

## How reliable is your diagnosis?

Probability-theoretical considerations of uncertain examination results and expert opinions

## Wie belastbar ist Deine Diagnose?

Wahrscheinlichkeitstheoretische Betrachtungen unsicherer Untersuchungsergebnisse und gutachterlicher Äußerungen

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### ABSTRACT

The effectiveness and justification of every therapy and other clinical decisions is based on a correct diagnosis. However, many types of test results can contain uncertainties that may lead to clinically incorrect decisions. The same applies to the reliability of expert opinions for legal disputes. Adequate communication of diagnostic and expert uncertainties in the examination report or expert opinion is therefore crucial for avoiding incorrect decisions. The liability of the person providing the service is also affected. However, uncertain or even erroneous findings can have various causes, only some of which are known to the examining or commissioning person. This article provides an overview of 3 different types of susceptibility to errors using the example of pathological biopsy and cytology examinations, which can also be transferred to other veterinary disciplines in a similar way. A solid understanding of the possible sources of error as well as adequate communication and discussion of case-specific, limited probabilities in investigation reports and expert opinions make a significant contribution to avoiding incorrect decisions. However, commonly used terms such as “highly probable”, “suspected” or “cannot be ruled out” are sometimes interpreted in unclear or divergent ways, which are explained here with recommendations for uniform use. This is intended to enable the person making the decision, if necessary, to initiate further diagnostic

tests or gather further evidence in the context of all other available data in order to reduce the risk of error as far as possible.

## ZUSAMMENFASSUNG

Die Effektivität und Rechtfertigung jeder Therapie und anderer klinischen Entscheidungen basieren auf einer korrekten Diagnose. Doch viele Arten von Untersuchungsergebnissen können Unsicherheiten enthalten, die unter Umständen zu klinischen Fehlentscheidungen führen können. Ähnliches gilt für die Belastbarkeit von Gutachten für gerichtliche Auseinandersetzungen. Daher ist die adäquate Mitteilung diagnostischer und gutachterlicher Unsicherheiten im Untersuchungsbericht bzw. Sachverständigenutachten entscheidend für die Vermeidung von Fehlentscheidungen. Auch die Haftbarkeit der Person, die die Leistung erbringt, ist davon betroffen. Unsichere oder gar fehlerhafte Befunde können jedoch diverse Ursachen haben, von denen nur ein Teil der untersuchenden oder der beauftragenden

Person bekannt sind. Dieser Beitrag bietet eine Übersicht über 3 verschiedene Arten von Fehleranfälligkeiten am Beispiel pathologischer Biopsie- und Zytologieuntersuchungen, die so oder ähnlich auch auf andere tierärztliche Disziplinen übertragbar sind. Ein solides Verständnis der möglichen Fehlerquellen sowie die adäquate Kommunikation und Diskussion fallspezifischer, eingeschränkter Wahrscheinlichkeiten in Untersuchungsberichten und Gutachten tragen wesentlich dazu bei, Fehlentscheidungen zu vermeiden. Bei den üblicherweise eingesetzten Begriffen wie „mit hoher Wahrscheinlichkeit“, „Verdacht auf“ oder „nicht auszuschließen“ bestehen jedoch teils unklare bis abweichende Interpretationen, die hier mit Empfehlungen für einen einheitlichen Gebrauch erläutert werden. Damit soll die entscheidende Person in die Lage versetzt werden, im Kontext aller übrigen verfügbaren Daten nötigenfalls weitere Diagnostik bzw. Beweiserhebung zu veranlassen, um die Irrtumswahrscheinlichkeit so weit wie möglich zu reduzieren.

## Introduction and background

Sometimes it is a matter of momentous decisions: Is the cost-intensive therapy justified? Should the leg be amputated? Can only euthanasia end the suffering? And in court, it is all about finding an appropriate verdict. However, examination results and forensic expert opinions often contain a certain degree of uncertainty due to insufficient data, which can lead to misjudgements. Against this background, an area of tension regularly arises between the expectations of the client and the actual feasibility of a probability statement. Knowledge of the various types and causes of uncertainties and their appropriate communication in individual cases can therefore help to avoid incorrect decisions.

