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**CALCIUM PYROPHOSPHATE CRYSTAL
DEPOSITION IN PATIENTS WITH
KNEE JOINT DISEASE**

Thesis
Submitted for partial fulfillment of M.D.
(Internal Medicine)

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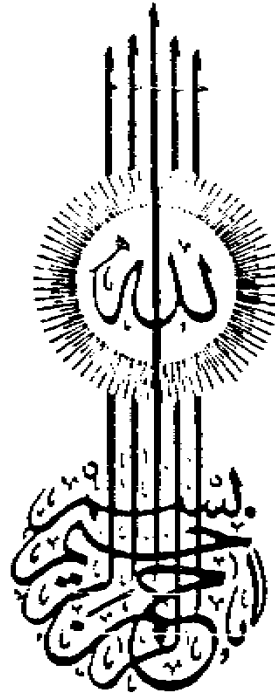
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سبحانك

لا علم لنا إلا ما علمتنا إنك أنت العليم الحكيم

صدق الله العظيم

(آية ٣٢ سورة البقرة)



To every one printed an idea or fingers'
tips in this work and to those I missed
them through my busyness in particular
Diana and Aya

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INTRODUCTION

INTRODUCTION

The use of compensated polarized light microscopy for the examination of joint fluid from patients with acute inflammatory synovitis, led to the detection of calcium pyrophosphate dihydrate (CPPD) crystals (1). It was discovered in 1961 by McCarty and, Hollander (1), and Kohn et al in 1962 (2). The term pseudogout was coined to describe the acute inflammatory gout like attacks that are produced by these weakly birefringent crystals with positively elongated sign (3). Pseudogout includes acute and chronic inflammatory as well as degenerative joint damage (2).

The term "crystal synovitis" was devised to describe joint inflammation generated from urate (1) or calcium pyrophosphate (CaPPi) crystal forms (1, 3 - 7) calcium oxalate (8), and later to include iatrogenic crystals of injected corticosteroid (9). It was apparent that the disease chondrocalcinosis familiaris described by Zitnan and Sitaj in 1958 (10), was linked to pseudogout, because of similar attacks of acute synovitis.

The term chondrocalcinosis referred to the detection, usually by roentgenograms or autopsy studies, of calcium (Ca) mineral salts in the articular fibrous or hyaline cartilages (3).

Some patients with pseudogout have a radiographically distinctive degenerative arthropathy with structural joint changes (11,12) and may be associated with para-articular calcification, (pyrophosphate arthropathy).

McCarty in 1975 (13) has distinguished six different clinical patterns for calcium pyrophosphate dihydrate crystal deposition disease (CPDD).

[A] Pseudogout

[B] Pseudo-rheumatoid arthritis

[C] Pseudo-osteoarthritis with episodic superimposed acute attacks.

[D] Pseudo-osteoarthritis without acute attacks

[E] Asymptomatic (Lanthenic) type

Less common presentations

[F1] pseudoneuropathic without suspected neuropathic proprioceptive deficit.

- [F2] Pseudotabetic with suspected neuropathic proprioceptive deficit, and
- Post traumatic.

It is important to exclude septic arthritis and gout from pseudogout. In variable cases CPDD has grown in association with a wide variety of diseases.

This work was performed to study this disease in Egypt for the first time, using the polarized microscopy, the polarized phenomenon peculiar to these crystals and a number of other crystals properties were discussed.

THE FOLLOWING HEADINGS WERE STUDIED

- The polarizing microscopy and other methods for crystals identifications.
- Synovial fluid analysis
- Knee joint effusions and particular crystals induced arthropathies.
- Pyrophosphate (PPi) metabolism.
- Associated disease with CPDD.

The investigation and the pathologic material which had been performed to this work, were proposed to

- [a] Realize the frequency of CPDD among patients with knee joint complaints.
- [b] Delineate the frequency and characteristic features of CPDD, according to Mc Carty clinical patterns.
- [c] Define and correlate clinical, radiographical and pathological abnormalities of CPDD with that of other knee joint diseases.
- [d] Consider the sensitivity and specificity of the diagnostic criteria of CPDD.

As part of this work is directed to the study of knee joint crystals, in general crystals are defined as:

Crystal is a solid matter with regular internal structure consisting of individual atoms arranged in a tridimensional pattern, called the crystal lattice. It is bounded by plane faces and edges as expression of the orderly internal arrangement of molecules (14). The shape depends on the concentration of the mother solution, pH, temperature, and nucleated factors. The crystallization of a given compound results in characteristic shape, outline, or habit which are

retained and repeated as the crystal grows. Internal symmetry gives a predicted effect on polarized light and on an electron beam conferring its phlogistic activity to certain types of crystals.

