Colloids and Surfaces B: Biointerfaces 208 (2021) 112092

Contents lists available at ScienceDirect

Colloids and Surfaces B: Biointerfaces

journal homepage: www.elsevier.com/locate/colsurfb

Diagnostic tests based on pattern formation in drying body fluids – A mapping review

Maria Olga Kokornaczyk [a,b,*], Natalia Borisovna Bodrova [b], Stephan Baumgartner [a,c,d]

[a] Society for Cancer Research, 4144, Arlesheim, Switzerland
[b] International Research Group on Very Low Dose and High Dilution Effects (GIRI), Dornach, Switzerland
[c] Institute for Integrative Medicine, University of Witten/Herdecke, Herdecke, Germany
[d] University of Bern, Institute of Complementary and Integrative Medicine, Bern, Switzerland

ARTICLE INFO

Keywords:
Diagnostic test
Patterns
Crystallization test
Desiccating body fluids
Ferning

ABSTRACT

There are numerous diagnostic tests based on pattern formation in desiccating body fluids, where the pattern or some of its characteristics constitute the diagnostic test outcome. However, partially due to the development in different time periods, and partially due to publications in languages different from English, most of these diagnostic tests exist as separate approaches and have never been grouped, systematized, nor compared with each other. In the present mapping review, we performed a wide literature search with the aim to collect all diagnostic tests based on pattern formation in desiccating body fluids. Furthermore, we grouped the identified diagnostic tests according to their experimental protocols, type of body fluids investigated, and target conditions, and propose so for the first time a classification of different diagnostic tests based on pattern formation in desiccating body fluids. The literature search revealed 1603 publications, out of which 141 were included into the review. Following three main classification criteria (way of deposition of the fluid for desiccation, addition of reagents, and spatial restrictions during evaporation), we identified six different methods; following a further classification concerning the analyzed body fluid we identified 30 different diagnostic tests based on pattern formation in evaporating body fluids. Amongst these tests are well-known procedures such as ferning tests (tear ferning for the assessment of tear film quality, saliva and cervical mucus ferning for the detection of the fertile period, and amniotic fluid ferning for the diagnosis of fetal membrane rupture), whereas other tests are less well-established. In the latter group, the most frequently investigated body fluids were serum, saliva, and blood; the most frequently addressed target conditions were cancer, inflammation, and benign tumors. We recommend conducting further systematic reviews and meta-analyses concerning groups of methods addressing the same target condition.

1. Introduction

Pattern formation in desiccating body fluids has triggered the interest of scientists for many years. According to our knowledge, the first publication regarding this topic, addressing the evaporation-induced formation of NaCl crystals in solutions containing urea, was by Jean-Baptiste Romè de l'Isle in 1783 [1]. Since then, literally all body fluids, including secretions (tears, saliva, sweat, urine, cervical mucus, sperm, wound leakages, discharges), liquid biopsies (blood, cerebrospinal fluid, follicular fluid, pleural effusion), and blood derivatives (serum and plasma) have been studied for their pattern forming characteristics in the course of desiccation. The studies focused mainly on the detection of structural differences in dried residues of body fluids obtained from diseased vs. control donors, and the potential of such differences for medical diagnosis (diagnostic test based on pattern formation in desiccating body fluids; further on called diagnostic patterning test, DPT).

Many different DPTs have been developed, varying in their methodological procedures concerning- besides the body fluid to be analyzed-, also, *inter alia,* its dilution degree, addition of reagents, volume of the body fluid (or solution containing the body fluid) needed to obtain a pattern, way of solution deposition on the substrate before drying, evaporation conditions, and, finally, pattern evaluation procedures. These numerous DPTs represent a highly differentiated field nowadays.

* Corresponding author at: Society for Cancer Research, Kirschweg 9, 4144, Arlesheim, Switzerland.
E-mail address: m.kokornaczyk@vfk.ch (M.O. Kokornaczyk).

https://doi.org/10.1016/j.colsurfb.2021.112092
Received 27 April 2021; Received in revised form 30 August 2021; Accepted 31 August 2021
Available online 1 September 2021

There are tests which are well established and commonly used, and others which still are experimental. Furthermore, there are well-known tests, but also tests with limited dissemination, for instance due to the language of publication being other than English (mainly Russian or German), or because they were developed, and are mostly still used, in small and rather closed scientific communities. Finally, there are tests where the working principle is clear, and others where it is partially or completely unknown. The lacking cohesion of different DPTs is also due to the fact that a common nomenclature is missing (e.g. the same method can be named differently, for instance, *desiccation of a sitting serum droplet on a glass substrate* may be named *droplet evaporation* or *wedge dehydration* method).

However, despite these differences, all DPTs rely on the same phenomenon and can be considered to represent a single group of methods. Therefore, the aim of the present mapping review [2] is to give a complete overview of all DPTs based on evaporation-induced pattern formation in body fluids and to classify them according to their experimental protocols and the body fluids applied. The publications included serve to identify all DPTs documented in literature. In our opinion, an overview of the different DPTs may have a positive impact on the unification of these approaches; in addition, by comparing the different protocols, new insights into the working principle of these diagnostic tests might be revealed.

2. Materials and methods

2.1. Literature search

Articles, book chapters, and books were collected from scientific databases (PubMed and Web of Science) using the following search terms: (((blood OR serum OR plasma OR biofluid OR “body fluid” OR “bodily fluid”) AND (evaporat* OR desiccat* OR dried OR dry)) OR (“ferning test” OR “crystallization test” OR “crystallisation test” OR “wedge-shaped dehydration” OR “copper chloride crystallization” OR “copper chloride crystallisation” OR “bolen test”)) AND pattern AND diagnos*. The database e-Library Russia was searched with corresponding terms in Russian. Suitable literature was also collected by contacting experts in the research field in question. Additionally, literature reference lists were searched by hand for further relevant publications. Literature regarding the copper chloride biocrystallization method was also collected from the Goetheanum library (Dornach, Switzerland) and E. Pfeiffers Archives (i.e. a collection of scanned articles and documents found in E. Pfeiffers laboratory, USA). Publications in English, German, Russian, French, and Polish were considered. There was no limit regarding publication year. We collected literature regarding diagnostic applications in both human and in veterinary medicine.

2.2. Inclusion criteria

For the present mapping review, we considered (i) experimental studies on the diagnosis of diseases or detection of physiological processes (e.g. fertile period, pregnancy), in which *in vitro* methods based on evaporation-induced pattern formation in body fluids have been applied, and (ii) reviews concerning such experimental studies. Moreover, the result of the diagnostic test had to depend on the pattern characteristics. For veterinary medicine, we included only studies where naturally occurring disorders or physiological processes were investigated.

2.3. Exclusion criteria

We did not consider basic research studies nor commentaries. Experimental studies in which the desiccated residues of biological fluids represented a specimen subjected to further analysis by means of other methods (e.g. spectrometry) were also excluded. Furthermore, publications regarding recognized DPTs were subjected to a restriction in publication number (see: identification of recognized diagnostic pattering tests). Regarding veterinary medicine, studies employing the artificial induction of diseases in animals were excluded.

2.4. Criteria for identification of recognized diagnostic patterning tests

A DPT was considered a recognized approach if (i) there was at least one publication published by a health institution or health organization containing recommendations on the DPT application in diagnostics, or if (ii) there was at least one peer-reviewed publication which used the DPT as a reference standard. These criteria were established for the purpose of the present mapping review.

2.5. Extraction of information from the publications and classification of the experimental protocols

From each included publication, the following information was extracted and listed in a table:

(i) author(s) and publication year,
(ii) way of deposition of the evaporating liquid,
(iii) use of reagents,
(iv) spatial restrictions of the liquid during evaporation,
(v) type of body fluid analyzed,
(vi) target condition, and
(vii) pattern evaluation technique.

Experimental protocols identical in terms of conditions (ii-iv) were considered a method, whereas those identical in conditions (ii-v) were considered a DPT.

This classification was established for the purpose of the present mapping review.

3. Results

3.1. Literature search

As shown in Fig. 1, the literature search of the databases according to the chosen searching terms and other sources identified a total of 1569 publications; further 34 publications were added following the search of the reference list. After removing duplicates and irrelevant literature, 342 publications remained which were subjected to a further screening according to the inclusion criteria. We identified four tests which fulfilled our criteria for recognized diagnostic approaches (ferning tests applied to (i) tears for analysis of the tear film quality [3], (ii) amniotic fluid for the diagnosis of ruptured fetal membranes [4], (iii) saliva [5], and (iv) cervical mucus [6] for the detection of the fertile period), and limited the number of publications of each of these DPTs. Finally, 141 articles, book chapters, books, and case reports establishing the diagnosis of different diseases and physiological states in humans and animals based on pattern formation in desiccating body fluids were identified; these publications were included into the present mapping review.

3.2. Classification of the collected experimental protocols into methods

As shown in Fig. 2a, we first classified the experimental protocols identified into methods according to three following characteristics: (1) mode of liquid deposition, (2) reagents added, and (3) spatial restrictions of the liquid during evaporation.

(1) We identified four different modes of liquid deposition: deposition into (i) films, (ii) smears and swabs, (iii) droplets, and (iv) as bulk liquid in a dish.

(2) The comparison of experimental protocols showed that in most cases no reagents were used and the pattern formation process was

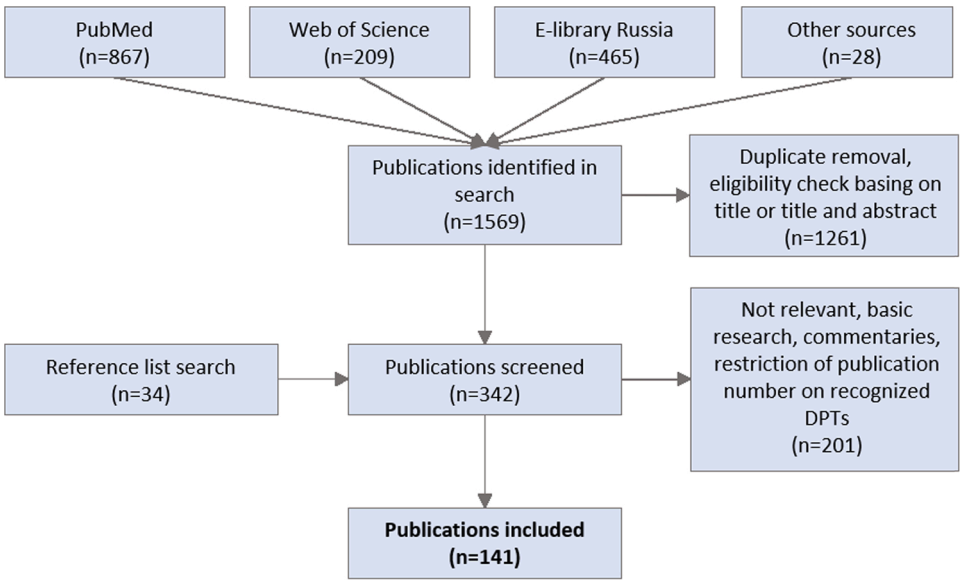


Fig. 1. Flow chart depicting the literature search.

spontaneous; if reagents were added, it was mostly a single type of salt (NaCl, KCl, or $CuCl_2$) which was used to induce crystallization.