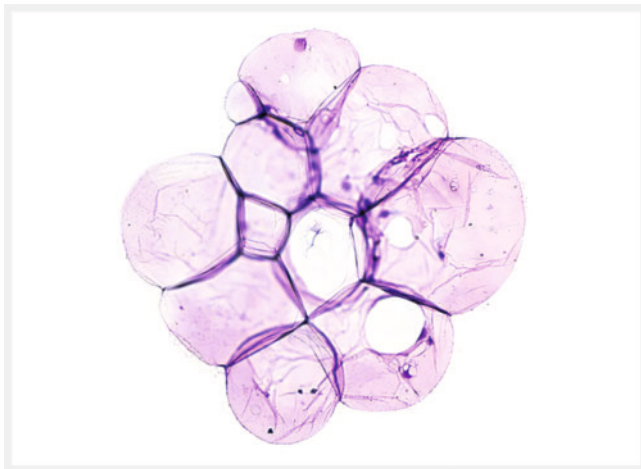
Uncertainties and the risk of misjudgement due to incomplete data are an integral part of many veterinary activities. However, they are unpleasant and are therefore often suppressed, overlooked or not communicated, which can lead to a wide range of inappropriate consequences for humans and animals. Certain diagnostic disciplines are more sus-

ceptible to this than others. The more complex the basis for an assessment, the more prone to error it must be assumed to be. In radiology, for example, inconsistency between diagnosticians is considered to be its most important Achilles heel [1]. In pathological biopsy, cytology and autopsy diagnostics in particular, a large number of influencing factors can limit the certainty of judgment in the case of ambiguous findings. In view of the increasing desire of patient owners for maximum diagnostic and therapeutic care and at the same time an increased tendency towards legal disputes in the event of treatment failure, certainty of judgment is likely to become increasingly important. An even higher level of complexity and thus the probability of error can be assumed for some forensic assessment procedures. But are we aware of them and do we always deal with them appropriately?

► **Table 1** In principle, 3 different types of uncertainties can be considered, which have different consequences for their recognition and communication.

► **Tab. 1** Prinzipiell können 3 verschiedene Arten von Unsicherheiten betrachtet werden, die unterschiedliche Konsequenzen für ihre Erkennung und Kommunikation haben.

Type	Sources of uncertainty
Type 1	Uncertainties that are inherent in the method and are generally known to professionals. In principle, they are foreseeable and should therefore be taken into account when selecting the method used. Such uncertainties can be influenced to a limited extent both during sampling and when carrying out the test procedure.
Type 2	Case-typical or case-specific uncertainties resulting from insufficient diagnostically relevant information from the sample or from the information on which the expert opinion is based. The examiner recognizes this uncertainty and formulates a vague opinion. Non liquet statements are used in the examination report or an intuitive, subjective and rough assessment of a probability based on the terms listed in ► <b>Table 2</b> . This expresses the competence and uniqueness of the investigator [1]. The consequence of such uncertainties may be a recommendation for further investigations or the procurement of information in court proceedings.
Type 3	Uncertainties due to bias and noise that are usually not apparent to either the person commissioning the study or the person conducting the study. These can distort the results of the study systematically and directionally (bias) or randomly and undirected (noise) [1]. Both often remain unrecognized but can be reduced by procedural hygiene measures.



► **Fig. 1** The reliability of a cytological diagnosis depends in particular on the representativeness of the sample and the accompanying information in the examination order. The sample shown here (400x magnification) will usually lead to the diagnosis of “lipoma” in the case of a brief clinical report such as “dog, cutaneous mass”. However, depending on the exact localization of the sample and the clinical context, it could also be unchanged subcutaneous adipose tissue, a well-differentiated but infiltrative lipoma, omentum parts in an umbilical hernia or pelvic cavity adipose tissue in a perineal hernia. The final diagnosis requires consideration of the overall clinical context. Source: Achim D. Gruber.

► **Abb. 1** Die Belastbarkeit einer zytologischen Diagnose hängt auch von der Repräsentativität der Probe und den Begleitinformationen im Untersuchungsauftrag ab. Das hier abgebildete Muster (600-fache Vergrößerung) wird bei einem kurzen Vorbericht wie „Hund, Umfangsvermehrung Haut“ üblicherweise zur Diagnose „Lipom“ führen. Je nach genauer Entnahmelokalisation und klinischem Kontext könnte es sich jedoch auch um unverändertes Unterhautfettgewebe, ein gut differenziertes, aber infiltratives Lipom, Omentumanteile in einer Nabelhernie oder Beckenhöhlenfettgewebe in einer Perinealhernie handeln. Die finale Zuordnung erfordert eine Betrachtung im klinischen Gesamtkontext. Quelle: Achim D. Gruber.