REVIEW OF THE LITERATURE

THE POLARIZING MICROSCOPY

The polarizing microscope is a special instrument designed for the study of minerals and inorganic crystals (15,16).

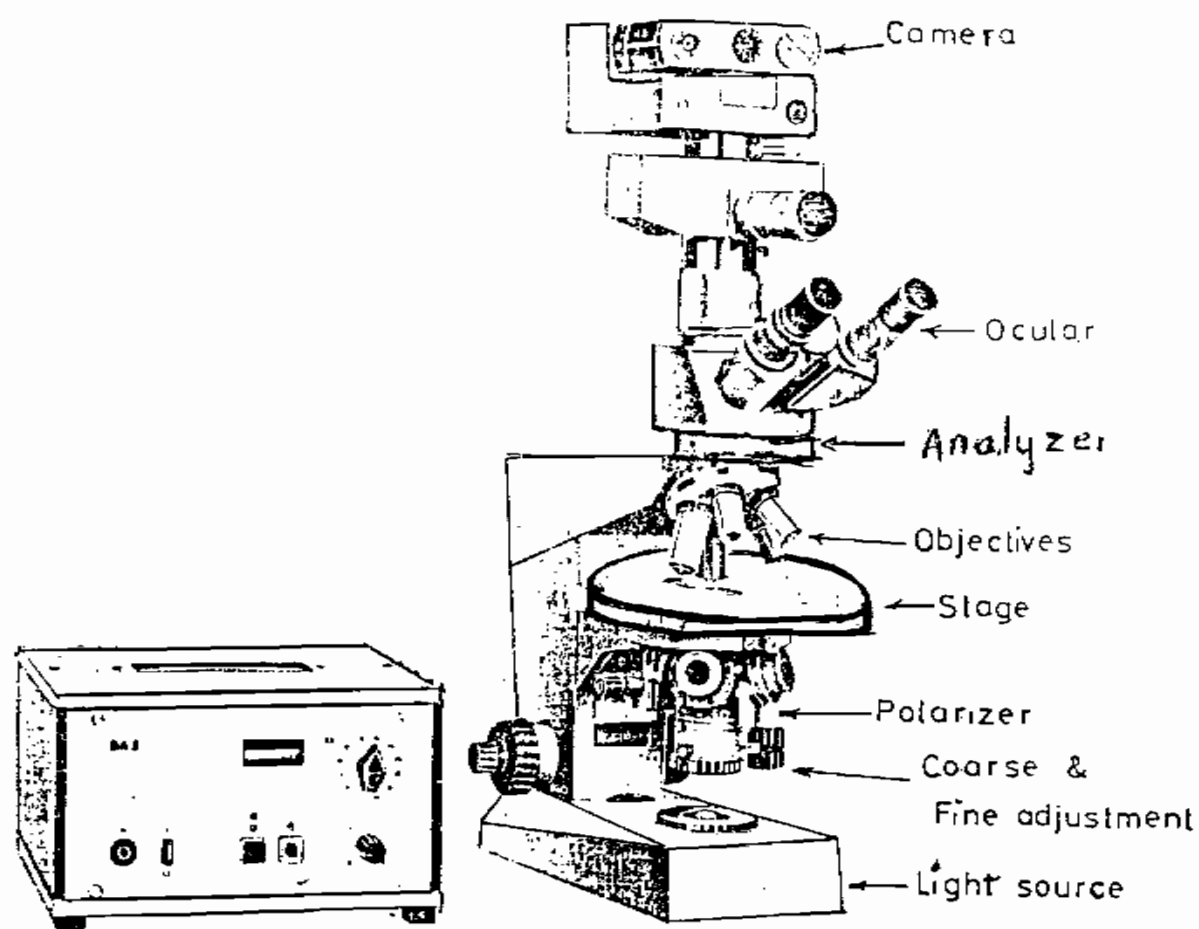
The main parts of the polarizing microscope are illustrated in Fig [1]. It contains of additional parts than the ordinary microscope.