(3) The experimental protocols varied regarding spatial restrictions during desiccation of the liquid: (i) in case of films, the body fluid was flattened by means of a cover glass (i.e. restricted from the top), (ii) smears, swamps, and droplets had no other spatial restrictions besides the substrate, and (iii) the bulk liquid was desiccated in a round 100 mm diameter dish (or Petri-dish), i.e. with restrictions along the perimeter.

Based on the comparison of the experimental protocols, a total of six methods could be differentiated: (i) desiccation of body fluid films under a cover glass, (ii) desiccation of body fluid smears or swabs, (iii) desiccation of body fluid droplets *per se*, (iv) desiccation of droplets of watery solutions of ashed body fluid, (v) desiccation of body fluid droplets with addition of reagents, and (vi) desiccation of body fluid bulk solutions with added reagents.

3.3. Classification of the collected experimental protocols into diagnostic patterning tests

As shown in Fig. 2b, in a next step, the experimental protocols within each of the six methods were classified according to the body fluid analyzed. Any such group of experimental protocols concerning the same method and body fluid was considered a diagnostic patterning test (DPT).

As shown in Fig. 2c, in total 30 DPTs could be identified, most concerning the desiccation of body fluid (BF) droplets *per se* (14 DPTs), followed by desiccation of BF droplets with reagents (6 DPTs), desiccation of bulk solutions with reagents (4 DPTs), desiccation of BF smears and swabs (3 DPTs), then films (2 DPTs), and finally desiccation of droplets of watery solutions of ashed BF (1 DPT). The body fluids most frequently applied in diagnostic tests were serum and saliva (4 DPTs for each BF), followed by blood and urine (3 DPTs for each BF). Other fluids, e.g. plasma, tears, amniotic fluid, cervical mucus and sweat, were used in one DPT each; there were also single studies regarding DPT applied on menstrual fluid, tonsil discharge, follicular fluid, peritoneal fluid, lymph, pleurical cavity fluid, cerebrospinal fluid, wound exudate, and endometrial washouts.

3.4. Description and comparison of the identified methods

As presented in Fig. 2a, the identified DPTs may be classified into six methods, depending on the characteristics of their experimental protocols.

Desiccation of body fluid films is a less known approach described in three studies only. The body fluid to be analyzed is placed on a microscope slide and flattened by covering it with a cover glass. The desiccation process lasts longer than in other methods; however, the phase transition occurs in a protected environment (e.g. lesser relative humidity shifts and drafts); moreover, this approach results in a homogenous thickness of the desiccating liquid layer. Due to the size of the specimen, selected pattern sections were subjected to evaluation; the choice of pattern sections may constitute a source of bias.

Desiccation of body fluid smears or swabs is used mainly with dense, mucous body fluids (e.g. cervical mucous) unlikely to form into droplets. The body fluid is deposited on a microscope slide by different means: a spatula, or, in case of saliva, a spoon, or by pressing the slide directly on the tongue. Therefore, the specimen may be of varying thickness and size. Evaporation takes place under ambient room conditions. In case of smears, pattern sections were subjected to evaluation.

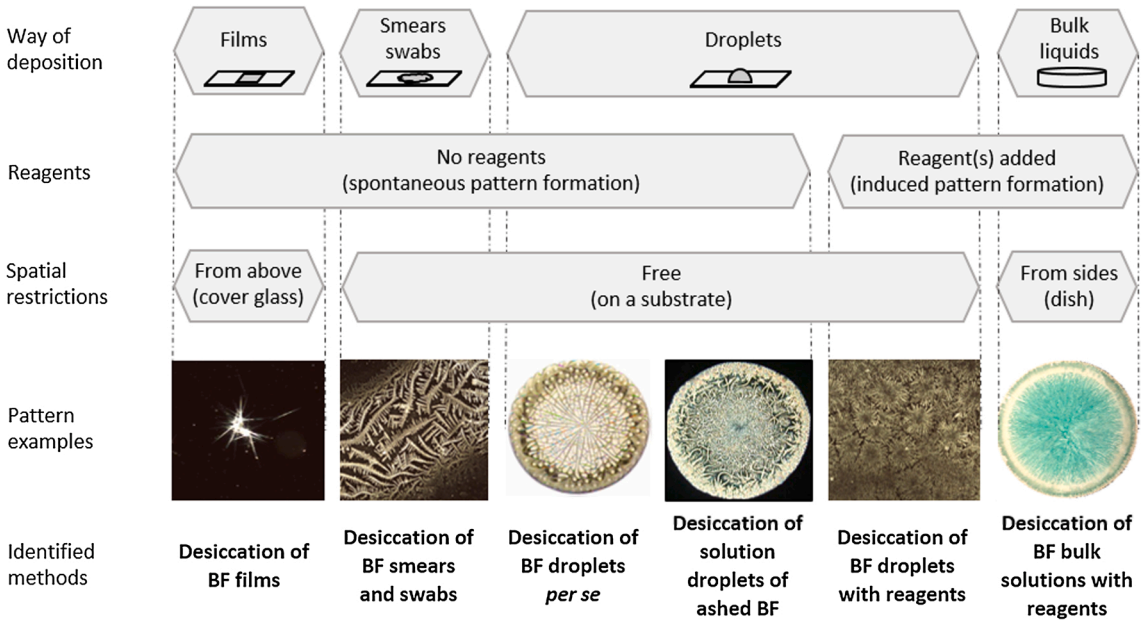
Desiccation of body fluid droplets *per se* was applied on the largest number of different body fluids. The method consists in evaporation of droplets of undiluted body fluids placed on microscope slides. Two experimental studies introduced a modified method based on a slight inclination of the substrate (slides) after droplet deposition, causing the droplets to run off a little and to dry in a different form. Since no reagents are used, the pattern formation depends strictly on the body fluid characteristics and can consist in crystallization, agglomerating, breaking of the surface (formation of so-called cracks), or can combine different pattern formation mechanisms. The multiplicity of possible resulting patterns may represent a challenge for the evaluation.

Desiccation of solutions droplets of ashed BF is a method derived from Spagyric medicine. It consists in incinerating the sample and subsequent evaporation of droplets obtained by preparing a watery solution of the sample's ash. Due to the sample's incineration, patterns are formed predominantly in course of crystallization.

Desiccation of body fluid droplets with addition of reagents consists of the evaporation of droplets of body fluids with additives, mostly salts (NaCl and KCl), which induce pattern formation and promote the formation of crystalline structures. As the reagents are added in form of a watery solution, the body fluids become slightly diluted.

In most experimental studies based on BF droplet desiccation (desiccation of BF droplets *per se*, droplets of solutions of ashed BF, and BF droplets with reagents), the evaporation process took place under ambient room conditions. There were only a few studies where an

a. Classification into methods



b. Classification into DPTs

Serum	✓		✓		✓	✓
Saliva	✓	✓	✓		✓	
Blood			✓	✓		✓
Urine			✓		✓	✓
Plasma			✓			
Tears			✓			
Amniotic fluid		✓				
Cervical mucus		✓				
Sweat			✓			
Other BFs*			+ 7 other BFs		+ 3 other BFs	+ 1 other BF

c. Number of DPTs identified

DPTs	2	3	14	1	6	4

Fig. 2. Classification of the diagnostic tests into (a) methods regarding (i) way of deposition of the evaporating liquid, (ii) addition of reagents, and (iii) spatial restrictions during evaporation, and into (b) diagnostic pattering tests (DPTs) regarding the type of analyzed body fluid; (c) number of DPTs identified.
In (a) pattern examples: the third, fourth and sixth image from the left are reused from [11] (with permission of Voprosy Onkologii) [146], (with permission of HIS Spagyrik Institute), and [90] (with permission of Scientific Section of Goetheanum, Dornach, Switzerland), respectively.
BF – body fluid; * - menstrual fluid, tonsil discharge, follicular fluid, peritoneal fluid, lymph, pleurical cavity fluid, cerebrospinal fluid, wound exudate, and endometrial washouts.

evaporation chamber or an incubator was used in order to control temperature and relative humidity. In some studies, the droplet volume was predefined (from 0.2 μL in case of tear droplets to 100 μL in case of saliva droplets); however, in most studies the droplet volume was not defined and could vary between the droplet replicates. For pattern evaluation, the whole specimen was considered. The droplet patterns consisted of zones and required a microscopic evaluation.

The **copper-chloride biocrystallization (desiccation of body fluid bulk solutions with reagents)** was developed by E. Pfeiffer in the thirties of the 19th century and is still being studied today by different research groups. To the body fluid, a watery copper chloride solution is added; the so obtained crystallizing solution is poured onto dishes and desiccated mostly in a crystallization chamber under controlled conditions. The macroscopic patterns are evaluated visually regarding the presence of specific structures.

In Table 1, basing on the information extracted from the publications, the background-knowledge of the authors, and the number of available publications per method, some possible advantages and disadvantages of the methods are listed related to their methodological aspects.

3.5. Description of the identified diagnostic pattering tests and their target conditions

Table 2 and 3 present the different DPTs identified as used in human and veterinary medicine, respectively. The DPTs are classified according to body fluid investigated, method, and target condition; the tables contain also information about the applied pattern evaluation technique.

3.5.1. Diagnostic patterning tests applied on serum

As shown in Table 2a, we identified four DPTs applied on serum:

Table 1
Comparison of the methods based on pattern formation in drying body fluids considering possible advantages and disadvantages of some of their methodological aspects.

Possible advantages	Possible disadvantages
Desiccation of BF films (under a cover-glass)	
• Uniform film thickness • Possibly smaller sensitivity to external relative humidity changes during drying • Simple methodology	• Long drying process • Need for the choice of specimen section(s) for evaluation • Method in experimental stage • Small number of publications
Desiccation of BF smears and swabs	
• Short analysis time (depending on the fluid and evaporation conditions) • Simple methodology • Large number of publications • Recognized diagnostic tests within the method	• Unequal thickness of the specimen • Need for the choice of specimen section(s) for evaluation • Sensitive to external drying conditions • Sensitive to substrate characteristics
Desiccation of BF droplets *per se*	
• Short analysis time (depending on the fluid and evaporation conditions) • Simple methodology • Large number of publications • Possible evaluation of whole specimen • Recognized diagnostic tests within the method	• Patterns are results of multiple pattern forming mechanisms (depending on the BF and drying conditions) • Sensitive to external drying conditions • Sensitive to substrate
Desiccation of solution droplets of ashed BF	
• Patterns are a result of one single mechanism only (crystallization) • Possible evaluation of whole specimen	• Time-consuming • Method in experimental stage • Small number of publications • Sensitive to external drying conditions • Sensitive to substrate
Desiccation of BF droplets with reagents	
• Short analysis time • Patterns are mostly a result of one pattern forming mechanism due to reagent addition (crystallization) • Possible evaluation of whole specimen	• Small number of publications • Method in experimental stage • Sensitive to external drying conditions • Sensitive to substrate
Desiccation of BF bulk solutions with reagents	
• Large number of publications • Well described methodological protocol including visual evaluation procedure • Possible evaluation of whole specimen	• Time-consuming • Method in experimental stage • Special laboratory equipment is needed • Sensitive to external drying conditions • Sensitive to substrate

desiccation of films [7,8], droplets *per se* [8–29], droplets with addition of reagents [19,30], and the copper-chloride biocrystallization [31].

