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Viewpoint

Pseudogout, chondrocalcinosis, CPPD et al: crystal clear. . . or clear as mud?—The time has come to reconsider the nomenclature of calcium pyrophosphate deposition

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ABSTRACT

Scientific interest in calcium pyrophosphate deposition (CPPD) has been limited by several challenges. These include difficulties in diagnosis due to diverse clinical presentations, the lack of classification criteria, the absence of standardised diagnostic modalities, underrecognition in clinical care, and, most significantly, the lack of evidence-based treatments. Consequently, CPPD was often regarded as the 'poor cousin' of gout. Fortunately, in recent years, CPPD has garnered increased attention from the rheumatology community. Milestones such as the first American College of Rheumatology/European Alliance of Association for Rheumatology classification criteria, the European Alliance of Association for Rheumatology recommendations for the use of imaging in clinical practice, validated OMERACT ultrasound definitions and scoring system, and the OMERACT core domain sets for CPPD have significantly advanced the field. Yet, unresolved issues regarding CPPD nomenclature hold back advancement in both research and clinical practice. The terminology surrounding CPPD remains inconsistent in the scientific literature, with numerous terms and acronyms used to describe the condition and its manifestations. For example, many 'pseudosyndromes' (eg, pseudogout) and purely radiographic descriptors (eg, chondrocalcinosis) are still commonly used by clinicians and researchers interchangeably,

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as either the name of the condition or one of its clinical or radiographic manifestations. This lack of standardisation complicates communication among health care professionals, researchers, and between doctors and patients, creating insurmountable barriers to effective care and research advances. In this viewpoint, we highlight the value of standardised terminology, drawing parallels with other rheumatic diseases. We aimed to explore the historical evolution of CPPD nomenclature, assess the impact of previous standardisation efforts, and propose a possible way for a common language.

Language is the most essential tool for communication. When different terms are used to describe the same disease or aspect of a condition, especially with inconsistent or inhomogeneous terminology, clarity is diminished, and effective communication is compromised [1]. This issue affects not only technical terminology to be used among health care professionals but, even more critically, communication with patients. In the case of calcium pyrophosphate deposition (CPPD), the problem extends beyond inconsistent terminology to include the multiple abbreviations used to refer to both the crystals and the condition itself [2]. The situation mirrors the biblical Tower of Babel, where fragmented language created confusion and hindered understanding [3].

THE VALUE OF A COMMON TERMINOLOGY: INSIGHTS FROM OTHER RHEUMATIC DISEASES

The importance of clear and consistent terminology is underscored by other examples in rheumatology. One notable shift is the transition from ankylosing spondylitis to axial spondyloarthritis, which reflects a deliberate effort to adopt a more precise language for describing disease by emphasising the anatomic focus of disease (axial) and removing the term ankylosing, which carries a negative prognostic connotation, as the associated degree of structural damage may take years to develop or may not occur at all [4]. The standardisation of the nomenclature of axial spondyloarthritis has been supported by numerous publications on the topic and has been embraced by international scientific groups. For instance, the ASAS working group renamed itself from 'ASsessment of Ankylosing Spondylitis' working group to 'Assessment of SpondyloArthritis International Society'. Furthermore, there has been a proposal to officially redefine the ASDAS acronym, changing its meaning from 'Ankylosing Spondylitis Disease Activity Score' to 'Axial Spondyloarthritis Disease Activity Score'. These initiatives have significantly increased the use of the term axial spondyloarthritis in both clinical practice and scientific literature, promoting greater alignment in the field.

CPPD TERMINOLOGY: FROM THE ORIGINS TO THE CURRENT DISARRAY

In 1962, McCarty et al [5] coined the term pseudogout to describe acute arthritis flares resembling gout but caused by non-urate crystals. They later identified these crystals as calcium pyrophosphate dihydrate and introduced the term CPPD to refer to the crystals [6]. They proposed 5 clinical phenotypes, many of which were labelled with the prefix pseudo due to their resemblance to other rheumatic conditions [7]. The condition was defined as calcium pyrophosphate dihydrate crystal deposition disease [7], although some called it pyrophosphate arthropathy [8] or pyrophosphate synovitis [9]. Moreover, the term chondrocalcinosis, initially used to describe the radiographic appearance of CPPD [10], became common to describe the condition itself [11] (Fig).