## Sources of uncertainty

The reliability of an assessment of vague or complex relationships is based on a variety of factors, including personal expertise (education and training, experience, etc.), active self-questioning, cognitive abilities and the quality of the structured approach to the analysis [1]. At the same time, numerous procedural and case-specific sources of interference often affect the result. These will be divided into 3 types here for systematic consideration of their causes and with a view to their communicability: 1) foreseeable, process-specific uncertainties, 2) case-specific, recognizable uncertainties and 3) uncertainties that are not expected or recognizable (► **Table 1**).

Such a differentiation is crucial for the professional handling of susceptibility to errors in everyday veterinary and forensic practice, among other things by sharpening the focus on the responsibilities, accountabilities and, not least, liabilities of all parties involved. In each individual case, however, all 3 types are to be expected as sources of error to a greater or lesser extent, with an additive effect on the overall uncertainty.

Dealing with uncertainties and sources of error probably requires greater attention.

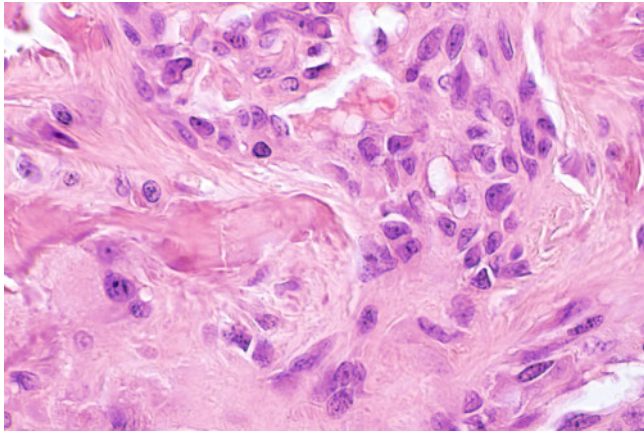
These relationships are illustrated below using the example of microscopic biopsy and cytology examinations.

## Type 1: Foreseeable, process-typical uncertainties

Histological examination is generally regarded as the gold standard in the diagnosis of most tumors, forms of inflammation and other tissue changes. The clear identification of specific microscopic patterns allows the pathologist in most cases to make a clear assignment to a specific entity, its cause, in the case of tumors the assessment of a complete excision, the expected course (prognosis) and many other aspects relevant to decision-making. What is the susceptibility to error here, assuming good expertise and excluding any sample mix-ups? The representativeness of the sample for the entirety of the change is decisive. Even in basic veterinary studies, students are taught that a histological specimen is only a few  $\mu\text{m}$  thick. If you imagine a typical canine skin tumor to be the size of a gymnasium, the pathologist would look at a thumb-thick, roughly centrally located slice of it under the microscope. Even if a second, perpendicular plane is used to assess the resection margins, 99.9 % of the tumor remains unseen. The consequences for the reliability of the assessment of the resection margin are obvious. Nevertheless, this degree of representativeness is sufficient for most histological examinations.

The situation is different for inhomogeneous or more complex lesions. Frequent examinations also include removed canine spleens with masses suspicious of tumor growth. Hematomas often represent the lion’s share of the volume of the mass, whereas the actual cause, such as a life-threatening hemangiosarcoma or only a nodular hyperplasia of the white pulp typical for aged patients, may be very small [2]. Consequently, there is an increased risk of a false-negative diagnosis if the much smaller lesion that caused the hemorrhage did not make it under the microscope by chance. In the picture of the gym, the viewer of a few, hopefully representative, sections could easily miss an elephant standing in the corner of the hall. In routine examination practice, this risk can be reduced by thorough lamination and sample selection as well as an increase in the number of microscopic slides. However, there are practical limitations here, which virtually rule out any claim to a reliable, complete examination. The proportion of underdiagnosed splenic tumors is probably underestimated [2].

