders, pulmonary thromboembolism, and acute anaemia.
2. **Expiratory effort:** breathing is also audible and deep, with an abdominal component. It is associated with obstructive intrathoracic disease caused by bronchial damage (trauma/contusion, asthma, collapse, etc.), intrathoracic tracheal injury (trauma/contusion, collapse, oesophageal or tracheal obstruction), etc.
3. **Restrictive breathing:** characterised by rapid breathing, with very little expansion of the rib cage and no associated sounds. The most common problems that give rise to this type of pattern are pleural cavity alterations, loss of chest wall integrity, and neuromuscular issues.
4. **Inspiratory and expiratory effort:** there is not usually any associated breath sounds and the respiratory effort is similar to previous patterns. It is a sign of lower respiratory and lung parenchyma disorders, as well as nonrespiratory system alterations: cardiac, neuromuscular, metabolic (uraemia, metabolic acidosis, heatstroke), or systemic conditions (shock, haemorrhaging, sepsis).

So, when faced with a patient with respiratory distress, we should ask ourselves:

- **Is there greater inspiratory or expiratory effort?**
- **Can we hear any obvious sounds?**
- **Is breathing rapid and shallow?**
- **Does the rib cage move in coordination with the respiration?**





4. INDIVIDUALISE THE DIAGNOSTIC PLAN

With regard to *S* 's problems, anorexia is a nonspecific sign that can appear in practically any disease or stressful situation; therefore, our plan will focus on the respiratory distress with tachypnoea and crackling sounds. The patient's condition requires rapid action and a careful assessment.

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What is the approach with such a patient?

The first step is to check that the patient has an open airway, adequate breathing, a stable cardiovascular system, and does not show any signs of pain or neurological deficit. By minimising the animal's level of stress we can perform minimally invasive or tolerable procedures such as a quick chest or abdominal ultrasound and, if they tolerate it, a blood sample should be drawn, a peripheral catheter inserted, sedation administered (if necessary), and oxygen provided while the vet performs examination, auscultation, and palpation:

- **Examination** to identify *S* 's respiratory pattern:
  - Difficulty: yes, mixed (inspiratory/expiratory)
  - Frequency: tachypnoea
  - Noisy breathing: no
  - Thoracoabdominal synchrony: yes
- **Auscultation** , systemic and bilateral:
  - Heart: no murmur, normal heart rate, no arrhythmia
  - Lung fields: increased sounds, mild crackling sounds.
- **Palpation** in search of rib cage abnormalities:
  - Chest wall compromise: no

By narrowing down and characterising *S* 's respiratory distress, we can individualise the diagnostic plan and focus on a parenchymal lung disease. The possible differential diagnoses for *S* are shown below.

DIFFERENTIAL DIAGNOSIS FOR MIXED RESPIRATORY DISTRESS AND PARENCHYMAL LUNG DISEASES

- Cardiogenic or noncardiogenic pulmonary oedema
- Pneumonia (viral, bacterial, parasitic)
- Pulmonary contusion
- Pulmonary haemorrhage due to coagulopathies
- Neoplasm
- Pulmonary thromboembolism

What is most likely in *S* 's case?

Given that she is a young animal from an uncontrolled environment, with an incomplete vaccination plan, and does not have any heart murmurs or history of trauma, the most likely diagnosis is infectious pneumonia, although other causes cannot be ruled out without conducting additional tests. In this type of patient, these conditions would account for the other findings such as crackling sounds and tachypnoea due to the presence of material in the alveoli and ventilation/perfusion alterations.

Which additional tests should be considered?

While stabilising the patient, a quick chest ultrasound could be performed to rule out pneumothorax by evaluating the sliding sign to detect any B-lines compatible with alveolar or interstitial patterns due to the present of alveolar material and to discard cavitary effusions. Once the animal is stable, chest X-rays should be taken to determine whether there is a lung pattern and its distribution, and to rule out the presence of any masses. A blood analysis is also recommendable, including an arterial blood gas test to assess the patient's acid–base balance, oxygenation, and ventilation and a blood count to detect white cell alterations or anaemia (e.g. due to cavitary bleeding or thrombocytopaenia), as is a blood chemistry analysis and a urinalysis.

In such cases, and particularly in young animals, it is important to perform a stool test with both sedimentation and faecal flotation to rule out the presence of any parasites responsible for a respiratory infection. In *S* 's case, the presence of acute dyspnoea is suggestive of acute decompensation more than an acute process in itself, so we cannot rule out the possibility of a chronic process.