In 2011, a European Alliance of Association for Rheumatology (EULAR) CPPD task force attempted to standardise CPPD nomenclature via a consensus paper based on expert opinion

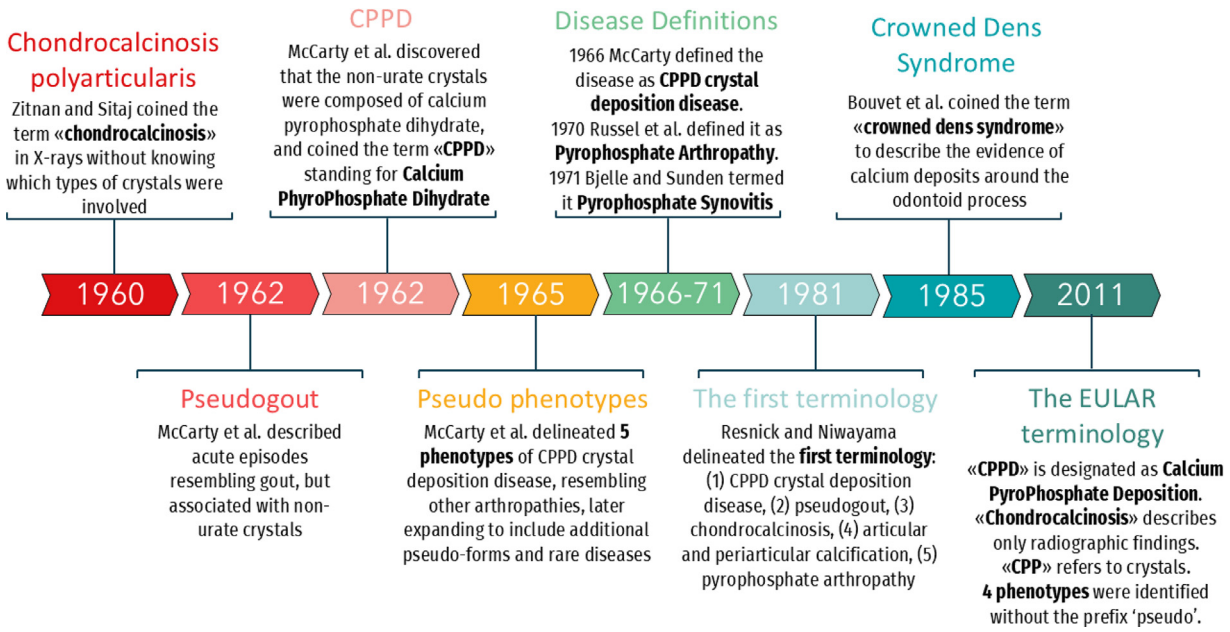

Figure. Timeline of the fundamental steps in calcium pyrophosphate deposition description. Adapted from Sirotti et al [3]. CPDD, calcium pyrophosphate deposition disease; CPP, calcium pyrophosphate; EULAR, European Alliance of Association for Rheumatology.

[12]. Their recommendations aimed to eliminate the pseudo prefix and restrict the term chondrocalcinosis to describe radiographic findings (Fig). For the first time, CPPD was specified to stand for calcium pyrophosphate (CPP) deposition, referring to the umbrella term for all instances of CPP crystal occurrence, including the asymptomatic form, while the pathogenic crystals were referred to as CPP crystals. Moreover, the task force outlined 4 distinct phenotypes: (i) asymptomatic CPPD, (ii) osteoarthritis with CPPD, (iii) acute CPP crystal arthritis, and (iv) chronic CPP crystal inflammatory arthritis.