It is clear from these examples that both the collection of the diagnostic sample by the veterinarian and the sectioning in the pathology department can have a significant effect on the degree of uncertainty of the result. The same has been documented many times for false-negative diagnoses of prostate carcinomas [3] or other small or difficult-to-access changes in humans. This type of susceptibility to error is inherent to the procedure and entity, known and therefore predictable. Since all of this is also the subject of basic veterinary studies, uncertainties in this category can



► **Fig. 2** Example of an uncertain microscopic finding from an osteosarcoma in a dog (HE staining, 400x). Such a specimen is often used to decide whether the limb should be amputated from a few tiny biopsies of a suspected tumor. As shown here, some osteosarcomas in certain regions can show virtually identical patterns to active, reparative and regenerative callus formation after a fracture. As long as there are no clear guidelines for the procedure, the pathologist must decide on the degree of certainty of her or his diagnosis on her or his own responsibility. Second and third opinions as well as additional biopsy examinations may increase the degree of certainty, but the decision to amputate always requires a complex consideration in the overall clinical context. Source: Achim D. Gruber.

► **Abb. 2** Beispiel eines unsicheren mikroskopischen Befundes aus einem Osteosarkom eines Hundes (HE-Färbung, 400-fach). Anhand eines solchen Präparates soll oft aus wenigen, winzigen Biopsien von einer tumorverdächtigen Knochenveränderung entschieden werden, ob die Gliedmaße zu amputieren ist. Wie hier dargestellt, können manche Osteosarkome in bestimmten Regionen quasi identische Muster aufweisen wie eine aktive, reparative und regenerative Kallusbildung nach einer Fraktur. Solange klare Leitlinien für das Vorgehen fehlen, muss die Pathologin eigenverantwortlich über den Sicherheitsgrad ihrer Diagnose entscheiden. Zweit- und Drittmeinungen sowie zusätzliche Biopsieuntersuchungen können diesen erhöhen, jedoch erfordert die Entscheidung über eine Amputation immer ein komplexes Abwägen im klinischen Gesamtkontext. Quelle: Achim D. Gruber.

be assumed to be fundamentally known to veterinarians. As a rule, they no longer need to be disclosed in every specific case. However, there may be justified exceptions, for example in the case of known limitations of a new test procedure.

The same applies with regard to the representativeness of the sample for cytological examinations of fluids or tissue fine needle aspirates (► **Fig. 1**). Since the relationship between sample size and actual extent of the lesion is often even less favorable here and cytological smears usually lack important information, for example on structural tissue context, they are generally considered to be more susceptible to various uncertainties than histological examinations. In principle, these uncertainties are also inherent to the method, can be assumed to be generally known by specialists and are therefore not usually reported unless there is a specific discrepancy with available clinical information. The situation is different in the case of additional, but case-specific and recognizable uncertainties, which are assigned to risk type no. 2.

## Type 2: Case-specific, recognizable uncertainties

Once again, the example of pathology illustrates what may also apply to many other diagnostic disciplines. Even with a high number and high representativeness of microscopic sections of a tumor, diagnostically relevant patterns may be missing or remain vague. For example, histogenetically decisive differentiation criteria may be missing in advanced malignant, de-differentiated tumors. In other cases, it may be difficult to distinguish between reactive hyperplasia and neoplasia due to a lack of decisive patterns (► **Fig. 2**).

The judgment must then inevitably contain a certain degree of uncertainty, which the person making the assessment is aware of. In addition to individual expertise and various interfering factors known as situational noise (see below), such as the current ability to concentrate, experience and intuition ultimately play a decisive role in assessing the degree of uncertainty [1]. Since this type of uncertainty is highly case-specific, the pathologist is aware of it and it is decisive for further clinical decisions, it must be communicated in the report. In the simplest case, this is done with the addition of “suspected” or “suspicious for” associated with the diagnostic judgment, possibly with the mentioning of differential diagnoses. In addition, it may be more valuable to state an estimated *degree of probability*.

As a rule, only type 2 uncertainties should be mentioned in diagnostic reports or expert opinions. In individual cases, however, there may also be reasons to report other obvious uncertainties.

There have been various, often inconsistent and sometimes contradictory proposals for standardized formulations of uncertainty levels in the literature [4–10]. Some of them equate specific terms with percentage probabilities, such as a 95 % certainty in the assessment “with a probability bordering on certainty” [4, 8]. Others assign the term “with high probability” to the same percentage and give a confidence level of 99.99 % for “almost certain” [7]. Still other authors fundamentally reject a reference to a numerical percentage of probability as a pseudo-accuracy and rely solely on the usual meaning of the terms in German language [9]. Although the desire for an assessment similar to a measurement due to the pseudo-objective feeling it conveys is understandable, it is of a dubious nature without a reliable database. Specific or a range of percentages in this regard cannot add precision to a vague estimate and are not compatible with principles of evidence-based medicine.