5. ESTABLISH A DEFINITIVE DIAGNOSIS OR REASSESS THE DIFFERENTIAL DIAGNOSIS

The test results were:

- Blood count: no significant findings.
- Blood chemistry: no significant findings.
- FeLV/FIV tests: negative.
- Chest X-rays (Fig. 1): there is a multifocal and diffuse alveolar pattern in various lung lobes compatible with pneumonia of a parasitic, bacterial, viral, or fungal

origin; while less probable causes are haemorrhaging, contusion, or pulmonary oedema.

After assessing *S* 's X-rays, a stool test was performed and revealed numerous *Aelurostrongylus* spp. larvae, leading to a definitive diagnosis of verminous pneumonia.

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FINAL TREATMENT PLAN AND EVOLUTION

Treatment was based on the administration of anthelmintic drugs to eliminate the parasite and its larval forms. The patient progressed favourably, healing completely after a few weeks of treatment.

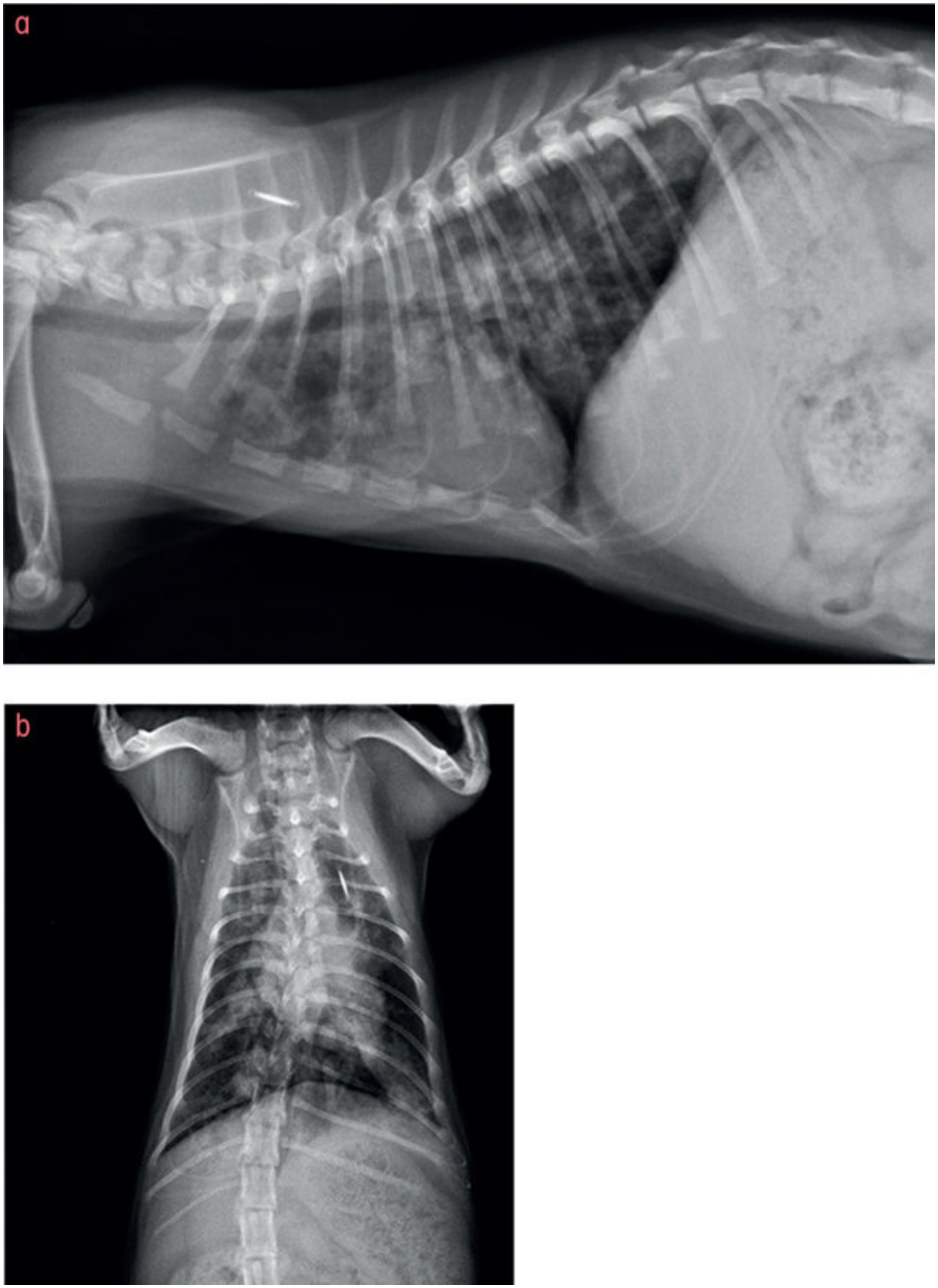
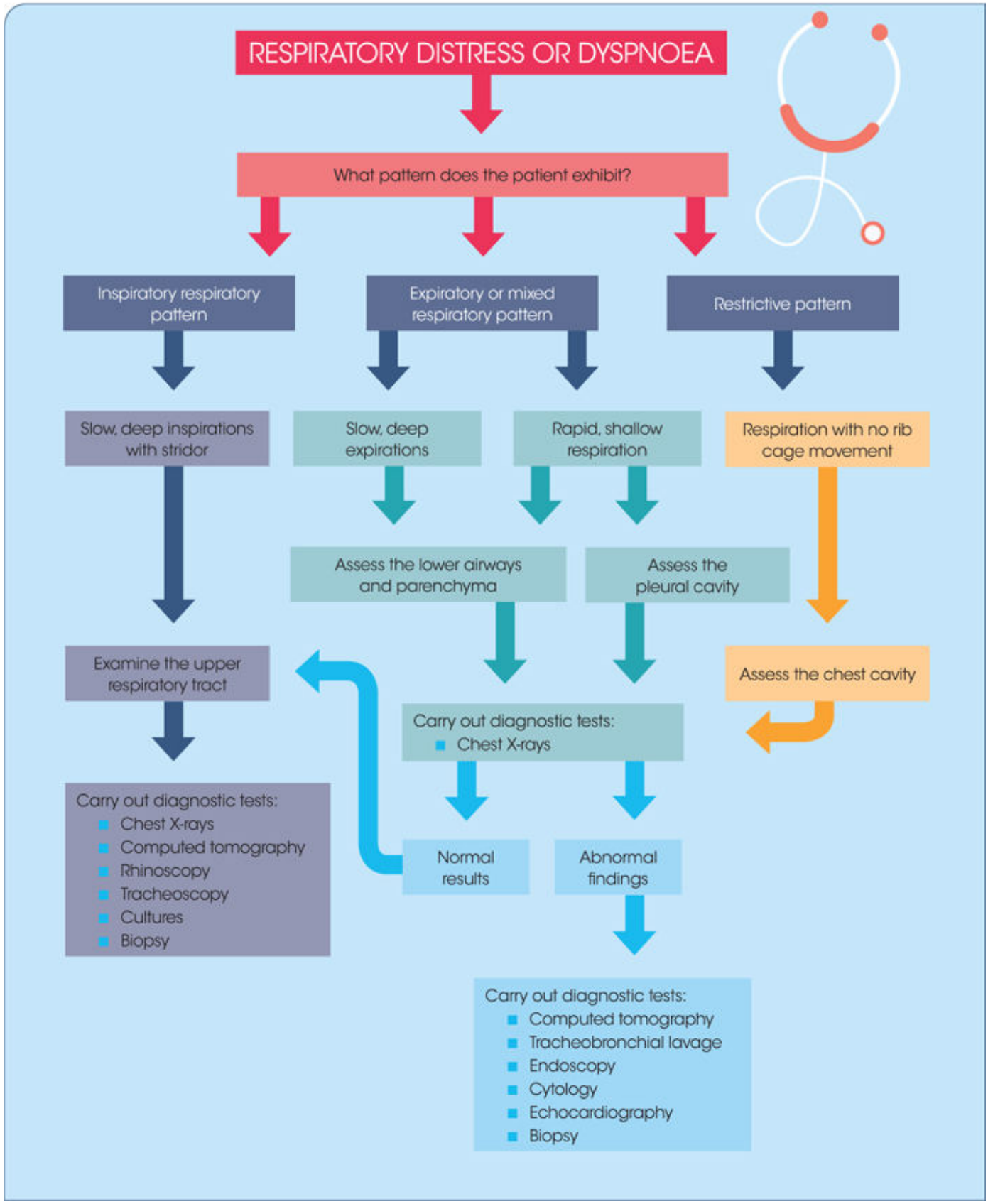


FIGURE 1. Lateral (a) and ventrodorsal (b) chest X-rays of the patient showing a multifocal, diffuse alveolar pattern in the lung lobes.

DIAGNOSTIC ALGORITHM FOR RESPIRATORY DISTRESS (DYSPNOEA)



BRIEF REVIEW OF…

PULMONARY PARASITOSIS IN CATS

WHICH LUNG PARASITES ARE IMPORTANT IN CATS?

Aelurostrongylus abstrusus, Troglostrongylus brevior , and *Capillaria aerophila* (also known as *Eucoleus aerophilus*) are currently considered the most significant lung parasites with the broadest distribution.