A recent systematic literature review (SLR) examined the terminology commonly used to describe CPPD, revealing significant inconsistencies across the literature [13]. Among 886 articles analysed from 2000 to 2022, the most frequent label used to designate the condition remains pseudogout, appearing in nearly half of the article, followed by chondrocalcinosis and calcium pyrophosphate deposition disease (CPDD). Controversy also surrounds the appropriate abbreviation for the condition −CPPD or CPDD? Although CPPD was the most used abbreviation, it predominantly referred to calcium pyrophosphate deposition disease, rather than calcium pyrophosphate deposition as recommended by the EULAR. This reflects ongoing confusion on the significance of the final letter 'D'. Another key issue identified was the inconsistent use of the term chondrocalcinosis, which has been applied variably to describe the condition itself, its elements, and its states. Furthermore, the frequent use of pseudoterms to describe different condition's states remains prevalent in the literature.

IMPACT OF THE 2011 EULAR TERMINOLOGY RECOMMENDATION

The SLR demonstrated that terms such as chondrocalcinosis and pseudogout are still deeply rooted in the terminology despite the 2011 EULAR recommendations [12]. To evaluate the impact of these recommendations, a comparison of data from before and after 2011 was conducted, driving this viewpoint (Table). Between 2000 and 2011, the most frequently used term to describe the condition was pseudogout (52%), followed by chondrocalcinosis (33%) and calcium pyrophosphate dihydrate crystal deposition disease (19.7%). Unfortunately, only a slight improvement was observed after 2011. While the use of pseudogout decreased to 43.7%, it remained the most used term, followed by calcium pyrophosphate deposition disease (31.5%) and chondrocalcinosis (22.8%). The term proposed by the EULAR taskforce, calcium pyrophosphate deposition, was scarcely adopted, appearing in just 1.1% of articles before 2011 and increasing to only 5% after 2011.

The abbreviation CPPD also exhibited a shift in usage before and after 2011. Before 2011, it predominantly referred to calcium pyrophosphate dihydrate in the context of crystals, whereas after 2011, it was used to describe the condition as calcium pyrophosphate deposition disease. However, this usage still does not align precisely with the EULAR recommendation, which advocated for calcium pyrophosphate deposition, omitting the term disease, as CPPD was meant to include also the asymptomatic form.

In contrast, terms referring to crystals showed better adherence to the recommendations. Before 2011, calcium pyrophosphate dihydrate (abbreviated as CPPD) was the most frequently used term, but it transitioned to calcium pyrophosphate with the abbreviation CPP after 2011, in line with EULAR's guidance.

The use of pseudoterminology has lessened for describing certain phenotypes following the publication of the EULAR recommendations. Nevertheless, pseudogout remained the most used term to describe 'an episode of acute arthritis' and 'recurrent acute arthritis' both before and after 2011. The recommended term, acute CPP crystal arthritis, was found in only 1.2% of articles before 2011 and increased to 32.9% of articles after 2011−reflecting the research community's openness to new terminology for this condition state. A more significant shift occurred in the terminology for 'persistent inflammatory arthritis'. Before 2011, this was predominantly referred to as pseudorheumatoid arthritis, whereas after the EULAR recommendations, it was more frequently labelled as chronic CPP crystal arthritis. Similarly, 'osteoarthritis related to CPP crystals' underwent a terminological change. Before 2011, it was described using the pseudoterm pseudo-osteoarthritis. After 2011, it was more commonly referred to as CPPD-related/associated osteoarthritis, a term more closely aligned with EULAR's recommendations.

These analyses revealed that the EULAR recommendations had a moderate impact on scientific language and have failed to replace entrenched habits. The reason for this may be attributed to several factors: the absence of subsequent articles emphasising the importance of standardising terminology, insufficient endorsement of the recommendations by other scientific societies, the absence of an alignment in the International Classification of Diseases (ICD) coding system, or a lack of intervention by peer reviewers to correct the terminology used in submitted papers and promote greater alignment with the recommendations.

THE GOUT, HYPERURICEMIA AND CRYSTAL-ASSOCIATED DISEASE NETWORK NOMENCLATURE PROJECT FOR CPPD

An international initiative developed by the Gout, Hyperuricemia and Crystal-Associated Disease Network (G-CAN), is underway to agree on standardised terminology for CPPD, aiming to update inconsistencies and varied meanings of existing terms. Launched in 2022, the project began with an SLR to identify existing definitions and terms used to describe CPPD [13]. Following this, a Delphi consensus process involving leading experts is in progress to refine and standardise the scientific terminology. Moreover, the project also includes a third step for creating lay-friendly language, ensuring accurate, clear, and consistent communication with patients. This step seeks to overcome the linguistic barriers that have hindered the broader adoption of EULAR-recommended terminology in clinical practice.