The **desiccation of serum films** under a cover glass was applied for the examination of samples from patients suffering from laryngeal cancer, otitis media, rhino sinusitis [7] and asthma [8]; pattern evaluation consisted in stating the presence of specific form characteristics (markers).

Out of DPTs applied on serum, the **desiccation of droplets *per se*** was described in the largest number of experimental studies. A typical serum pattern is composed of an outer and an inner zone and contains both cracks and structures (Fig. 3a). The patterns can show great variety in regularity and quantity of the crack patterns, as well as the density and morphology of the structures. The studies collected used the serum drop patterns for diagnosing cancer [9–17] (Fig. 3a, b), diabetes mellitus [20,21], hepatitis [18], and other types of inflammation. In most cases, pattern evaluation was done visually and consisted in stating the presence and quantity of specific structures interpreted as markers of specific processes taking place in the body, as for instance malignant processes, inflammation, sclerotic processes, and intoxication. In few studies, the pattern evaluation consisted in the measurement or count of structures (e.g. measurement of zone radiuses, crack length, branching angles, count of plates) [18,19,24], measurements of the phase transition dynamics by means of acoustic mechanical impedance [15], and application of machine learning algorithms [16].

In two studies, the **evaporation of serum solution droplets, containing reagents**, L-leucine [30] and sodium chlorate [19], was applied to examine samples from cancer and hepatitis patients, respectively.

In one study, serum samples of cancer patients were analyzed by means of the **copper-chloride biocrystallization** [31].

3.5.2. *Diagnostic pattering tests applied to saliva samples*

The collected literature described four DPTs applied to saliva samples: desiccation of films [7], smears [5,32–36], droplets *per se* [37–53], and droplets with reagent addition [54] (Table 2b).

The **desiccation of salivary films** was reported in a study for the detection of otitis media [7].

The **desiccation of salivary smears** (the so-called **salivary fern test**, as the forming patterns resemble fern leafs) represents a well-known procedure for the detection of the fertile period [5]. The working principle of this DPT relies on the correlation between the fern tendency and the sodium chloride level in saliva. Before and during ovulation, estrogen causes saliva sodium chloride levels to rise, which, in turn, is responsible for intense fern. The evaluation of fern patterns is done visually by simple visual inspection or comparison to reference pictures exhibiting different degrees of fern tendency. Despite the rather low accuracy caused *inter alia* by numerous factors influencing the fern properties of saliva (i.e. smoking, eating or brushing teeth prior to the analysis, different disorders), this test is recommended for women as a helpful tool for family planning [5, 34–36]. There exist analysis kits including small microscopes for carrying out salivary fern tests at home [32].

The **desiccation of saliva droplets *per se*** as a diagnostic tool was proposed for the detection of cancer [37], diabetes mellitus [38–40], other diseases [17,19,41–44,47], as well as dental disorders [48–53]. Interestingly, in none of these applications the fern complexity was assessed (as in the salivary fern test) but other pattern characteristics were evaluated, as for instance different shapes of dendrites or count of the dendrite tips.

One study reported on the use of **desiccation of saliva droplets with reagents** for the detection of ulcer and coronary heart disease [54].

3.5.3. *Diagnostic pattering tests applied to blood samples*

Full blood was analyzed by means of three DPTs: desiccation of blood droplets *per se* [55,56,58–70,135], desiccation of watery solutions of ashed blood samples [71–73], and the copper-chloride biocrystallization [74–97] (Table 2c).

The **desiccation of blood droplets *per se*** was first applied by Bolen, who had observed that patterns forming in dried blood drops put on slides directly from a pierced finger differed between cancer and control patients [55,56,135]; the DPT was further studied also by other authors [58–64]. The underlying mechanism of the test was reported to possibly relate to differences in blood density between cancer and control patients. The pattern evaluation was done only visually and consisted in classifying the pattern type in accordance to its structure homogeneity. The test was reported to give false-positive results in pregnancy and tuberculosis. All studies on the Bolen test were published between 1942 and 1974. Recently, the desiccation of blood droplets *per se* was studies for other target conditions, including uterus myoma [66], as well as thalassemia and jaundice in children [69]. Moreover, it could be shown that physiological conditions such as the donor's blood-group [67] and the performance of physical activity just before the sample collection [68] may influence the emerging formations. In a recent study, patterns were evaluated by deep learning algorithms [68].

The **desiccation of watery solutions of ashed blood samples** was

Table 2
Diagnostic tests based on pattern formation in desiccating body fluids applied in human medicine.

Author (Year)	Target condition	Pattern evaluation
a. SERUM		
Desiccated films		
Shatokhina & Sambulov (2016) [7]	Cancer (laryngeal), otitis media, rhinosinusitis	Visual, presence of specific structures (markers)
Shirokaya et al (2013) [8]	Asthma	Visual, presence of specific structures (markers)
Desiccated droplets *per se*		
Ardzha (2013) [9], Shatokhina et al (2009) [10], Shatokhina & Shabalin (2010) [11], Shihlyarova et al (2015) [12], Shikhliarova et al (2013) [13], Kovacs et al (1984) [14], Yakhno et al (2005) [15]	Cancer	Visual, presence of specific structures (markers)
Killeen et al (2006) [16],	Cancer	Machine learning
Yakhno et al (2005, 2004) [15,17]	Cancer, paraproteinemia, hepatitis, liver disorders	Morphology, dynamics of drying process (acoustic mechanical impedance)
Levitan (2010) [18]	Hepatitis	Count of specific structure elements
Martusevich et al (2007) [19]	Chronic hepatitis and cirrhosis	Rating of specific structure elements by means of a scale
Maksimov (2010) [20], Sherbatyuk et al (2009) [21]	Diabetes mellitus (type 1 and 2)	Visual, presence of specific structures (markers) and their localization
Dementyev & Kulinich (2010) [22], Kulinich & Dementyev (2010) [23]	Inflammation of small pelvic organs	Visual, presence of specific structures (markers)
Shirokaya et al (2013) [8]	Rhinosinusitis and forecast of disease course	Visual, evaluation of structure complexity
Marinich & Borsukov (2012) [24]	Chronic calculous cholecystitis	Measurement of specific structures
Selivanenko (2013) [25]	Endocarditis	Visual, presence of specific structures (markers)
Shatokchina et al (2010) [26]	Ulcerative colitis, diarrheal syndrome (dehydration)	Visual, presence of specific structures (markers)
Shabalin & Shatokhina (2007) [27]	Sclerosis, acute heart insufficiency, chronic intoxication, inflammation	Visual, presence of specific structures (markers)
Streltsova & Tarasova (2009) [28]	Tuberculosis	Visual, presence of specific structures (markers)
Zoeva (2016) [29]	Abnormal uterine bleeding	Visual, presence of specific structures (markers)
Desiccated droplets with reagents		
Martusevich et al (2007) [19]	Hepatitis	Visual, presence of specific structures (markers)
Teichmann (1964) [30]	Cancer (L-leucin crystallization)	Visual, presence of specific structures (markers)
Desiccated bulk solutions with salts (copper chloride biocrystallization)		
Teichmann & Zierbarth (1973) [31]	Cancer, tuberculosis	Visual, presence of transverse formations
b. SALIVA		
Desiccated films		
Shatokhina & Sambulov (2016) [7]	Otitis media	Visual, presence of specific structures (markers)
Desiccated smears		
Food and Drug Administration [5], Fehring & Gaska (1998) [32], Guida et al (1999) [33], Patel & Desai (2018) [34] Su et al (2017) [35]	Fertile period*	Visual, ferning complexity grading by scale
El-Miedany et al (1999) [36]	Sjögren's syndrome	Visual, ferning complexity grading by scale
Desiccated droplets *per se*		
Denisov et al (2006) [37]	Cancer (prostate), benign hyperplasia	Dendrite shapes, multivariate analysis
Myachina et al (2016) [38], Selifanova et al (2005) [39]	Diabetes mellitus	Visual, presence of specific structures within zones, zone measurement
Denisov et al (2005) [40]	Diabetes mellitus	Dendrite shapes, multivariate analysis
Denisov (2004) [41]	Gastro-intestinal disorders	Algorithm for evaluating different structure types
Lebedev-Stepanov et al (2018) [42]	Endogenous intoxication	Computerized image recognition
Chemicosova & Guyaeva (2008) [43]	Intoxication through exposure to herbicides	Visual, classification into 3 main pattern types
Martusevich et al (2014) [44], Martusevich & Kamakin (2007) [45]	Liver alveococcosis	Measurement of specific structures
Pattanasuttinont et al (2007) [46]	Fertile period	Visual, ferning complexity grading by scale
Belskaya et al (2011) [47]	Physical activity	Visual, crystallization intensity rating
Domenyuk et al (2016) [48]	Bite disorders	Visual, crystallization intensity rating
Kaskova et al (2019) [49], Pancu et al (2015) [50], Spinei et al (2014) [51], Spinei et al (2013) [52], Voloshina (2018) [53]	Caries, dental erosion lesions, enemal acid resistance, inflammatory periodontal disease, gastro esophageal reflux (microcrystallization for odontogenic disorders)	Microcrystallization index: visual, count of dendrite tips

(*continued on next page*)