IS IT POSSIBLE TO DIFFERENTIATE BETWEEN THEM OR OTHER LUNG DISEASES BASED ON CLINICAL SIGNS?

The clinical signs derive from bronchopulmonary effects similar to feline asthma; in fact, it is easy to confuse the two if this point is not considered in the differential diagnosis. It is impossible to differentiate between the parasites based on the clinical presentation.

With *A. abstrusus* , the clinical signs depend on several factors such as the degree of infestation, the animal's overall health and its immune response. So, animals may have a subclinical infection or show moderate to severe signs sometimes including fatal cases of pneumonia in young or immunocompromised animals. The most common clinical signs vary depending on the factors explained earlier, but they include cough, sneezing, haemoptysis, nasal discharge, dyspnoea, tachypnoea, as well as apathy and weight loss in more severe cases.

In the case of *C. aerophila* , the infection courses with no clinical signs or affected animals may suffer respiratory distress. Adult parasites cause lesions to the trachea and lungs, giving rise to clinical signs similar to those triggered by *A. abstrusus* . Patients tend to have a dry cough that is complicated by opportunistic bacterial infections.

T. brevior infections are more common in young animals; the clinical signs are akin to those caused by the two previous parasites and depend on the same factors. Potentially irreversible pulmonary hypertension has also been described in the case of *T. brevior* infections.

WHICH OTHER PARASITES CAN CAUSE COUGH?

In general, all intestinal nematodes can have stages of larva migrans that affect the lungs. Infections caused by *Dirofilaria immitis* , *Angiostrongylus vasorum* , and some protozoa such as *Toxoplasma* spp. can also produce respiratory signs.

HOW ARE THEY TRANSMITTED?

Animals become infected with *C. aerophila* by ingesting larvae in the environment (in the cough or faeces of infected animals) or by eating infected earthworms. Earthworms are considered intermediate hosts. Infections due to *Aelurostrongylus* and *Troglostrongylus* are caused by the ingestion of intermediate hosts (snails, slugs) or parasitised hosts such as mice, birds, lizards, or snakes. Vertical transmission from infected mothers to their offspring has been reported in the case of *Troglostrongylus* .

WHAT CHANGES ARE REVEALED BY CHEST X-RAYS?

In mild cases, chest X-rays may appear normal, while in more severe cases there is evidence of a diffuse interstitial or alveolar peribronchial pattern.

WHICH ARE THE BEST DIAGNOSTIC TECHNIQUES FOR DETECTING LUNG DISEASES CAUSED BY PARASITES?

Currently, the most reliable diagnostic techniques are stool tests and tracheobronchial lavage, but parasites can sometimes be observed in lung cytology. The stool test comprises the sedimentation test or Baermann technique, although this test requires 12–24 hours to allow the larvae to migrate correctly. It is important to analyse several different samples when conducting stool tests, as larvae can be eliminated intermittently.

The morphological study of L1 larvae can be used to identify the parasite involved in the lung condition. However, *Aelurostrongylus* and *Troglostrongylus* can have common features, which complicates differentiation. Therefore, the use of new diagnostic tools such as PCR is recommended to help better identify the parasites, and nowadays it can even be used for the diagnosis as it offers a high sensitivity and specificity.