- [1] It is equipped with two polarizing elements (the polarizing and analyzing prisms).
- [2] The microscope stage is rotary stage.
- [3] The presence of Bertrand lens.
- [4] The use of accessory plates for identification of crystals e.g mica plate, gypsum plate, and quartz wedge. It has the advantage of being used in studying crystals in
 - [a] Ordinary light in which the light consists of waves vibrating in all directions (perpendicular to the direction of propagation of the wave).
 - [b] Plane polarized light in which the light is allowed to pass through its vibrating direction East-West or North-South.
 - [c] Examination of crystals between crossed Nicols, both prisms are inserted in the path of light.
 - [d] Conoscopic study : Consists of examination between crossed Nicols in convergent polarized ligh with a Bertland lens.

ROUTINE OF CRYSTAL IDENTIFICATION

The general sequences of crystal observations are summerized in the following steps.

- [1] Examination of form and crystallographic properties (cleavage, parting or fracture and shape of crystals).
- [2] Examination of optical properties
 - [a] Color and pleochroism, whether colorless or colored on rotation of the microscope stage in plane polarized light.
 - [b] Refractive index and relief, the appearance of crystal outlines is called relief and it depends on the difference in refractive index between the crystal and the surrounding medium. It shows low or high relief. Refractive index can be measured by using sets of immersion liquids with specific refractive indices.



otic photomicrograph equipment

FIG. [1]: THE POLARIZING MICROSCOPY

[3] Examination of crystals under crossed nicols

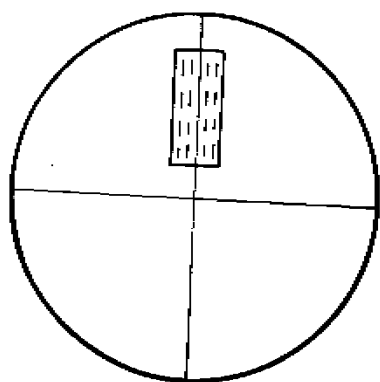
[a] Isotropic or anisotropic crystals:

- Isotropic crystals, which become dark when the nicols are crossed by rotating the microscope stage. It has one optic indicatrix with one (uniform) refractive index.
- Anisotropic crystals which transmit light when the nicols are crossed, of uniaxial or biaxial optic axis with two or three refractive indices subsequently. The optic axis is the only direction in the crystal in which light travelling along it, is not double refracted.

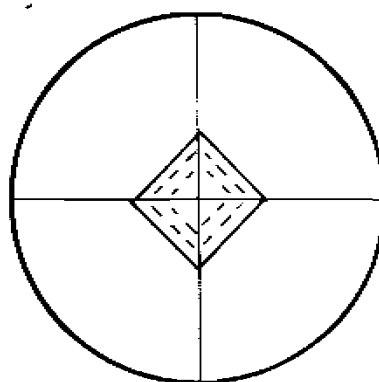
[b] Extinction, when an anisotropic crystal is examined between crossed nicols, the transmitted light will be colored (interference colors). If the microscope stage is turned, the crystal will become dark for four times during complete rotation, the crystal is then said to be extinguish. The position of extinction is to be parallel extinction, if extinction takes place when a prominent crystal edges are parallel to the cross hairs in the ocular which are oriented East-West and North-South. Symmetrical extinction, if at the extinction the cross hairs bisect the angle between crystal faces (45 degrees). Oblique extinction, if at extinction the crystal face is inclined to the cross, hairs [Fig 2 A,B,C].

[c] Interference colors, are produced by an anisotropic crystal between crossed nicols and the resulting colors appearing in white light are determined by,

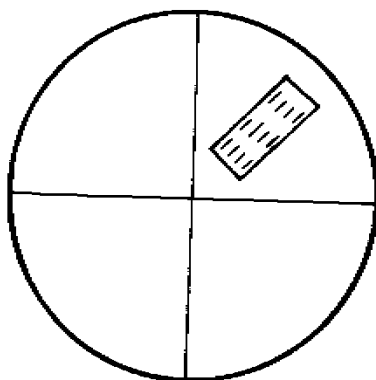
- The thickness of the crystal.
- The difference between the velocity of the two rays which the crystal breaks it under plane polarized light (a ray of light traversing the crystal is in general refracted into two rays that vibrate in planes at right angle to each other), and in turn is controlled by,
- The specific birefringence is determined by the difference between the lowest and highest index of refraction of the crystal and which may be weak or strong according to the difference in the amount of both indices. The birefringence can be measured by observing the interference colors, and by measuring the number of wave lengths between the two indices



A- Parallel



B- Symmetrical



C- Inclined

FIG. [2]: THE POSITION OF EXTINCTION