Table 2 (*continued*)

b. SALIVA		
Desiccated droplets with reagents		
Simonova et al (2014) [54]	Ulcer, coronary heart disease	Visual, presence of specific structures (markers)
c. BLOOD		
Desiccated droplets *per se*		
Bolen (1942, 1950, 1954) [55,56,57], Finnegan et al (1950) [58], Grueber and Huppertz (1952) [59], Hawk et al (1951) [60], Huettl et al (1955) [61], Pinskaia & Sergeeva (1973) [62], Vaughn et al (1952) [63], White et al (1952) [64]	Cancer, different types (Bolen test)	Visual, uniformity of the central and outer zone
Gruner (1941) [65]	Cancer	Visual, presence of specific structures
Feofilova (2016) [66]	Uterus myoma	Measurement of specific structures
Feofilova (2013) [67]	Blood group	Measurement of specific structures
Hamadeh et al (2020) [68]	Exhaustion after physical exercise	Deep learning algorithms
Bahmani et al (2017) [69]	Thalassemia, jaundice (in children)	Measurement of specific structures
Chen et al (2016) [70]	Review (blood and plasma)	–
Desiccated droplets of watery solutions of ashed body fluids		
Franz et al (2013) [71]	Colon polyps	Visual, connection or disconnection of structures with the droplet edge
Gruner (1994) [72], Schockert (2009) [73]	Treatment or external factor influence (beneficial or harmful)	Visual, comparison of shapes, complexity and harmony of structures
Desiccated bulk solutions with salt (copper chloride biocrystallization)		
Bali & Marathe (2017) [74], Barth (1990) [75], Bornholt (2010) [76], Garn (1950) [77], Gruner (1940) [78], Gulati et al (1994) [79], Jung (1953) [80], Kuczkowski (1995) [81], Makkar et al (2020) [82], Mehrota et al (2017) [83], Pfeiffer & Miley (1939) [84], Rascher & Trumpp (1939) [85], Rawat et al (2019) [86], Sarode (2013) [87], Shaikh (2012) [88], Tarigoppula (2018) [89]	Cancer, different types, precancerous conditions	Count and localization of transverse formations
Knijpenga (2020) [90], Selawry (1957) [91]	Cancer, benign conditions, inflammations, organ dysfunctions, physiological stages	Visual, presence and localization of specific forms
Quadeer (1988) [92]	Cancer, benign conditions, inflammations	Visual, presence and localization of specific forms
Vara et al (2015) [93], Shibata et al (2000) [94]	Diabetes mellitus	Visual, presence and localization of specific forms
Cocude et al (1994) [95]	Silicosis	Visual, presence and localization of specific forms
Pfeiffer (1975) [96]	Different diseases, treatment influence	Visual, presence and localization of specific forms
Pfeiffer (1957) [97]	Review	–
d. URINE		
Desiccated droplets *per se*		
Shatokhina & Shabalin (2010) [11]	Cancer	Visual, presence of specific structures (markers)
Martusevich et al (2014) [44]	Postoperative liver alveococcosis	Measurement of specific structures
Shabalin et al (2015) [98]	Disorders in long-living persons (atherosclerosis and organ dysfunctions)	Visual, presence and localization of specific structures
Desiccated droplets with reagents		
Martusevich & Kamakin (2007) [45]	Liver alveococcosis	Measurement of specific structures
Desiccated bulk solutions with salts (copper chloride biocrystallization)		
Trumpp & Rascher (1939) [99]	Pregnancy	Visual, presence of specific structures
e. PLASMA		
Desiccated droplets *per se*		
Abramov et al (2016) [100], Brzecki et al (1989) [101], Obukhova et al (2011) [102], Rapis (2002) [103]	Cancer	Visual, presence of specific structures, uniformity
Firsova et al (2012) [104]	Pancreatitis (different degrees of severity)	Visual, presence of specific structures, uniformity
Kim (2008) [105]	Chronic tonsillitis	Visual, presence of specific structures, uniformity, symmetry
Shuasheva (2012) [106]	Rheumatoid arthritis (treatment influence)	Visual, presence of specific structures within zones
Yakhno et al (2005) [15]	Different states in women: non-pregnant, normal pregnancy, premature delivery, threatened abortion	Morphology, dynamics of drying process (acoustic mechanical impedance)
Karpukhina et al (2011) [107]	Encephalopathy (treatment influence)	Measurement of specific structures
f. TEARS		
Desiccated droplets *per se*(ocular ferning)		
Costagliola et al (2001) [108], Li et al (2007) [109], Nebbioso et al (2018) [110], Peponis et al (2002) [111]	Tear film quality under treatment influence*	Visual, ferning intensity grading by scale
Masmali et al (2018) [112], Parodi et al (2001) [113], Pezzi et al (2004) [114], Rolando et al (1988) [115], Vaikoussis et al (1994) [116]	Tear film quality in disease (diabetes mellitus, retinal detachment keratoconjunctivitis sicca, Vogt-Koyanagi-Harada syndrome, cystic fibrosis, Sjögren's syndrome)*	Visual, ferning intensity grading by scale
Beden et al (2008) [117]	Tear film quality in premature and mature newborns*	

(*continued on next page*)

Table 2 (*continued*)

f. TEARS		
Srinivasan et al (2007) [118]	Tear film quality in postmenopausal women*	Visual, ferning intensity grading by scale
Gajta et al (2015) [119]	Tear film quality in computer-users*	Visual, ferning intensity grading by scale
Masmali et al (2014) [120]	Ocular ferning test, review*	Visual, ferning intensity grading by scale
g. AMNIOTIC FLUID		–
Desiccated smears (amniotic fluid ferning)		
Bilodeau (1963) [121], Ferron & Fogelson et al (2014) [122], Gaddey et al (2011) [123], Hutchison et al (2020) [4], Rogers et al (2016) [124]	Rupture of membranes*	Visual, detection of thin crystallizations of amniotic fluid (different from thick patterns of cervical mucus)
h. CERVICAL MUCUS		
Desiccated smears		
GP Notebook (2018) [6], Neumann & Lehfeldt (1955) [125], Patel & Desai (2018) [34]	Early pregnancy, fertile period*	Visual, ferning intensity grading
i. SWEAT		
Desiccated droplets *per se*		
Farahmand et al (2012) [126], Ferrer-Clavete et al (1990) [127]	Cistic fibrosis	Visual, crystallization intensity grading (presence of NaCl crystals)kkkk
j. OTHER		
Desiccated droplets *per se*		
MENSTRUAL FLUID:, Ukhanova (2016) [128], Ukhanova et al (2015) [129], Zoeva (2016) [29]	Myoma, abnormal bleeding	Visual, presence of specific structures
TONSIL DISCHARGE: Shatokhina & Sambulov (2016) [7]	Tonsillitis	Visual, presence of specific structures
FOLLICULAR FLUID: Turbinkova et al (2017) [130]	Inflammation, infertility	Visual, presence of specific structures
PERITONEAL FLUID, LYMPH, PLEURICAL CAVITY FLUID: Firsova et al (2012) [104]	Pancreatitis (different degrees of severity)	Visual, presence of specific structures
SYNOVIAL FLUID: Shabalin & Shatokhina (2007) [27]	Osteoarthritis	Visual, presence of specific structures
Desiccated droplets with reagents		
WOUND EXUDATE: Shatokhina et al (2008) [131], Shatokhina & Sambulov (2016) [7]	Malignancy and complications of odontogenic origin, healing prognosis after surgery	Visual, formation of bubbles (markers)
ENDOMETRIAL WHASHOUTS: Shvaryov (2015) [132]	Ovarian disorders (malignant and benign), chronic uterus inflammation	Visual, presence of specific structures, zone measurement
LIQUOR CEREBROSPINALIS: Strom-Olsen & Kite (1942) [133]	Mental disorders	Visual, ranking in accordance to a scale
Desiccated bulk solutions with salts (copper chloride biocrystallization)		
LIQUOR CEREBROSPINALIS: Neritin & Kirjakov (1977) [134]	Cancer, inflammations of the central nervous system	Visual, presence of specific structures

LEGEND: * - recognized diagnostic patterning tests; literature was subjected to quantity restriction.

applied in few studies as a means for the detection of colon polyps [71] and also for monitoring the overall health condition (e.g. following a medical treatment) [72,73].

According to the collected literature, the **copper chloride biocrystallization of blood** samples (desiccation of bulk solutions with reagents) represents the DPT with the longest scientific tradition with publication years of experimental studies ranging from 1939 to 2020 [74–97]. Depending on whether the presence of a patient was possible in the laboratory [91], one fresh blood drop from the fingertip or a blood drop dried on filter paper and shipped to the laboratory was dissolved in water; to the resulting hemolysate a watery copper chloride solution was added. The crystallizing solution was poured on dishes (100 mm diameter) and desiccated in a crystallization chamber. In most cases, the macroscopic patterns were evaluated visually for the presence of specific structures, as for instance transverse, star-like, or hollow formations, which in numerous studies were reported to indicate cancer, inflammation, and benign tumors, respectively [91,92]. Besides formations indicating disease processes, specific organ-structures were reported to occur, indicating the organ affected by the disease [91,95]. Some authors observed that the location of formations in the macroscopic pattern indicated zones of the human body [88,96]. Most studies on the copper chloride biocrystallization reported the possibility to detect cancer (Fig. 3c, d), including early cancer stages and pre-cancerous conditions [74–92,97]. This DPT was also applied for the detection diabetes mellitus [93,94], silicosis [95], and other diseases [91].

3.5.4. *Diagnostic pattering tests applied to urine samples*

Urine was analyzed by means of three DPTs (Table 2d).

Desiccation of urine droplets *per se* was studied for detection of cancer [11], different disorders in long-living persons [98], and liver alveococcosis [44]; the last was also detected by **desiccating droplets with the addition of reagents** [45]. The pattern evaluation consisted in visual inspection and search for specific structures (markers), or the measurement of different formation elements.

One study proposed the **copper-chloride biocrystallization** of urine as a test to detect a pregnancy [99]. The proposed acting principle relies on the alternation of hormone levels present in urine during pregnancy, leading to a specific structure formation.

3.5.5. *Diagnostic pattering tests applied to plasma samples*

As shown in Table 2e, **desiccation of droplets *per se*** was used for the analysis of plasma samples with the purpose of detecting cancer [100–103], inflammatory conditions including pancreatitis, chronic tonsillitis, and arthritis [104–106], and pregnancy as well as pregnancy pathologies [15]. One study analyzed the efficacy of treatment in patients with encephalopathy [107]. In case of plasma patterns, the evaluated features were pattern uniformity, division into zones, presence of specific structures, and the crack length and angle. One study evaluated the dynamics of zone transition by measuring acoustic mechanical impedance [15].

Table 3
Diagnostic tests based on pattern formation in desiccating body fluids as applied in veterinary medicine and farm animals.

BODY FLUID: Author (date)	Target condition / animal	Pattern evaluation
Desiccated smears		
SALIVA: Kubatova & Federova (2016) [136], Padro-Carmona et al (2010) [137], Ravinder et al (2016) [138]	Fertile period, optimal matting time / Borneo orangutans, bitches, water buffaloes*	Visual, ferning intensity grading by scale; box fractal dimension measurement
CERVICAL MUCUS: Bernardi et al (2015) [139], Cortes et al [140], Luno et al (2016) [141]	Detection of fertile period / Holstein cows, sows*	Visual, ferning intensity grading by scale
Desiccated droplets*per se*		
TEARS: Williams and Hewitt (2017) [142], Coassin et al (2005) [143]	Diagnosing and treating of keratoconjunctivitis sicca in dogs*	Visual, ferning intensity grading by scale
BLOOD: Yakhno (2015) [144]	Leukosis and tuberculosis / cattle	Dynamics of drying process (acoustic mechanical impedance)

LEGEND: * - recognized diagnostic patterning tests; literature was subjected to quantity restriction.

3.5.6. *Diagnostic pattering tests applied to tear samples*

The **desiccation of tear droplets *per se*** (the so-called **tear ferning test**) (Table 2f) is a commonly used DPT for accessing the tear film quality [120]. The test has been mainly applied for the purpose of evaluating changes in the tear film quality following medical treatment [108–111] and for the detection of different diseases [112–116]. There were also studies assessing tear film quality in newborns [117], post-menopausal women [118] and computer-users [119]. In this test, undiluted tear droplets were left to desiccate on microscope slides; the resulting crystalline structures, resembling fern leafs, were then observed under a microscope and evaluated by scoring the ferning tendency by means of a scale comprised of reference pictures. The scientific rationale for this test is based upon a strong correlation between the salt content in tears and tear film quality.