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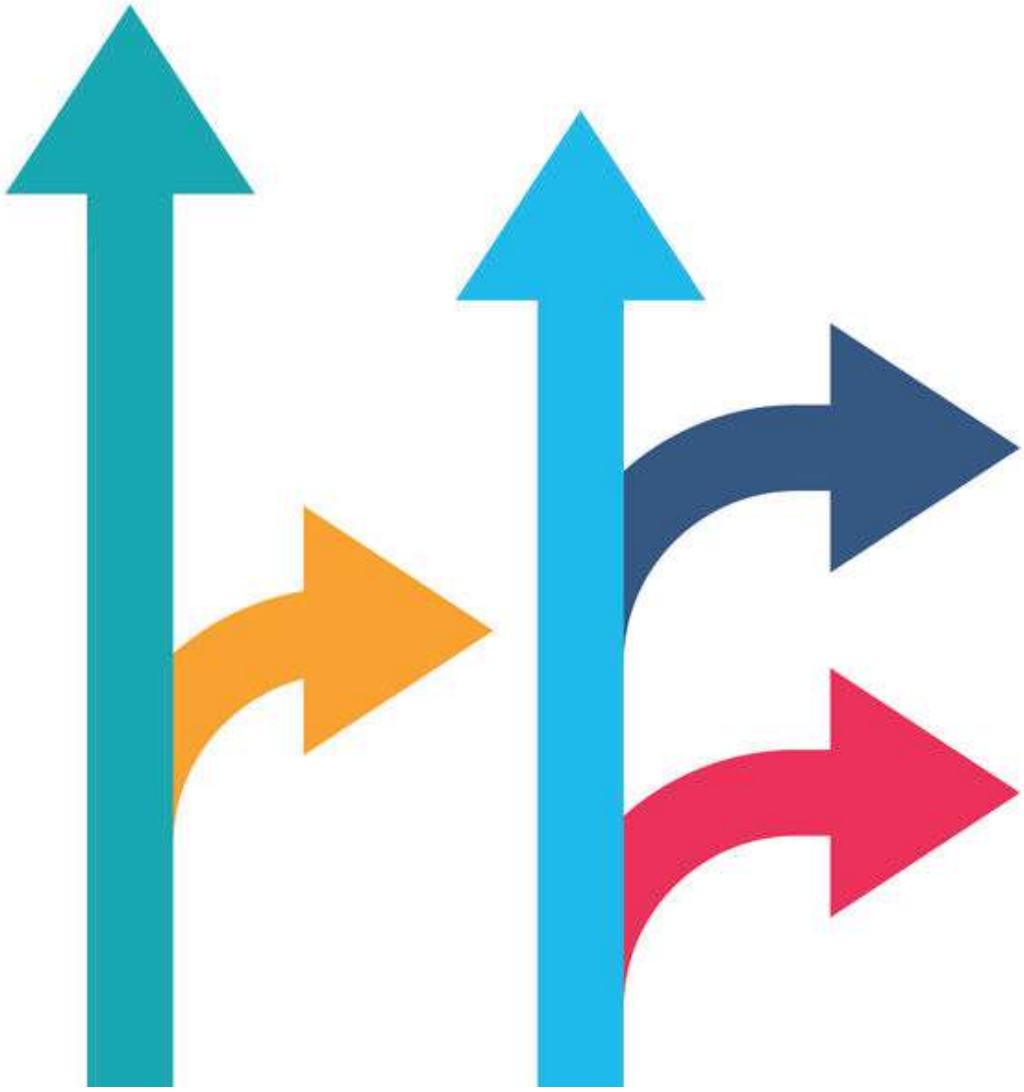
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CLINICAL REASONING IN A CASE OF RESPIRATORY DISTRESS

8



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8 CLINICAL REASONING IN A CASE OF RESPIRATORY DISTRESS

CLINICAL CASE
RESPIRATORY DISTRESS

_S_ , an entire female common European kitten around 3 months old, was brought to our clinic having suffered from tachypnoea for 3 days and anorexia over the last 24 hours. The patient was taken in from the street 1 month before the consultation in apparently healthy condition. The veterinarian completed deworming and external antiparasitic treatment then administered the first dose of trivalent vaccine.

In the physical examination, _S_ had respiratory distress (inspiratory and expiratory) accompanied by severe tachypnoea (140 bpm) and slight generalised crackling noted upon pulmonary auscultation. No other relevant findings were observed in the rest of the exam.



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REASONING APPLIED TO THE CASE

Based on the available information, go through the first two steps of clinical reasoning:
1. Identify the animal's problems.
1. Prioritise the problems .





1. IDENTIFYING THE ANIMAL'S PROBLEMS

The patient has the following problems:
- Respiratory distress
- Tachypnoea
- Pulmonary crackles
- Anorexia



2. PRIORITISE THE PROBLEMS

In this case, it seems reasonable to assume that the respiratory distress, tachypnoea, and pulmonary crackles are related and correspond to the patient's main problems. The anorexia is probably secondary to the respiratory process.

Take these premises and proceed with the next two steps in the clinical reasoning procedure:
3. Structure and organise the animal's problem.
4. Individualise the diagnostic plan.





3. STRUCTURING AND ORGANISING THE PROBLEM (DIFFERENTIAL DIAGNOSIS)

The initial approach to a patient with respiratory distress includes locating the affected regions and creating a list of preliminary differential diagnoses based on the anamnesis and findings from the physical examination. Determining the location is essential for the best possible management of the problem.

So, when dealing with a patient such as *S* , we need to answer the following questions.

How can we detect the presence of respiratory distress?

Respiratory distress and tachypnoea (increase in respiration frequency) are closely related, as frequency and the effort required to breath increase as compensatory mechanisms to cope with respiratory failure. A patient with these signs may also exhibit mouth breathing (an indication of severe respiratory failure in cats), cyanotic mucosae, increased breath sounds, anxiety, distressed facial expression, orthopnoeic position (extension of the head and neck in dogs, sphinx position in cats), and paradoxical respiration (the abdomen and chest move in opposite directions with each breath).