The Pathology Section of the German Veterinary Medical Society (DVG) saw a need to standardize the terms used. At its Annual General Meeting on March 10, 2024, after discussion and consideration of the options, the standard listed in ► **Table 2** was proposed for the formulation of uncertainty levels. This consensus hardly differs from similar proposals in earlier veterinary standard textbooks [4, 5, 8], but deliberately avoids any reference to percentages.

► **Table 2** Recommended gradation of degrees of probability in the formulation of diagnoses and expert statements. The meaning of the words corresponds to the general understanding of common language use. Equivalent percentages were omitted due to a lack of basis.

► **Tab. 2** Empfohlene Abstufung von Wahrscheinlichkeitsgraden bei der Formulierung von Diagnosen und gutachterlichen Äußerungen. Die Bedeutung der Worte entspricht dem allgemeinen Sprachverständnis. Auf äquivalente Prozentzahlen wird aufgrund fehlender Basis verzichtet.

Degree of probability	
1	certain (diagnosis without further additions) or “diagnostic of”
2	with a probability bordering on certainty
3	with high probability (= highly probable)
4	likely/probable
5	balanced probability (2 or more possibilities appear similarly likely)
6	less likely
7	unlikely (= hardly likely)
8	impossible (= impossible, unthinkable)

No rules or criteria can be formulated for the practical use of the individual terms. Instead, the person making the judgment decides purely subjectively and intuitively using all available information based on their own expertise, experience, literature, etc. It is, so to speak, a professional personal achievement that can, in principle, be questioned.

The assessment of “certain” raises the fundamental question of how certain a diagnosis can actually be. There is no doubt that each diagnosis formulated as “certain” – as an expression of a lack of recognizable differential diagnoses from the current perspective of the person making the judgement – is also subject to all the other uncertainties of types 1 and 3 mentioned here. Although these can never be ruled out as inherent to the procedure and generally known (type 1) or unrecognizable (type 3), they do not need to be explicitly mentioned. This also reflects the individuality and fundamental situational dependence of each diagnosis or expert assessment [1].

## Formulation of probabilities with percentages

Expressing a probability as a percentage can be justified if it is based on scientific evidence. For example, numerous studies have determined the survival probabilities for certain time intervals after a specific tumor diagnosis. With reference to such literature data, it can therefore be appropriate and legitimate to speak of average survival probabilities of XY% after 3, 6 or 9 months after diagnosis. The use of percentage probabilities may be similarly justified for a variety of other scientifically supported medical contexts.

## Formulation of uncertainties without gradual differentiation: *Non liquet* statements

In some cases, an uncertainty is of a more fundamental nature without a recognizable reference to a degree of probability. In such cases, terms known as *non liquet* (Latin for “it is not clear”) formulations are used. They are intended to express the fact that a situation cannot be assessed on the basis of the available data or that an expert question cannot be answered. In other words: there are alternative explanations and further information must be obtained, usually through additional investigations, in order to be able to assess a connection with certainty or at least more certainty. This group includes terms such as “possible”, “suspicious for”, “cannot be ruled out”, “comes into consideration” and “no evidence of”. This category also includes the phrases “resembling”, “indicative of”, “suggestive of”, “consistent with”, and “compatible with”, which may suggest a higher probability to the reader, but are generally regarded as *non-liquet* statements.

Case-specific, recognizable uncertainties should be discussed in the epicrisis/comment section of a diagnostic report or expert opinion, whereby suggestions for solutions to increase certainty can also be submitted to the person commissioning the investigation or the court.

## Consequences in the form of clinical or judicial decisions

All the uncertainties mentioned so far must be taken into account for the clinical decision (such as amputation, complex therapy or euthanasia) in the full complexity of the clinical context, usually also with the involvement of the patient’s owners. The plausibility of each piece of the puzzle and the coherence of the overall picture must always be critically scrutinized by the responsible clinician before a potentially momentous decision is made. In cases of doubt, a dialog with the pathologist can often help in the decision-making process.

The same applies to the judicial verdict, whereby judges are generally free in their case-specific assessment of evidence both in criminal proceedings (Section 261 of the German StPO) and in civil proceedings (Section 286 of the German ZPO). However, the court must regularly rely on experts to provide the deciding judges with expertise in a specific field of knowledge, such as pathology or forensics, which they do not have or do not have in full [11].