3.5.7. *Diagnostic pattering tests applied to amniotic fluid samples*

Desiccation of amniotic fluid smears or the so-called **amniotic fluid ferning test** (Table 2g) was used in the past to detect a premature rupture of fetal membranes and a resulting risk of abortion [121]. Nowadays, the test is recommended for diagnosing the rupture of fetal membranes only during labor [4,122–124]. In this test, smears of vaginal secretion are left to dry. The working principle relies on a clear difference in formation shapes between the fine arborizations developing out of the leaking amniotic fluid and thick structures developing out of cervical and vaginal mucus which can be detected by means of a visual inspection of the smear (Fig. 3e).

3.5.8. *Diagnostic pattering tests applied to cervical mucus samples*

The **desiccation of cervical mucus smears** or the so-called **cervical mucus ferning test** (Table 2h) depends strongly on changing sodium chloride levels prior and during ovulation. The test was used for the detection of the fertile period [6,34] and proposed for the detection of early pregnancy [125]. Similar to salivary ferning, the ferning tendency is assessed here by a visually inspecting the patterns.

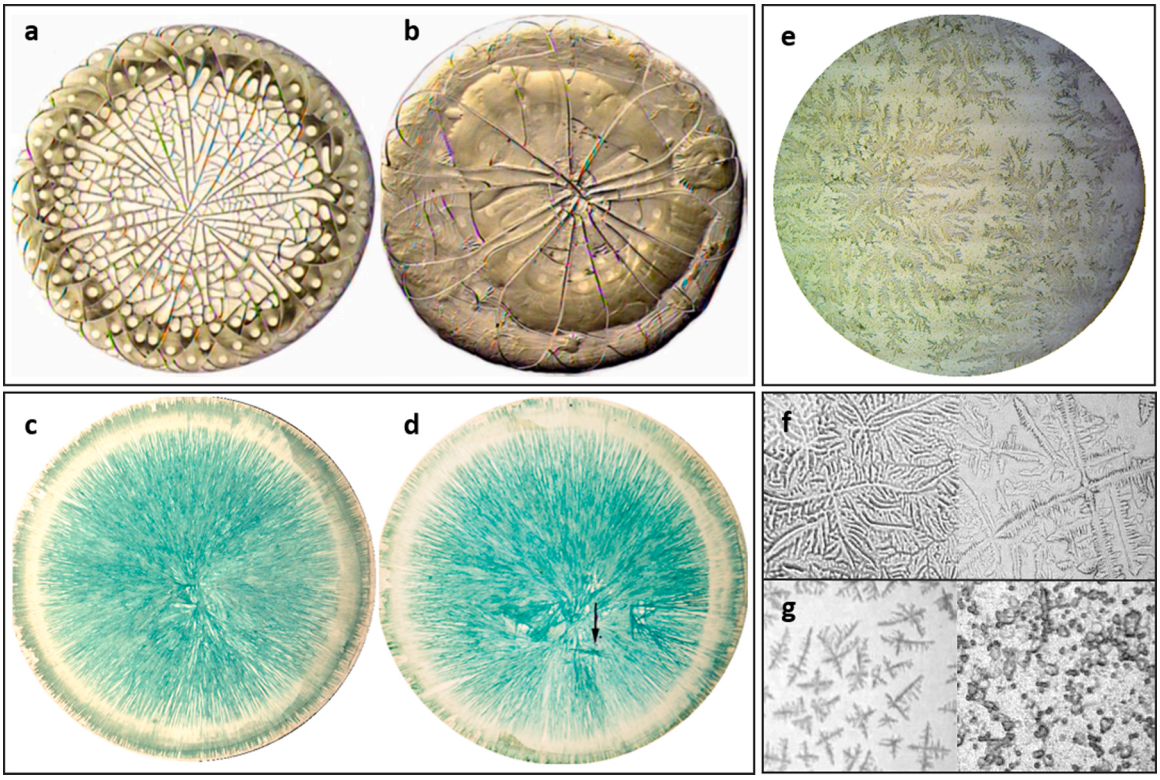


Fig. 3. Examples of patterns obtained in diagnostic patterning tests in human (a-e) and veterinary medicine (f, g). Desiccated serum droplet of a healthy person (a) and a cancer patient (b); copper-chloride biocrystallization pattern of blood from a healthy person (c) and a cancer patient (d; transverse formation marked with arrow); ferning obtained from amniotic fluid (e); and tear ferning patterns obtained from dog tears of a healthy animal (f) and animal with dry eye disease (g). Images reused (a,b) from [11] with permission of Voprosy Onkologii; (c,d) from [90] with permission of Scientific Section of Goetheanum, Dornach, Switzerland; (e) from [147] with permission of Wikimedia Commons; (f, g) from [142] with permission of Open Veterinary Journal.

3.5.9. Diagnostic pattering tests applied to sweat samples

The **desiccation of sweat droplets *per se*** or the so-called **sweat crystallization test** (Table 2i) is a DPT used for the detection of cystic fibrosis [126,127]. Cystic fibrosis patients have an increased amount of sodium chloride in sweat, which in turn leads to an increased crystallization tendency.

3.5.10. Diagnostic pattering tests applied to other body fluids

As shown in Table 2j, we further identified 11 DPTs applied to menstrual fluid [29,128,129], tonsil discharge [7], follicular fluid [130], lymph, pleurical cavity fluid [104], synovial fluid [27], wound exudate [7,131], endometrial washouts [132], and cerebrospinal fluid [133, 134]. These DPTs were performed using three methods: **desiccation of droplets *per se***, **desiccation of droplets with reagent addition**, and **copper-chloride biocrystallization**. In all these DPTs, the fluid used was related to the diagnosed disorder; e.g. pattern formation in menstrual fluid was studied for the diagnosis of uterus myoma and abnormal bleeding, in tonsil discharge for the detection of tonsillitis, in synovial fluid for the detection of osteoarthritis, and in cerebrospinal fluid for the detection of central nervous system and mental disorders.

3.5.11. Diagnostic pattering tests of animal body fluids used in veterinary medicine

Regarding DPTs based on pattern-formation in animal body fluids (Table 3), most studies applied the desiccation of saliva [136–138] and cervical mucous smears [139–141] for the purpose of detecting the fertile period. These ferning tests were applied on farm animals, such as cows [139,140], sows [141], bitches [137], and water buffaloes [138]; one study was performed on Bornean orangutans kept in a zoo [136].

Two other studies reported on the use of the droplet desiccation method in the case of dogs suffering from dry eye (Fig. 3f, g) [142,143], and on bovine blood samples with the purpose of detecting leucosis and tuberculosis [144].

4. Discussion

Among the DPTs identified in the present mapping review, tests collectively known as "ferning tests" are broadly recognized and used. There are four such tests based on the evaporation of smears or droplets *per se* using samples of tears [120], saliva [5], amniotic fluid [4], and cervical mucus [6]. Their working principle is well understood, since the target condition triggers a modification in the composition of each body fluid. During desiccation, the so modified body fluid leads to structures that are clearly distinguishable from those created in absence of the target condition. In all ferning tests, the evaluation criterion of the patterns is the ferning tendency, e.g. complexity and quantity of the dendritic structures. Besides the four before-mentioned ferning tests, also the sweat crystallization test for the detection of cystic fibrosis may be added to this category.

In other DPTs, in particular those applied to more complex body fluids, such as blood [70] and serum [16], the relationship between target condition, fluid composition, and the resulting pattern may be multifactorial and dependent, besides on the target condition, *inter alia,* on age, general state, diet, and medication (i.e. conditions not necessarily related to the target condition) [91]. In all these DPTs, pattern evaluation consists in the identification of specific structures, and not in evaluating their complexity and quantity (ferning). These structures are DPT-specific, and are named after shapes they resemble or after the target condition they indicate (e.g. leaf-like structures, tongs, transverse formations, hollow forms, or intoxication markers, inflammation markers, organ-specific forms). One pattern may contain different kinds of structures and therefore indicate the presence of different target conditions in one sample analysis. It was also reported in several studies concerning the copper-chloride biocrystallization method, that a combination of specific structures (e.g. transverse formation indicating cancerous conditions together with liver-specific formations) may indicate both the type of disorder and the affected organ (e.g. liver carcinoma).

In DPTs, pattern evaluation resembles the diagnostic test reading. In most of the studies presented here, pattern evaluation was performed visually. In some studies, specific formation elements were measured or quantified. In a few more recent studies, computerized techniques based on pattern recognition and deep learning were applied. The recent development of computerized image evaluation tools might remarkably improve the quality of image evaluation and allow for analysis in comparison with large image databases.

Recently, desiccated residues of body fluids were also subjected to spectroscopic analysis [145]. We did not consider this method in the present mapping review since its evaluation is not strictly based on the emerging patterns or their characteristics.

The target conditions addressed most often in DPTs are those diagnosed by ferning tests, i.e. tear film quality, detection of fertility, and rupture of fetal membranes. Besides these target conditions, cancer has been the condition addressed in most studies (52 studies), followed by benign tumors (11 studies), inflammatory condition (11 studies), and different organ dysfunctions (11 studies). There were also studies regarding the diagnostics of diabetes mellitus (7 studies), diseases related to viral infections (7 studies), dental problems (6 studies), and other target conditions (represented by 5 or less studies).

To the best of our knowledge, this mapping review is the first one to include all DPTs on desiccating body fluids and to classify them in accordance to their experimental protocols. Although there have been a number of review articles published in this field [70,120] they each report only on one or a few of these methods, respectively.

In the present review, we did not assess the quality of the experimental studies nor evaluate the accuracy of the diagnostic tests. Such evaluations, in form of systematic reviews and meta-analyses, should be carried out in further studies on groups of DPTs concerning the same target condition. One such target condition would be malignant diseases, addressed in a considerable number of experimental studies.

Furthermore, some of the DPTs presented here were reported to exhibit highly promising features, such as the possibility to (i) diagnose several disorders in one analysis run [91], or to (ii) monitor patients' health conditions during the course of disease or following a medical treatment [91,95,110]. These DPTs should also be assessed regarding quality and test accuracy in further systematic reviews.

Maria Olga Kokornaczyk: conceptualization, resources, investigation, data curation, writing of the original draft; **Natalia Borisovna Bodrova**: resources, investigation, and translation of the Literature in Russian; **Stephan Baumgartner**: supervision, reviewing.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] J.-B.R. De L'Isle, Crystallographie, JBL. (1783) 379.
[2] S.S. Samnani, M. Vaska, S. Ahmed, T.C. Turin, Review typology: the basic types of reviews for synthesizing evidence for the purpose of knowledge translation, J. Coll. Physicians Surg. 27 (10) (2017) 635–641.
[3] A.M. Masmali, C. Purslow, P.J. Murphy, The tear ferning test: a simple clinical technique to evaluate the ocular tear film, Clin. Exp. Optom. 97 (2014) 399–406.
[4] J. Hutchison, H. Mahdy, J. Hutchison, Stages of Labor, StatPearls Treasure Island (FL), StatPearls Publishing, 2020, 2020.
[5] Administration UFD. Ovulation (Saliva Test, 2018.
[6] GPnotebook. Ferning (cerviacl mucus), 2018.