What causes respiratory distress?

We know that breathing is the process in which carbon dioxide is exchanged for oxygen. This requires coordination between the regulatory (receptors at both a central and peripheral level that are sensitive to changes in CO_2 , O_2 , and temperature) and anatomical elements (airways and respiratory muscles), followed by adequate oxygen transport to the tissues.

Based on the origin, that is, which element is affected, respiratory distress can be classified as:

1. **Upper respiratory diseases:** oral cavity, pharynx, larynx, and extrathoracic trachea. These cases are often characterised by inspiratory dyspnoea and rales, stridor, or cough. Some examples include laryngeal paralysis, brachycephalic syndrome, hypothyroid patients, upper respiratory tract neoplasms, trauma, and inflammation, etc. Patients with these problems cannot dissipate heat, so close attention must be paid to the possibility of hyperthermia.
2. **Lower respiratory diseases:** intrathoracic trachea and bronchi. Typical signs of these problems are expiratory effort and wheezing upon auscultation; patients may have a cough. For example: feline asthma or chronic bronchitis in dogs.
3. **Parenchymal lung diseases:** involving the bronchi, interstitium, alveoli, and vasculature. There is a notable increase in breath sounds and crackling can be detected upon auscultation. This classification includes cases of pulmonary oedema, pneumonia (bacterial, viral, parasitic, haematogenous), neoplasms, etc.
4. **Pulmonary thromboembolism (PTE):** in the case of PTE, it is essential to identify and treat the underlying cause and reduce the risk of its recurrence. Any process involving systemic inflammation can result in a procoagulant state that predisposes patients to PTE.
5. **Pleural cavity diseases:** these patients exhibit a restrictive respiratory pattern, in other words, short, shallow breathing cycles and paradoxical respiration. It may be impossible to auscultate heart and lung sounds during the physical examination. Some examples are pneumothorax, haemothorax, chylothorax, pyothorax, diaphragmatic hernia, etc.
6. **Rib cage alterations:** respiratory distress in these patients is due to the destabilisation of ribcage structures and courses with a lot of pain as well as concurrent alterations such as pulmonary contusion or pneumothorax. Examples include flail chest or penetrating wounds.
7. **Abdominal distension:** the pressure the abdomen exerts on the chest prevents the lungs from expanding during inspiration. These patients normally have tachypnoea rather than dyspnoea and the abdominal distension is evident.
8. **Respiratory distress-like syndromes:** although known by this expression, they do not originate within the respiratory system. For example, behavioural changes such as fear or excitation, or metabolic disorders such as respiratory acidosis, anaemia, hypotension, and hyperthermia.

Another means of classifying dyspnoea, and which can be carried out rapidly in the physical examination, is observing the **respiratory pattern** . As we have already seen, there are diseases with characteristic respiratory patterns, although there is a lot of variation and each case may present more than one pattern. The main respiratory patterns are:

1. **Inspiratory effort:** characterised by inspiratory sounds (rales, stridor, cough), mouth breathing, dilated nostrils, and the corner of the mouth withdrawn caudally. This pattern is seen in animals with obstructive diseases of the upper airways or lung parenchyma, heart diseases, neuromuscular disorders, pulmonary thromboembolism, and acute anaemia.
2. **Expiratory effort:** breathing is also audible and deep, with an abdominal component. It is associated with obstructive intrathoracic disease caused by bronchial damage (trauma/contusion, asthma, collapse, etc.), intrathoracic tracheal injury (trauma/contusion, collapse, oesophageal or tracheal obstruction), etc.
3. **Restrictive breathing:** characterised by rapid breathing, with very little expansion of the rib cage and no associated sounds. The most common problems that give rise to this type of pattern are pleural cavity alterations, loss of chest wall integrity, and neuromuscular issues.
4. **Inspiratory and expiratory effort:** there is not usually any associated breath sounds and the respiratory effort is similar to previous patterns. It is a sign of lower respiratory and lung parenchyma disorders, as well as nonrespiratory system alterations: cardiac, neuromuscular, metabolic (uraemia, metabolic acidosis, heatstroke), or systemic conditions (shock, haemorrhaging, sepsis).

So, when faced with a patient with respiratory distress, we should ask ourselves:

- **Is there greater inspiratory or expiratory effort?**
- **Can we hear any obvious sounds?**
- **Is breathing rapid and shallow?**
- **Does the rib cage move in coordination with the respiration?**





4. INDIVIDUALISE THE DIAGNOSTIC PLAN

With regard to *S* 's problems, anorexia is a nonspecific sign that can appear in practically any disease or stressful situation; therefore, our plan will focus on the respiratory distress with tachypnoea and crackling sounds. The patient's condition requires rapid action and a careful assessment.