As previously mentioned, the EULAR recommendations on CPPD terminology have faced challenges in gaining widespread acceptance, likely due to several factors. First, since 2011, CPPD has seen a remarkable advance in research [14–17], and as understanding of its clinical manifestations and pathogenetic mechanisms grows [18,19], more precise terms are required to accurately describe the condition. For instance, while the condition itself is referred to as calcium pyrophosphate deposition, no consensus exists for its symptomatic form, which has been spontaneously termed calcium pyrophosphate deposition disease in recent publications. Another area of imprecision lies in the use of the term chondrocalcinosis, which is often applied broadly to

Table
The most frequently used labels representing the condition, the crystal, the condition element, and the condition states, presented in comparison before and after the 2011 EULAR recommendations on CPPD terminology

Concept	Before 2011		After 2011	
	Total no. of distinct labels	Most used labels, no. of papers (%)	Total no. of distinct labels	Most used labels, no. of papers (%)
The condition				
Condition name	46	Pseudogout, 145/279 (52.0) Chondrocalcinosis, 92/279 (33.0) Calcium pyrophosphate dihydrate crystal deposition disease, 55/279 (19.7)	51	Pseudogout, 220/504 (43.7) Calcium pyrophosphate deposition disease, 159/504 (31.5) Chondrocalcinosis, 115/504 (22.8)
Condition acronym	10	CPPD, 60/97 (61.9) CPDD, 12/97 (12.4) CC, 12/97 (12.4)	13	CPPD, 252/293 (86.0) CPDD, 27/293 (9.2) CC, 19/293 (6.5)
Condition acronym meaning	24	Calcium pyrophosphate dihydrate, 44/123 (35.8) Calcium pyrophosphate deposition disease, 15/123 (12.2) Calcium pyrophosphate dihydrate deposition disease, 11/123 (8.9)	24	Calcium pyrophosphate deposition disease, 89/298 (29.9) Calcium pyrophosphate deposition, 66/298 (22.1) Calcium pyrophosphate dihydrate, 29/298 (9.7)
The crystal				
Crystal name	7	Calcium pyrophosphate dihydrate, 206/271 (76.0) Calcium pyrophosphate, 47/271 (17.3) Calcium pyrophosphate dehydrate, 16/271 (5.9)	10	Calcium pyrophosphate, 233/446 (52.2) Calcium pyrophosphate dihydrate, 166/446 (37.2) Calcium pyrophosphate dehydrate, 45/446 (10.1)
Crystal acronym	8	CPPD, 196/210 (93.3) CPP, 10/210 (4.8) CCP, 1/210 (0.5)	7	CPP, 203/341 (59.5) CPPD, 138/341 (11.1) CCP, 2/341 (0.6)
The condition element				
Evidence of crystal deposition on radiography	13	Chondrocalcinosis, 106/153 (69.3) Calcification, 56/153 (36.6) Deposit, 6/153 (3.9)	15	Chondrocalcinosis, 179/246 (72.8) Calcification, 83/246 (33.7) Deposit, 11/246 (4.5)
The condition states				
Asymptomatic evidence of crystal deposition on radiography	9	Chondrocalcinosis, 4/13 (30.8) Asymptomatic chondrocalcinosis, 4/13 (30.8) Incidental radiographic finding, 1/13 (7.7)	13	Chondrocalcinosis, 11/25 (44.0) Asymptomatic chondrocalcinosis, 7/25 (28.0) Incidental radiographic finding, 1/25 (4.0)
Acute peripheral articular inflammation triggered by the presence of crystals	22	Pseudogout, 44/86 (51.2) Acute pseudogout, 10/86 (11.6) Acute arthritis, 5/86 (5.8)	36	Pseudogout, 69/164 (42.1) Acute CPP crystal arthritis, 54/164 (32.9) Acute arthritis, 16/164 (9.8)
Recurrent acute peripheral articular inflammation triggered by the presence of crystals	9	Pseudogout, 6/18 (33.3) Pseudorheumatoid arthritis, 3/18 (16.7) Pseudogout attacks, 3/18 (16.7)	12	Pseudogout, 10/28 (35.7) Acute recurrent CPP arthritis, 4/28 (14.3) Recurrent arthritis, 3/28 (10.7)
Persistent peripheral articular inflammation triggered by the presence of crystals	12	Pseudorheumatoid arthritis, 12/30 (40.0) Chronic arthritis, 8/30 (26.7) Chronic arthropathy, 1/30 (3.3)	19	Chronic CPP crystal arthritis, 27/58 (46.6) Pseudorheumatoid arthritis, 13/58 (22.4) Chronic arthritis, 7/58 (12.1)
Symptomatic osteoarthritis related to crystal deposits	24	Pseudo-osteoarthritis, 13/51 (25.5) CPP crystals deposits with osteoarthritis, 7/51 (13.7)	30	CPPD-related/associated osteoarthritis, 31/77 (40.3) Pseudo-osteoarthritis, 12/77 (15.6)