[7] S.N. Shatokhina, V.I. Sambulov, Structures of non-cellular tissues of the body and their importance in otorhinolaryngology, Almanac of Cinical Medicine. 44 (2016) 857–865.
[8] A.V. Shirokaya, V.M. Svistushkin, S.N. Shatokhina, V.N. Shabalin, Evaluation of the efficiency of the treatment of patients with polypous rhinosinusitis and forecast for disease course, Rossijskaya Otolaringologiya. 63 (2013) 96–104.
[9] A.Y. Ardzha, Y.V. Przhedetskiy, G.A. Nerodo, A.I. Shikhliarova, T.A. Kurkina, Self-organization of the blood serum in patients with excesive ovarian cancers under chemiotherapy in combination with ingaron, Int. J. Exp. Educ. 10 (2013) 226–232.
[10] S.N. Shatokhina, A.S. Balkanov, N.N. Petrushkina, V.N. Shabalin, Features of blood serum systemic organization in patients with brain glioblastoma during adjuvant radiotherapy, Al'Manakh Klinicheskoj Mediciny. 21 (2009) 49–51.
[11] S.N. Shatokhina, V.N. Shabalin, Markers of malignant growth in the morphological pattern of human biological liquid, Voprosy Oncologii. 56 (2010) 293–300.
[12] A.I. Shihlyarova, E.A. Sheiko, G.Z. Sergostyants, T.A. Kurkina, Morfostructur's features of serum of blood from the lung affected with the malignant tumor, Sovremennye Problemy Nauki i Obrazovaniya. 4 (2015) 315–321.
[13] A.I. Shikhliarova, E.M. Nepomnyaschaya, S.A. Mashurova, T.P. Protasova, The morphological features of the solid-state film of the blood serum in the soft tissues sarcoma metastasis patients, Int. J. Appl. Fundam. Res. 7 (2013) 62–65.
[14] A. Kovacs, A. Vertesy, L. Szalai, S. Adami, L. Urbancsek, Z. Simon, et al., A New Technique for Diagnosing Cancer by Inspecting Blood Serum, Humana Press INC Clifton, New Jersey, 1984, pp. 307–314.
[15] T.A. Yakhno, V.G. Yakhno, A.G. Sanin, O.A. Sanina, A.S. Pelyushenko, N. A. Egorova, et al., The informative-capacity phenomenon of drying drops, Ieee Eng. Med. Biol. Mag. (2005) 96–104.
[16] A.A. Killeen, N. Ossina, R.C. McGlennen, S. Minnerath, J. Borgos, V. Alexandrov, Protein self-organization patterns in dried serum reveal changes in B-cell disorders, Mol Diag Ther. 10 (2006) 371–380.
[17] T.A. Yakhno, V.G. Yakhno, A.G. Sanin, O.A. Sanina, A.S. Pelyushenko, Protein and salt: spatiotemporal dynamics of events in a drying drop, Tech. Phys. 49 (2004) 1055–1063.
[18] B.N. Levitan, A.R. Umerova, D.M. Abjalilova, A.K. Ayupova, The types of blood serum structural organization in chronic hepatitis and liver cirrhosis, Astrakhanskiy Medicinskiy Zhurnal. 5 (2010) 94–97.
[19] A.K. Martusevich, Y. Zimin, A. Bochkareva, Morphology of dried blood serum specimens of viral hepatitis, Hepat. Mon. 7 (2007) 207–210.
[20] S.A. Maksimov, O.P. Blagovechenskaya, G.V. Vavin, S.F. Zinchuk, Features of the structural organization of solid phase of whey of blood of patients with a diabetes, Medicina v Kuzbasse. 1 (2010) 33–36.
[21] T.G. Sherbatyuk, O.V. Zanozina, N.N. Borovkov, E.S. Klincova, Possibility of estimation of oxidizing stress for patients by diabetes Mellitus of type 2 be method of wedge-shaped dehydration, Rossijskiy Medico-biologichekkiy Vestnik Imeni Academika IP Pavlova. 4 (2009) 92–97.
[22] K.A. Dement'ev, S.I. Kulnich, The method of evaluating severity of inflammatory diseases of small pelvis organs by the method of blood serum clinoid dehydration, Sibirskiy Medicinskiy Zhurnal. 6 (2010) 81–84.
[23] S.I. Kulinich, K.A. Dementev, Method of pelvic inflammatory disease severity evaluating using wedge-shaped dehydration, part 2, Byulleten VSNC SO RAMS 76 (2010) 43–46.
[24] T.V. Marinich, A.V. Borsukov, The use of spheric dehydration method of biological fluids in the clinic of general medicine, Zdrove dlya Vsekh. 1 (2012) 3–6.
[25] V.T. Selivanenko, V.A. Dudakov, M.A. Martakov, S.N. Shatokhina, Integrated management of valve infective endocarditis in patiens with heart diseases, Grudnaya i Serdechno-Sosudistaya Khirurgiya. 5 (2013) 50–56.
[26] S.N. Shatokhina, T.S. Mishurovskaya, G.V. Tsodikov, New opportunities of early diagnosis of ulcerative colitis, Al'Manakh Clinicheskoj Mediciny. 23 (2010) 56–59.
[27] V.N. Shabalin, S.N. Shatokhina, Diagnostic markers in the structures of human biological liquids, Singapore Med. J. 48 (2007) 440–446.
[28] Y.N. Streltsova, L.G. Tarasova, The role of serm collagen type III autoantibodies and atructural and optical properties in the evaluation of reparative processes in children with tuberculosis, Tuberkulez i Bolezni Legkih. 87 (2009) 29–33.
[29] A.R. Zoeva, Structural characteristics of biological fluids of patients with abnormal uterine bleeding, J. Scienticic Articles Health Educationin Millennium 18 (2016) 205–209.
[30] B. Teichmann, Ueber die Verwertbarkeit Der Kristallisation Von L-Leuzin in Kontakt mit Seren Von Krebskranken Zur Krebsdiagnose, Acta Biol Med German. 13 (1964) 758–768.
[31] B. Teichmann, D. Ziebarth, [Effect of acid on crystallizator tests in tumor diagnosis. Cryoscopic measurements and crystallization tests. II. Crystallization studies], Arch. Geschwulstforsch. 42 (1973) 151–162.
[32] R.J. Fehring, N. Gaska, Evaluation of the Lady Free Biotester in determining the fertile period, Contraception. 57 (1998) 325–328.
[33] M. Guida, G.A. Tommaselli, S. Palomba, M. Pellicano, G. Moccia, C. Carlo Di, et al., Efficacy of methods for determining ovulation in a natural family planning program, Fertil. Steril. 72 (1999) 900–904.
[34] D.K. Patel, A.N. Desai, Comparative analysis of salivary ferning versus cervical ferning test as a predictor of ovulation, Int. J. Recent Adv. Multidisciplinary Res. 5 (2018) 3936–3941.
[35] H.W. Su, Y.C. Yi, T.Y. Wei, T.C. Chang, C.M. Cheng, Detection of ovulation, a review of currently available methods, Bioeng. Transl. Med. 2 (2017) 238–246.
[36] Y.M. El-Miedany, S.M. E-H, M.A. E-B, Validity of the saliva ferning test for the diagnosis of dry mouth in Sjogren's syndrome, Rev. Rhum. Engl. Ed 66 (1999) 73–78.
[37] A.B. Denisov, D.Y. Pushkar', S.A. Denisov, Use of saliva crystallogenic properties for early diagnostics of prostate cancer, Bull. Exp. Biol. Med. 142 (2006) 242–245.
[38] O.V. Myachina, A.A. Zuykova, A.N. Pashkov, N.M. Pichuzhkina, Features of major salivary glands, Zhurnal Anatomii i Gistopatologii. 5 (2016) 66–69.
[39] E.I. Selifanova, S.Y. Ivanov, A.M. Mkrtumyan, A.B. Denisov, M.V. Chachiashvili, Crystallization of oral fluid components in patients with type 1 diabetes mellitus, Bull. Exp. Biol. Med. 139 (2005) 18–20.
[40] A.B. Denisov, G.M. Barer, E.I. Selifanova, Crystallization of components oral fluid in diabetics in case of absence of crystal structures, Bull. Exp. Biol. Med. 140 (2005) 100–101.
[41] A.B. Denisov, Algorithm for evaluation of crystal figures obtained after drying of mixed saliva, Bull. Exp. Biol. Med. 7 (2004) 30–34.
[42] P.V. Lebedev-Stepanov, M.E. Buzoverya, K.O. Vlasov, Y.P. Potekhina, Morphological analysis of images of dried droplets of saliva for determination the degree of endogenous intoxication, J. Bioinform. Genomics 9 (2018) 1–5.
[43] T.S. Chemicosova, O.A. Gulyaeva, The morphological picture of the oral fluid as a diagnostic test to professional intoxication preclinically estimate, Paradantologya. 46 (2008) 7–10.
[44] A.K. Martusevich, V.A. Yanchenko, O.B. Zhdanova, F. Artese, L.A. Napisanova, R. Virbalene, Crystallization characteristics of biological fluids of patients with postoperative alveococcosis, Clin. Med. 6 (2014) 38–42.
[45] A.K. Martusevich, N.F. Kamakin, Crystallography of biological fluid as a method for evaluating its physiochemical characteristics, Bull. Exp. Biol. Med. 143 (2007) 385–388.
[46] S. Pattanasuttinont, W. Seseepapong, S. Suwajanakorn, The Salivary Ferning Test and Ovulation in Clomiphene Citrate-stimulated Cycles, 2007, pp. 876–883, 90.
[47] L.V. Belskaya, O.A. Golovanova, E.S. Shukailo, V.G. Turmanidze, Experimental study of crystallization in biological liquids, Vestn. Otd. Nauk. O Zemle Ran 3 (2011) 1–4.
[48] D.A. Domenyuk, B.N. Davydov, E.G. Vedeshina, S.V. Dmitrienko, Morphology of oral liquid solids as a diagnostic method for dentofacial anomalities, part 1, Institut Stomatologii. 3 (2016) 52–54.
[49] L.F. Kaskova, T.B. Mandziuk, O.I. Godovanets, L.P. Ulasevych, L.V. Kuzniak, Effect of PH and mineralizing properties of the oral fluid on enamel acid resistance in children, World Med. Biol. (2019), 15.
[50] G. Pancu, S. Stoleriu, G. Iovan, A. Gheorghe, I. Nica, N. Tofan, et al., On the salivary microcrystallization index variation in patients with dental erosion lesions, Int. J. Med. Dentistry. 19 (2015) 189–193.
[51] A. Spinei, A.M. Picos, I. Romanciuc, A. Berar, A.M. Mihailescu, The study of oral liquid microcrystallization in children with gastro-esophageal reflux disease, Clujul Med. 87 (2014) 269–276.
[52] Spinei Iurie, Balteanu Olga, Spinei Aurelia, Stepco Elena, Crystallogenesis of oral fluid in the diagnosis of dental caries and inflammatory periodontal diseases in children, in: Proceedings of the 4th IEEE International Conference on E-Health and Bioengineering Iasi, Romania, November 21-23, 2013, 2013.
[53] I.M. Voloshina, V.V. Borisov, A.V. Sevbitov, A.A. Davidiants, S.N. Mironov, M. Y. Kuznetsova, et al., Distinctive features of microcrystallization of mixed saliva in children with different levels of activity of carious process, Asian J. Pharm. 12 (2018) 1017–1020.
[54] Z.G. Simonova, A.K. Martusevich, O.I. Shubina, V.L. Emanuel, Structural characteristics of biological fluids of patients with combined cardiovascular and gastrointestinal pathology, Clin. Med. 6 (2014) 64–70.
[55] H.L. Bolen, A review of experience with the blood pattern test from 1939 to 1953, Am. J. Surg. (87) (1954) 205–210.
[56] H.L. Bolen, The blood pattern as a clue to the diagnosis of malignant disease, J. Lab. Clin. Med. 27 (1942) 1522–1536.
[57] H. Bolen, Diagnostic Value of the Blood Pattern in Cancer, 1950.
[58] J.V. Finnegan, Comparison of Huggins' test with sedimantation rate, Weltmann reaction, and the Bolen test in cancer, J. Lab. Clin. Med. 35 (1950) 708–712.
[59] H.L. Grueber, A. Huppertz, Beitrag Zur Carzinomdiagnose Durch Bolen-Test, Aerztliche Wochenschrift. 7 (1952) 1130–1132.
[60] B.O. Hawk, G.E. Thoma, J.J. Inkley, An evaluation of the Bolen Test as a screening test for Malignancy, Cancer Res. 11 (1951) 157–160.
[61] A. Huettl, A. Csillag, L. Horvath, J. Vadasz, On the Significance and Causes of the Variability in Pattern of the Dried Drop of Blood (Bolen's Test), 2nd Departement of Surgery and Institute of Histology and Embryology, University Medical School, Budapest, 1955, pp. 309–322.
[62] I.I. Pinskaia, T.V. Sergeeva, Diagnostic value of studying a dried drop of blood in cancer (Bolen test), Khirurgiia (Mosk). 49 (1973) 24–27.
[63] A. Vaughn, W. Metzner, C. Annan, An evaluation of the Bolen blood pattern test for detecting cancer, Amercan J. Surg. (1952) 641–646.
[64] B.H. White, R.R. Rector, J.M. Miller, W.A. Oktavec, The Bolen test for cancer, Am. J. Surg. (1952) 356–357.
[65] O.C. Gruner, Periodic fluctuations in the blood picture in cancer and their bearing on radiation therapy, Can. Med. Assoc. J. (1941) 256–259.
[66] M.A. Feofilova, A.G. Lastovetskiy, O.G. Pavlov, E.I. Tomareva, Comparative crystallography of blood for women with uterine myoma and women-donors, J. New Med. Technol. 4 (2016) 145–153.
[67] M.A. Feofilova, Crystallographic picture of healthy women blood, Vesnik Slyzhby Krovi. 1 (2013) 16–19.