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What is the approach with such a patient?

The first step is to check that the patient has an open airway, adequate breathing, a stable cardiovascular system, and does not show any signs of pain or neurological deficit. By minimising the animal's level of stress we can perform minimally invasive or tolerable procedures such as a quick chest or abdominal ultrasound and, if they tolerate it, a blood sample should be drawn, a peripheral catheter inserted, sedation administered (if necessary), and oxygen provided while the vet performs examination, auscultation, and palpation:

- **Examination** to identify *S* 's respiratory pattern:
  - Difficulty: yes, mixed (inspiratory/expiratory)
  - Frequency: tachypnoea
  - Noisy breathing: no
  - Thoracoabdominal synchrony: yes
- **Auscultation** , systemic and bilateral:
  - Heart: no murmur, normal heart rate, no arrhythmia
  - Lung fields: increased sounds, mild crackling sounds.
- **Palpation** in search of rib cage abnormalities:
  - Chest wall compromise: no

By narrowing down and characterising *S* 's respiratory distress, we can individualise the diagnostic plan and focus on a parenchymal lung disease. The possible differential diagnoses for *S* are shown below.

DIFFERENTIAL DIAGNOSIS FOR MIXED RESPIRATORY DISTRESS AND PARENCHYMAL LUNG DISEASES

- Cardiogenic or noncardiogenic pulmonary oedema
- Pneumonia (viral, bacterial, parasitic)
- Pulmonary contusion
- Pulmonary haemorrhage due to coagulopathies
- Neoplasm
- Pulmonary thromboembolism

What is most likely in *S* 's case?

Given that she is a young animal from an uncontrolled environment, with an incomplete vaccination plan, and does not have any heart murmurs or history of trauma, the most likely diagnosis is infectious pneumonia, although other causes cannot be ruled out without conducting additional tests. In this type of patient, these conditions would account for the other findings such as crackling sounds and tachypnoea due to the presence of material in the alveoli and ventilation/perfusion alterations.

Which additional tests should be considered?

While stabilising the patient, a quick chest ultrasound could be performed to rule out pneumothorax by evaluating the sliding sign to detect any B-lines compatible with alveolar or interstitial patterns due to the present of alveolar material and to discard cavitary effusions. Once the animal is stable, chest X-rays should be taken to determine whether there is a lung pattern and its distribution, and to rule out the presence of any masses. A blood analysis is also recommendable, including an arterial blood gas test to assess the patient's acid–base balance, oxygenation, and ventilation and a blood count to detect white cell alterations or anaemia (e.g. due to cavitary bleeding or thrombocytopaenia), as is a blood chemistry analysis and a urinalysis.

In such cases, and particularly in young animals, it is important to perform a stool test with both sedimentation and faecal flotation to rule out the presence of any parasites responsible for a respiratory infection. In *S* 's case, the presence of acute dyspnoea is suggestive of acute decompensation more than an acute process in itself, so we cannot rule out the possibility of a chronic process.



5. ESTABLISH A DEFINITIVE DIAGNOSIS OR REASSESS THE DIFFERENTIAL DIAGNOSIS

The test results were:

- Blood count: no significant findings.
- Blood chemistry: no significant findings.
- FeLV/FIV tests: negative.
- Chest X-rays (Fig. 1): there is a multifocal and diffuse alveolar pattern in various lung lobes compatible with pneumonia of a parasitic, bacterial, viral, or fungal

origin; while less probable causes are haemorrhaging, contusion, or pulmonary oedema.

After assessing *S* 's X-rays, a stool test was performed and revealed numerous *Aelurostrongylus* spp. larvae, leading to a definitive diagnosis of verminous pneumonia.