The central question in all the areas mentioned is therefore: are the available findings or evidence sufficient for a clinical decision or judgment? If there are doubts about this, further investigations must be carried out or evidence obtained – if possible – before a potentially seriously wrong decision is made in order to increase the level of certainty to the required level.

But how much evidence is enough? In the clinic, it is usually a complex, subjective, sometimes intuitive decision, which always in-



cludes the liability of the person making the decision. You should always be aware of this! If a wrong decision was made that had justifiable consequences, the decision must be justified retrospectively on the basis of all documented evidence in order to avert liability as far as possible. The traceability of the basis for the decision and the conclusions drawn from this basis are crucial for this. The distinction between a service contract and a contract for work can also be of central importance in the consequences of a wrong decision, which depends heavily on the individual case. However, the type of contract does not change the requirements for evidence status.

In the case of expert assessments, the court must reach its own independent conclusion on the basis of the expert opinion by freely assessing the evidence [12]. The term “conviction” already expresses the fact that it is not possible to obtain findings in court that are comparable to scientific or even mathematical evidence. Consequently, the court can also deviate from the expert assessment under certain conditions, provided there are sufficient grounds for doing so in its opinion. Due to its own lack of expertise, the court regularly requires as clear a statement as possible on all questions posed in the expert opinion to be provided. For this reason, in both civil and criminal proceedings, a “certain” or “almost certain” statement is usually considered sufficient (see ► **Table 2**).

The certainty with which judicial questions can be answered depends to a large extent on the specific wording of the question. In this respect, it can be helpful to discuss the court’s questions with the responsible judge and, if necessary, to reformulate them together. In this way, optimally formulated questions can make it easier to convince the judge, which can depend heavily on the expertise of the expert person. The expert can and should act in an advisory capacity here.

## Conflicts between expectations and certainty

Several circumstances could lead pathologists to commit themselves in their judgment more often than would be justified. Ultimately, those commissioning an examination expect the result to be as clear as possible, justifying a clear clinical decision. Any uncertainty formulated in the process leads either to an increased risk of a clinically incorrect decision or further diagnostic effort, both of which are undesirable. If the examiner repeatedly makes vague diagnoses, her or his competence may be questioned. On the other hand, the pathologist may have a strong interest in protecting her- or himself against subsequent liability claims, which is best achieved by verbally limiting the certainty of the diagnosis. Depending on their mentality and experience, we therefore also know colleagues who either conspicuously often secure themselves in this respect with “suspected...” diagnoses or who commit themselves too often and thus have to accept the consequences of their own misdiagnoses.

Forensic experts are exposed to similar tensions when the court expects them to be “certain” or “almost certain” in their conclusions (see ► **Table 1**). However, the high complexity of many cases with numerous unknown influencing factors often leads serious and critical experts to place greater restrictions on their assessments than would be desirable in the eyes of the court for a clear verdict. In the end, the burden of decision always lies with the person providing the expert opinion as to whether he or she pragmatically contributes to a speedy procedure and possibly runs the risk of making a wrong decision, or whether reasonable doubt is grant-

ed appropriate room in accordance with the principle *in dubio pro reo* – and not least to safeguard against subsequent liability claims. In both clinical and forensic settings, professional competence, experience, structured procedural hygiene and consistent objectivity can help to avoid serious mistakes for all parties involved [1].

## Type 3: Unanticipated and unrecognizable uncertainties

A large number of other causes are known for deviations in the assessment of vague estimates, i. e. estimates with a certain degree of freedom. These have already been systematically investigated for medical and other areas of life and can be divided into 2 subtypes: *Bias* and *noise*[1]. The authors are not aware of any systematic studies on this in veterinary medicine, but by analogy with many other fields of activity with comparable decision-making processes, similar correlations must be assumed for our profession.

Bias leads to a mostly directional deviation due to a systematic error, comparable to the incorrect adjustment of a measuring device. Bias in various veterinary disciplines, such as pathology and forensics, can be caused by a lack of specialist knowledge, for example if the examiner is unaware of certain patterns in the assessment of malignant tumors. As a result, malignant neoplasms may regularly be underdiagnosed. On the other hand, personal traumatic experiences may possibly lead to certain entities being overdiagnosed, for example if a previous misdiagnosis is painfully remembered.