CPDD, calcium pyrophosphate deposition disease; CPP, calcium pyrophosphate; CPPD, calcium pyrophosphate deposition; CC: ChondroCalcinosis; CCP: CalCium Pyrophosphate.
Proportion and percentage refer to the articles in which at least 1 label is identified for each concept, with multiple labels possible per article.

describe any imaging features of articular calcification. This is particularly relevant now that more precise definitions of CPPD-related imaging findings are available on both plain radiography and other imaging modalities [20–22].

Further, any change in nomenclature must be widely supported by the scientific community, which requires broad expert involvement. To achieve this, the G-CAN initiative has invited all its members—over 250 experts from across the globe specialising in crystal-induced arthropathies—to contribute. This ensures comprehensive input into the Delphi surveys, and hopefully the new terminology should be able to foresee and cover also future directions of the research.

CONCLUSIONS

Achieving widespread changes in medical nomenclature is a gradual process, often requiring years to overcome entrenched habits and inconsistent practices. In the case of CPPD, the persistent use of outdated terms underscores the challenges of adopting standardised terminology, as noted in the SLR. The 2011

EULAR terminology represented an important step forward; however, its partial adoption reflects the ongoing need for greater consensus and implementation. While several terms were valuable when first introduced, advances in knowledge necessitate updates to language. The G-CAN nomenclature project will play a pivotal role in revising and promoting standardised terminology for CPPD. The full implementation of consistent terminology will require revisions to systems like the ICD coding, endorsement by major scientific societies, and active efforts from editors and peer reviewers to support alignment in publications. These changes, driven by the efforts of researchers and clinicians, will enhance communication, research, and improve patient care. Progress may be incremental, but it is an essential and transformative journey.

Competing interests

GF has received a research grant from Eli Lilly for an Investigator Initiated Trial in CPPD. All other authors have no competing interests regarding this article.

CRediT authorship contribution statement

Silvia Sirotti: Writing – review & editing, Writing – original draft, Visualization, Validation, Data curation, Conceptualization. **Charlotte Jauffret:** Writing – review & editing, Visualization, Validation, Methodology, Formal analysis. **Antonella Adinolfi:** Writing – review & editing, Visualization, Validation. **Edoardo Cipolletta:** Writing – review & editing, Visualization, Validation. **Daniele Cirillo:** Writing – review & editing, Visualization, Validation. **Luca Ingrao:** Writing – review & editing, Visualization, Validation. **Alessandro Lucia:** Writing – review & editing, Visualization, Validation. **Emilio Filippucci:** Writing – review & editing, Visualization, Validation. **Tristan Pascart:** Writing – review & editing, Visualization, Validation. **Sara K Tedeschi:** Writing – review & editing, Visualization, Validation. **Robert Terkeltaub:** Writing – review & editing, Visualization, Validation. **Nicola Dalbeth:** Writing – review & editing, Visualization, Validation. **Georgios Filippou:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Data curation, Conceptualization.

Contributors

SS and GF drafted the first version of the manuscript. CJ performed data analysis. All authors reviewed and approved the final version of the manuscript before submission. GF accepts full responsibility for the work, had access to the data, and controlled the decision to publish.

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