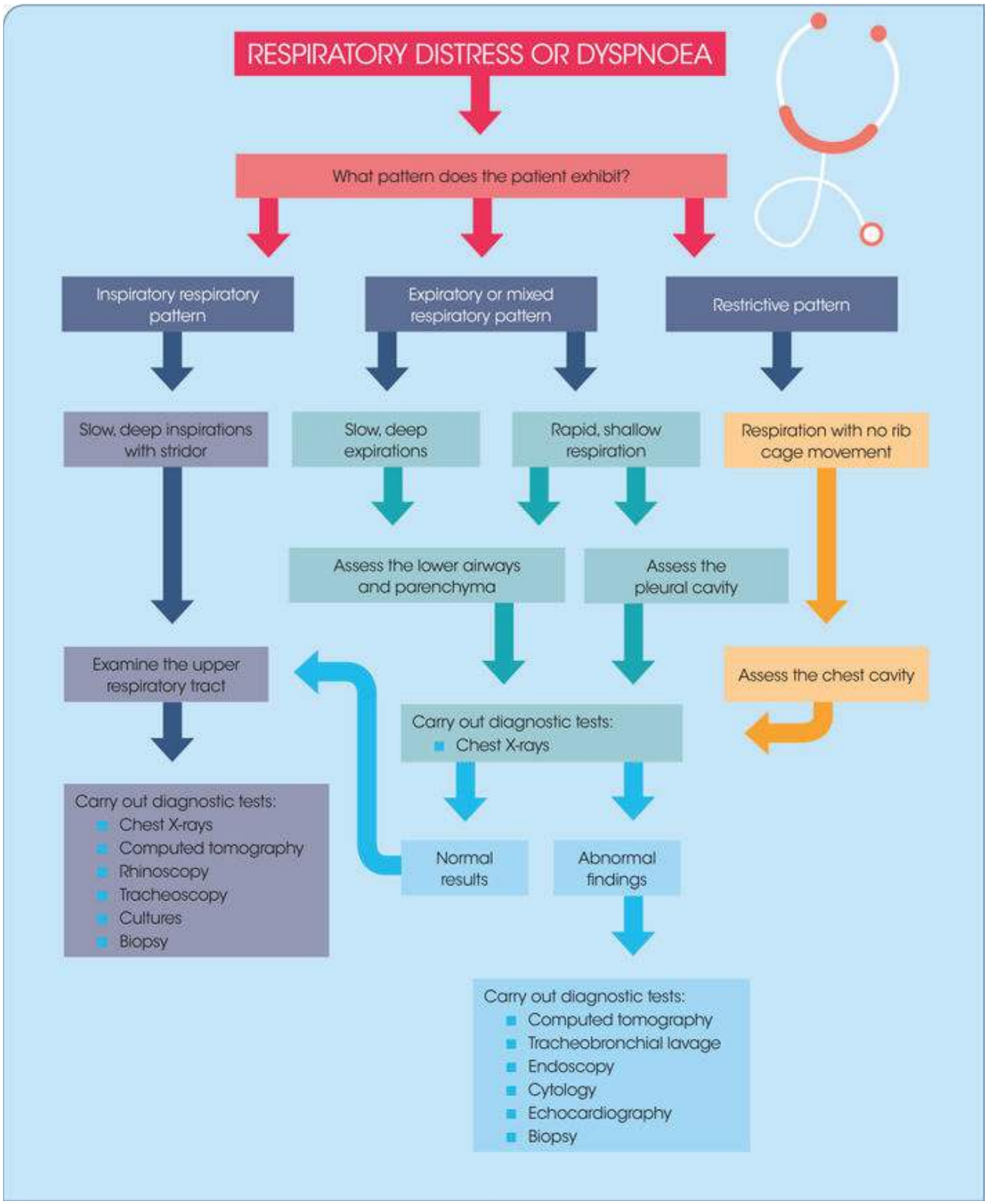
FINAL TREATMENT PLAN AND EVOLUTION

Treatment was based on the administration of anthelmintic drugs to eliminate the parasite and its larval forms. The patient progressed favourably, healing completely after a few weeks of treatment.



FIGURE 1. Lateral (a) and ventrodorsal (b) chest X-rays of the patient showing a multifocal, diffuse alveolar pattern in the lung lobes.

DIAGNOSTIC ALGORITHM FOR RESPIRATORY DISTRESS (DYSPNOEA)



BRIEF REVIEW OF…

PULMONARY PARASITOSIS IN CATS

WHICH LUNG PARASITES ARE IMPORTANT IN CATS?

Aelurostrongylus abstrusus, Troglostrongylus brevior , and *Capillaria aerophila* (also known as *Eucoleus aerophilus*) are currently considered the most significant lung parasites with the broadest distribution.

IS IT POSSIBLE TO DIFFERENTIATE BETWEEN THEM OR OTHER LUNG DISEASES BASED ON CLINICAL SIGNS?

The clinical signs derive from bronchopulmonary effects similar to feline asthma; in fact, it is easy to confuse the two if this point is not considered in the differential diagnosis. It is impossible to differentiate between the parasites based on the clinical presentation.

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The morphological study of L1 larvae can be used to identify the parasite involved in the lung condition. However, *Aelurostrongylus* and *Troglostrongylus* can have common features, which complicates differentiation. Therefore, the use of new diagnostic tools such as PCR is recommended to help better identify the parasites, and nowadays it can even be used for the diagnosis as it offers a high sensitivity and specificity.

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