Noise refers to random, undirected and undesirable deviations from the ideal judgment as a result of general life influences that are usually not perceived appropriately. Stress, fatigue, temporarily reduced ability to concentrate due to discomfort or personal grief are well-known causes that are also likely to play a not insignificant role in veterinary medicine. Depending on the cause and effect, a distinction is made between different types of noise [1], which will not be discussed in detail here.

Bias and noise generally have independent and additive effects on the overall degree of uncertainty [1]. Their consequences have been well studied in numerous fields of medicine, for example in relation to intra-observer variability and inter-observer variability in the formulation of vague or difficult diagnoses or the assessment of the proportion of actively dividing cells in a tumor [13, 14]. Here, repeated assessments by the same person at longer intervals or simultaneous assessments by different examiners can lead to sometimes significantly different results. However, bias and noise are regarded as “invisible enemies” that are usually unknown to those involved in the specific situation, but whose systematic combating is worthwhile in any case [1]. But how?

## Measures to reduce uncertainty

A solid understanding of the sources of uncertainty described here and a constant awareness of their possible presence should lead all those involved to deal with them appropriately. This article is intended to contribute to this. In addition, there are numerous targeted options for reducing certain sources of error [1].

A large number of process-oriented, structured quality assurance measures can be taken under the term “procedural hygiene”.

These include Standard Operating Procedures (SOP) for all steps of sample collection, processing and examination, both for automated and manual processes. For example, during surgical tumor removal, the validity of the histological assessment regarding its complete removal can be increased by marking the regions of concern to the surgeon with differently colored suture material or different numbers of knots made by the surgeon. In the pathology laboratory, the risk of false-negative findings of small tumors in a larger splenic hematoma can be countered by precise instructions for “complete lamination in 0.5 cm thick slices and embedding of all suspicious changes for microscopic examination”. Guidelines for microscopic findings have also been formulated in some disciplines for the most complete possible collection and communication of diagnostically relevant criteria [15–17]. Such guidelines may also provide for commenting on the quality and representativeness of the sample material obtained as part of quality feedback to the person taking the sample [16].

Even such SOPs can never completely rule out certain residual risks, as there are often limits to the effort required under practical conditions. The same applies to the number of tumor bed biopsies that can be examined in the case of cutaneous mass, the number of cytological preparations that can be examined and many similar scenarios. Here, the degree of representativeness of the samples can often be increased, but absolute certainty can never be achieved. Particularly in veterinary medicine, the costs incurred by the patient owners often set narrow limits on the effort required and the certainty that can be achieved.

A common measure to reduce diagnostic uncertainties is to obtain second or even third opinions from competent experts. The use of digitized histological or cytological specimens and sending them or viewing them via the Internet (telepathology) makes this procedure considerably easier. Second opinions should always be obtained impartially, i. e. without prior communication of the initial assessment in question, before a joint discussion of the case may follow. For this purpose, guidelines and standardized diagnostic algorithms are increasingly being used in human medicine, which are aimed at the measures to be taken to confirm the diagnosis in the case of uncertain findings. These include immunohistochemical or molecular procedures and, importantly, the taking and examination of further biopsies. Such guidelines can limit the scope for individual discretion and thus sources of error. Although second opinions and the follow-up examinations mentioned as examples are already common practice in veterinary medicine, structured guidelines for their use are still largely lacking.

Risks associated with diagnostic uncertainties can be reduced by, among other measures,

- knowledge of their types and causes,
- high quality training, experience, and continuing education,
- structured procedural hygiene,
- an actively self-questioning working style and
- open communication with the client.

Quantum leaps in the reduction of uncertainties are expected in the future from the use of computers, in particular artificial intelligence (AI), especially in the evaluation of complex images such as in radiology, pathology and cytology. However, most approaches in veterinary medicine are still in the testing phase [14]. However, many experts agree that AI will not be able to replace human judgment in more complex decision-making processes – at least not in the near future [1].

Despite all the procedural possibilities, a structured approach and the self-critical mind of a well-trained and experienced person remain the key elements in reducing errors. Increasing professional specialization can also be a great advantage, as long as one’s own competence limits are taken into account. Added to this is a solid knowledge of the sources of error described in this article, a case-specific consideration of them and the open communication of recognizable uncertainties with the client.

## Note

This is a reprint of an article that was first published in the *Deutsches Tierärzteblatt* (*Deutsches Tierärzteblatt* 2024; 72(7): 829–834).

## Conflict of interest

The authors declare no conflict of interest.

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