[68] L. Hamadeh, S. Imran, M. Bencsik, G.R. Sharpe, M.A. Johnson, D.J. Fairhurst, Machine learning analysis for quantitative discrimination of dried blood droplets, Sci. Rep. 10 (2020) 3313.
[69] L. Bahmani, M. Neysari, M. Maleki, The study of drying and pattern formation of whole human blood drops and the effect of thalassaemia and neonatal jaundice on the patterns, Colloids Surf. A Physicochem. Eng. Asp. 513 (2017) 66–75.
[70] R. Chen, L. Zhang, D. Zang, W. Shen, Blood drop patterns: formation and applications, Adv. Colloid Interface Sci. 231 (2016) 1–14.
[71] M. Franz, M. Scholz, S. Roeckl, L.I. Gomez, Detection of colon polyps by a novel, polymer pattern-based full blood test, J. Transl. Med. 11 (2013) 1–9.
[72] S. Gruner, Kristalloptischer nachweis von störfeldbelastungen mittels blutkristallisationsanalyse, in: M. Dräger (Ed.), Standort Als Risikofaktor, 1 ed., 1994, pp. 245–263. Reickl, Germany: Reichl Verlag, St. Goar.
[73] T. Schockert, H. Gegenbauer, F.A. Popp, Diagnose und Therapie mit spagyrischer Medizin: beobachtungen zur raschen Wirksamkeit der spagyrischen Heilmittel Homodot und Antihomodot mit der Regulationsdiagnostik nach Prof, Dr. Fritz-Albert Popp. Complementärmed Diagnose und Therapie. (2009) 6.
[74] S. Bali, R.R. Marathe, Crystallization test for early detection of malignancy, Int. Arch. Biomed. Clin. Res. 3 (2017) 46–49.
[75] J.G. Barth, Empfindliche Kristallisation Krebs Und Praekanzerose. Elemente Der Naturwissenschaft, 1990, pp. 42–50, 52.
[76] C. Bornholt, Darstellung Der Blutkristallisation Bzw. Kupferchloridkristallisation Unter Dem Gesichtspunkt Der Krebserkrankung. Onkologie, 2010, pp. 1–28, 5.
[77] W. Garn von, Blutkristallreaktion auf pathologische stoffwechselprodukte beim Karzinom, Archiv fuer Geschwulstforschung. 2 (1950) 238–245.
[78] O.C. Gruner, Experience with the Pfeiffer crystallization method for the diagnosis of cancer, Can. Med. Assoc. J. 43 (1940) 99–106.
[79] S.P. Gulati, O.P. Sachdeva, A. Sachdeva, V. Kakkar, Crystallization test for the detection of head and neck cancer, ORL. 56 (1994) 283–286.
[80] H. Jung, Beitraege Zur Kristallographischen Blutuntersuchung, Pharmascia. 7 (1952) 628–639.
[81] J. Kuczkowski, P. Zaorski, A. Betlejewski, Crystallization test in the patients with head and neck cancer, Otolartngol Pol. 49 (1995) 121–124.
[82] V. Makkar, M. Kamboj, A. Narwal, R.K. Kapoor, Potency of Pfeiffer's crystallization to analyze oral leukoplakia and squamous cell carcinoma, Asian Pac. J. Cancer Prev. 21 (2020) 517–522.
[83] H. Mehrota, H. Sadiq, R. Anjum, P. Goyal, P. Kasana, S.M. Shaikh, Crystallize to definitize cancer, Int. J. Sci. Res. 6 (2017) 312–315.
[84] E. Pfeiffer, G.P. Miley, The influence of blood of malignant and non-malignant origin upon the crystallization of copper chloride in: laboratory BR, (editor). Dornach, Switzerland: E. Pfeiffer Archive (1939).
[85] S. Rascher, J. Trumpp, Versuch einer Kristallographischen Karzinomdiagnose, Muenich med Wschr. 14 (1939) 544–545.
[86] G. Rawat, K. Kureel, A. Urs, An insight into crystallization test: a neoteric approach for screening premalignant and malignant lesions, J. Cancer Res. Ther. (2018), 0.
[87] S.C. Sarode, G.S. Sarode, S. Barpande, J.V. Tupkari, Efficacy of crystallization test for screening of oral squamous cell carcinoma with clinico-pathological correlation, Journal of Indian Dental Research. 24 (2013) 464–467.
[88] S.I. Shaikh, D.N. Kawale, C.V. Divan, A. Quadeer, A.R. Kharkar, Crystallization test for the detection of malignancy of the female genital tract, Int. J. Basic Med. Sci. 3 (2012) 118–124.
[89] R. Tarigoppula, B. Mujib, R. Naik, Effectiveness of crystallization test in screening of potentially malignant oral disorders and oral cancer, Indian J. Dent. Res. 29 (2018) 556–561.
[90] H. Knijpenga, Die Methode Der Empfindlichen Kristallisation Nach Ehrenfried Pfeiffer: Die Anwendung Auf Humanblut, Ein Lehrgang] Ehrenfried Pfeiffer's Sensitive Crystallization Method Appied on Human Blood: a Course.. Archiv-KN-Kristallisation: Sceintific Section of Goetheanmum, Dornach, Switzerland, 2020, p. 654.
[91] A. Selawry, O. Selawry, Die Kupferchloridkristallisation. Stuttgart, Germany: Gustav Fischer Verlag, 1957.
[92] A. Quadeer, New approach for detection of malignancy by crystallization test: govt, Medical College Nagpur (1988).
[93] J.T. Vara, H.K. Puneeth, A. Anuradha, M.A. Kiresur, S.G. Vijaya, B.S. Bagalad, Crystallization test: a diagnostic savvy of diabetes mellitus, Asian Acad. Res. J. Multidisciplinary. 2 (2015) 54–65.
[94] T. Shibata, S. Matsumoto, M. Kogure, T. Iguchi, A. Tanaka, T. Nagano, et al., Effects of diabetic human blood addition on morphology of cupric chloride dendrits grown from aqueous solutions, J. Cryst. Growth 219 (2000) 423–433.
[95] M. Cocude, J.G. Barth, B. Bruyet, P. Francois, Silikose - die staublunge der bergleute und ihre medizinische langzeitbetreuung, Elemente der Naturwissenschaft. 60 (1994) 49–63.
[96] Pfeiffer E. Sensitive crystallization processes: a demonstration of formative forces in the blood1975.
[97] E. Pfeiffer, An experimental method to detect finer changes in the blood and other body fluids, J. Appl. Nutr. 10 (1957) 1–4.
[98] V.N. Shabalin, D.S. Uvarova, S.N. Shatokhina, Features of urine biomineralization in long-livers, Vestnik RAMN. 70 (2015) 403–407.
[99] J. Trumpp, S. Rascher, E. Nachpruefung der, Pfeiffer'schen Angaben uber die moeglichkaeit einer Kristallographischen Diagnistik; versuch einer Hormonoskopie und schwangerschaftsdiagnose, Medizinische Wochenschrift. 26 (1939) 1049–1051.
[100] G.A. Abramov, Y.E. Zakharova, A.M. Zhumakaev, S.S. Zhumakaeva, L. B. Aytisheva, N.A. Chaykovskaya, The peculiarities of morphotypes of the teziogramms of blood plasma of patients with pancreatic cancer, Mezhdunarodnyj Zhurnal Prikladnykh Fundamentalnykh Issledovanij. 8 (2016) 297–301.
[101] A. Brzecki, A. Brzecka, E. Gruszka, P. Olejniczak, M. Cyrul, Dry drop blood plasma - a new approach in the diagnosis of neoplastic diseases, Mater. Med. Pol. 3 (1998) 170–174.
[102] L.M. Obukhova, A.V. Alyasova, K.H. Kontorshchikova, I.G. Terentyev, T. N. Gorshkova, O.N. Nikiforova, Structural and biochemical characteristics of human blood plasma in epithelial esophageal tumors, Vestnik Novyh Medizinskih Technologiy. 18 (2011) 27–30.
[103] E. Rapis, A change in the physical state of a nonequilibrium blood plasma protein film in patients with carcinoma, Tech. Phys. 47 (2002) 510–512.
[104] V.G. Firsova, V.V. Parshikov, Y.P. Potekhina, The peculiarities of hard biological phase fluids morphology in acute destructive pancreatitis, Annaly Khirurgicheskoj Gepatologii. 17 (2012) 79–85.
[105] M.P. Kim, Modern physical and chemical metods of research plasma blood in dynamics of treatment chronic tonsillitis in children, Rossijskaya Otolaringologiya. 37 (2008) 67–71.
[106] E.A. Shuasheva, Dynamic of Blood Serum Tesiographic Picture in Patietns With Rheumatoid Arthritis With Ozone /NO-low-frequency Ultrasonic Method of Treatment. Nauchno-meditisinskiy Zhurnal <Vestnik Avitsenny> Tadzhikskogo Gosudarstvennego Meditsinskogo Universiteta Imeni Abuali Ibni Sino, 2012, pp. 131–136, 4.
[107] M.B. Karpukhina, Y.P. Potekhina, E.A. Antipenko, A.V. Gustov, M.E. Busoverya, I. V. Shishpor, Dynamics of the morphological picture of blood plasma and cognitive functions on the background of neuroprotective therapy with discirculatory encephalopathy, Medicinskiy Almanakh. 14 (2011) 69–71.
[108] C. Costagliola, A. del Prete, C. Incorvaia, R. Fusco, F. Parmeggiani, A. di Giovanni, Ocular surface changes induced by topical application of latanoprost and timolol: a short-term study in glaucomatous patients with and without allergic conjunctivitis, Graefes Arch. Clin. Exp. Ophthalmol. 239 (2001) 809–814.
[109] M. Li, M. Zhang, Y. Lin, Q. Xiao, X. Zhu, S. Song, et al., Tear function and goblet cell density after pterygium excision, Eye (Lond). 21 (2007) 224–228.
[110] M. Nebbioso, M. Sacchetti, G. Bianchi, A.M. Zicari, M. Duse, P. del Regno, et al., Tear ferning test and pathological effects on ocular surface before and after topical cyclosporine in vernal keratoconjunctivitis patients, J. Ophthalmol. (2018). ID 1061276:11 pages.
[111] V. Peponis, M. Papathanasiou, A. Kapranou, A. Magkou, A. Tyligada, A. Melidonis, et al., Protective role of oral antioxidant supplementation in ocular surface of diabetic patients, Br. J. Ophthalmol. 86 (2002) 1369–1373.
[112] A.M. Masmali, Y.A. Maeni, G.A. El-Hiti, P.J. Murphy, T. Almubrad, Investigation of ocular tear ferning in controlled and uncontrolled diabetic subjects, Eye Contact Lens 44 (2018) 70–75.
[113] M.B. Parodi, S. Saviano, P. Panetta, G. Ravalico, Subretinal fluid ferning test in rhegmatogenous retinal detachment, Eur. J. Ophthalmol. 11 (2001) 156–159.
[114] P.P. Pezzi, M.P. Paroli, R. Priori, S. da Dalt, R. Corradini, Vogt-Koyanagi-Harada syndrome and keratoconjunctivitis sicca, Am. J. Ophthalmol. 137 (2004) 769–770.
[115] M. Rolando, F. Baldi, G. Calabria, Tear mucus crystallization in children with cystic fibrosis, Ophthalmologica. 197 (1988) 202–206.
[116] E. Vaikoussis, P. Georgiu, D. Nomicarios, Tear mucus ferning in patients with Sjogren's syndrome, Doc. Ophthalmol. 87 (1994) 145–151.
[117] U. Beden, D. Turgut-Çoban, C. Ayguń, I. Ulu-Guŋgör, Y. Süllu, D. Erkan, et al., Tear secretion and ferning patterns among premature and full-term newborns, Turk. J. Pediatr. 50 (2008) 155–159.
[118] S. Srinivasan, E. Joyce, L.W. Jones, Tear osmolality and ferning patterns in postmenopausal women, Optom. Vis. Sci. 84 (2007) 588–592.
[119] A. Gajta, D. Turkoanje, I. Malaescu, C.N. Martin, M.J. Koos, B. Jelicic, et al., Dry eye syndrome among computer users, AIP Conference Proceedings 1694 (2015), 040011.
[120] A.M. Masmali, C. Purslow, P.J. Murphy, The tear ferning test: a simple clinical technique to evaluate the ocular tear film, Clin. Exp. Optom. 97 (2014) 399–406.
[121] M. Ferron, R. Bilodeu, Amniotic fluid crystallization test for ruptured membranes, CMAJ 89 (1963) 1064–1067.
[122] N.S. Fogelson, P.C. Browne, S. Browne, A.R. Gregg, Second trimester amniotic fluid is reliably fern positive and alpha1-microglobulin positive: dispelling a labor deck myth, Am. J. Perinatol. 31 (2014) 389–392.
[123] H. Gaddey, J. Bailey, RF S, Ferning in amniotic fluid:is it a useful indicator of ruptured membranes? Clinical Inquiries. 60 (2011) 769–771.
[124] L.C. Rogers, L. Scott, J.E. Block, Accurate point-of-Care detection of ruptured fetal membranes: improved diagnostic performance characteristics with a Monoclonal/ Polyclonal immunoassay, Clin. Med. Insights Reprod. Health 10 (2016) 15–18.
[125] G. Neumann, H. Lehfeldt, The crystallization phenomenon of the cervical mucus in the diagnosis of early pregnancy, Am. J. Obstet. Gynecol. (1955) 70.
[126] F. Farahmand, N. Sadjadei, M.T. Haghi-Ashtiani, V. Modaresi, N. Rezaei, B. Pakseresht, Comparison of classic sweat test and crystallization test in diagnosis of cystic fibrosis, Iran Journal of Pediatry. 22 (2012) 102–106.
[127] J. Ferrer-Clavete, C. Ribes, C. Montero, Study of the forms of sweat crystallization in cystic fibrosis patiens, Acta Universitaris Carolinae Medica. 36 (1990) 89–92.
[128] Y.Y. Ukhanova, Method of wedge dehydration of menstrual fluid in diagnostics of proliferating hysteromioma, Novaya Nauka: Problemy i Perspektivy. 10 (2016) 46–50.
[129] Y.Y. Ukhanova, L.V. Dikaryova, E.G. Sharyov, A.K. Ayupova, An integrated approach to the diagnosis and evaluation of uterine myoma in growth rates, Opukholy Zhenskoj Reproduktivnoj Sistemy. 4 (2015) 71–75.
[130] L.I. Turbinkova, A.V. Samoylova, O.A. Marinova, S.G. Milaev, M.L. Albutova, Clinical value of follicular fluid morphology in patients with inflammatory

infertility genesis in outcome prognosis of assistedreproductive technology programs, Ul'Yanovskyj Medico-biologicheskyj Zhurnal. 1 (2017) 87–103.
[131] S.N. Shatokhina, Morphological marker anaerobic infection at pyoinflammatory diseases maxillofacial area, Al'Manakh Klinicheskoj Mediciny. 17 (2008) 283–286.
[132] E.G. Shvaryov, L.V. Dikaryova, D.L. Ovodenko, A.K. Ayupova, G.E. Shvaryov, Markers of endometrial biological fluids in the diagnosis of uterine adnexal tumors, Tumors Female Reprod. Syst. 11 (2015) 76–80.
[133] R. Strom-Olsen, Kite Ec, The sodium chloride crystallization test and its relation to the blood-C.S.F. Barrier, J. Ment. Sci. 88 (1942) 407–414.
[134] W.J. Neretin, W.A. Kirjakov, Eine Kristallographische Methode Zur Untersuchung Der Zerebrospinalfluessigkeit Bei Erkrankungen Des Zentralnervensystems, Psychiatr. Neurol. Med. Psychol. Beih. 29 (1977) 474–481.
[135] Bolen, Diagnostic Value of the Blood Pattern in Cancer, 1950.
[136] A. Kubatova, T. Fedorova, Saliva crystallization occurs in female Bornean Orangutans (Pongo pygmaeus): could it be a new option for monitoring of menstrual cycle in captive great apes? PLoS One 11 (2016), e0159960.
[137] B. Pardo-Carmona, M.R. Moyano, R. Fernandez-Palacios, C.C. Perez-Marin, Saliva crystallisation as a means of determining optimal mating time in bitches, J. Small Anim. Pract. 51 (2010) 437–442.
[138] R. Ravinder, O. Kaipa, V.S. Baddela, E. Singhal Sinha, P. Singh, V. Nayan, et al., Saliva ferning, an unorthodox estrus detection method in water buffaloes (Bubalus bubalis), Theriogenology. 86 (2016) 1147–1155.
[139] S. Bernardi, A. Rinaudo, P. Marini, Cervical mucus characteristics and hormonal status at insemination of Holstein cows, Iran. J. Vet. Res. 17 (2015) 45–49.
[140] M.E. Cortes, F. Gonzalez, P. Vigil, Crystallization of bovine cervical mucus at oestrus: an update, Rev. Med. Vet. (Toulouse) 28 (2014) 103–116.
[141] V. Luno, L. Gil, R.A. Jerez, C. Malo, I. Gale, I. de Blas, Crystallisation pattern of vestibular mucus and its relation to vestibular electrical resistance in cycling sow, Vet. Rec. 171 (2012) 298.
[142] D. Williams, H. Hewitt, Tear ferning in normal dogs and dogs with keratoconjunctivitis sicca, Open Vet. J. 7 (2017) 268–272.
[143] M. Coassin, A. Lambiase, N. Costa, A. De Gregorio, R. Sgrulletta, M. Sacchetti, et al., Efficacy of topical nerve growth factor treatment in dogs affected by dry eye, Graefes Arch. Clin. Exp. Ophthalmol. 243 (2005) 151–155.
[144] T.A. Yakhno, A.A. Sanin, R.G. Ilyazov, G.V. Vildanova, R.A. Khamzin, N. P. Astascheva, et al., Drying drop technology as a possible tool for detection leukemia and tuberculosis in cattle, J. Biomed. Sci. Eng. 08 (2015) 1–23.
[145] J.M. Cameron, H.J. Butler, D.S. Palmer, M.J. Baker, Biofluid spectroscopic disease diagnostics: a review on the processes and spectral impact of drying, J. Biophotonics 11 (2018), e201700299.
[146] HIS Spagyrik Institut. Die Auswertung der Kristalle. https://spagyrik.com/die-auswertung/2021.
[147] Wikipedia. Prelabor rupture of membranes. Wikipedia, the free Encyclopedia2018.