Congenital Hypertrophy of the Retinal Pigment Epithelium (CHRPE) as a screening marker for Familial Adenomatous Polyposis (FAP); literature review and screening recommendations (RCO2022.06901D4)

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Dovepress Clinical Ophthalmology

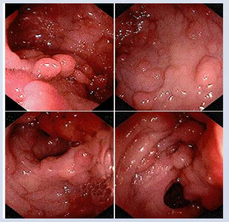
Introduction

- Familial adenomatous polyposis (FAP) carries an almost **100% lifetime colorectal cancer risk** warranting early detection in gene carriers.
- Congenital hypertrophy of the retinal pigment epithelium (CHRPE) is considered the **earliest** and **most-specific phenotypical marker of FAP.**
- This poster outlines our **systematic literature review** and **published screening recommendations** assisting clinicians in efficient, evidence-based FAP-associated CHRPE assessment.

Background

Familial Adenomatous Polyposis (FAP) [1]

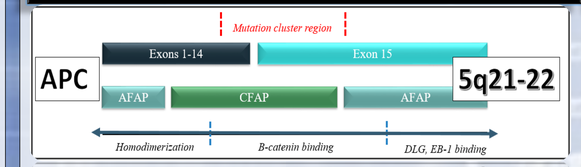
- Caused by germline mutation of the **Adenomatous Polyposis Coli (APC) gene**
- Autosomal dominant inheritance
- Birth incidence of **1 in 8,300**. [2]



Congenital Hypertrophy of the Retinal Pigment Epithelium (CHRPE)

- Congenital hamartoma of the retinal pigment epithelium (RPE).
- Lesions typically have **no visual significance** and almost no reported intraocular malignant potential.[2]
- Utility of CHRPE detection directed **towards identifying gene-carrier status of at-risk kindreds.**
- Literature variation exists regarding CHRPE nomenclature and subclassification which were streamlined in these guidelines presented.

Genetics [2]



Methods

- Systematic literature review and appraisal
- Comprehensive search strategy of online databases
- Criteria-led study inclusion graded according to NHMRC[2]
- Quantitative analysis, formulation of screening recommendation and morphological sub-analysis

WHO should be screened?

Individuals at increased risk of FAP:

- *First degree relative of individual with known APC gene mutation*
- *Asymptomatic FAP kindreds*

WHEN should screening commence?

- *10 years of age or prior to endoscopic evaluation*
- *Also acceptable at older and younger ages*

These guidelines are NOT appropriate for; symptomatic individuals or other hereditary non-polyposis or non-hereditary colorectal conditions.

Screening recommendations

Ocular Examination
(Dilated indirect ophthalmoscopy of both eyes)

Pigmented ocular fundus lesion observed?

Yes → **Documentation & Classification**

Document the following;

1. **Morphology** (refer to classification system adjacent)
2. **Total lesion number**
3. **Size** (disc-diameter (DD)
4. **Pigmentation** (hyperpigmented, hypopigmented, mixed)
5. **Laterality** (unilateral vs. bilateral)
6. **Location** (posterior pole, periphery)

Obtain fundus photography if available for monitoring. Consider ancillary testing (e.g. FAF, FA, OCT) if there is diagnostic uncertainty.

No → **Any of following features present?**

- ❑ Multiple lesions (cumulative total of ≥3 in one or both eyes)
- ❑ Lesion type A or B
- ❑ Bilateralism

Yes → *FAP-associated CHRPE*

Specificity 89%
PPV 94%

→ *Refer for early definitive testing. (endoscopic evaluation +/- genetic testing)*

No → *Sensitivity 79%*
NPV 71%

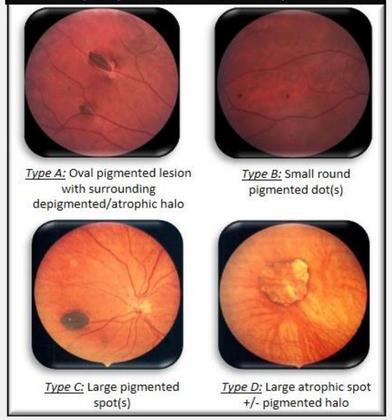
The absence of CHRPE cannot exclude FAP and should not preclude endoscopic and/or genetic testing

Continue with national colorectal cancer screening protocol at age-defined intervals

Cancer Council Australia

Found at: https://cancer.org.au/australia/Guidelines:Colorectal_cancer/Familial_adenomatous_polyposis

CHRPE morphological subclassification (adapted from Berk et al)[1-3]



Type A: Oval pigmented lesion with surrounding depigmented/atrophic halo

Type B: Small round pigmented dot(s)

Type C: Large pigmented spot(s)

Type D: Large atrophic spot +/- pigmented halo

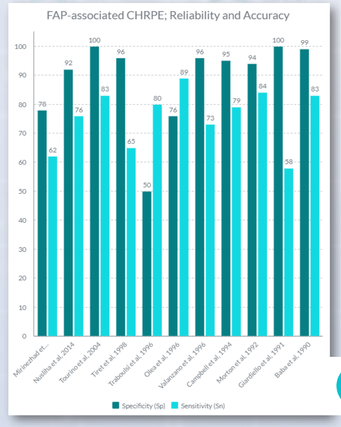
Results

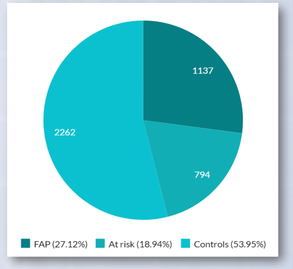
CHRPE as phenotypical marker FAP:

From 28 included studies:

- 4,451 participants







Morphological Sub analysis

1	**Total Lesion Number**	*FAP; 10.9, At-risk; 4.8*
2	**Laterality**	*Bilateralism (FAP); 69.4%*
3	**Size**	*<0.5DD: FAP 78.5%, At-risk; 82.0%*
4	**Location**	*Retinal periphery; 84.0%, central; 46.0%*
5	**Pigmentation**	*Pigmented; 61.5%, depigmented; 8.0%, Mixed; 30.5%*



Conclusion

- CHPRE is a **rapid, non-invasive phenotypical marker** for FAP.
- **Multiple lesion number (≥3)** and **bilateralism** have the greatest specificity for FAP.
- Absence of FAP-associated CHRPE cannot exclude polyposis and should not preclude further definitive testing.
- We advocate the use of ocular examination as part of **multimodal approach**, along with endoscopy and genetic testing, for **efficient, timely FAP assessment in at-risk individuals**

(1) *Chung DC, Rodgers LH. Clinical manifestations and diagnosis of familial adenomatous polyposis. Uptodate. [Internet] 2020 [updated 2020 Jul 21].* (2) Bonnet LA, Conway RM, Lim LA. Congenital hypertrophy of the retinal pigment epithelium (CHRPE) as a screening marker for familial adenomatous polyposis; systematic literature review and screening recommendations. Clin Ophthalmol. 2022;16:765-774. (3) Berk T, Cohen Z, McLeod RS et al. Congenital hypertrophy of the retinal pigment epithelium as a marker for familial adenomatous polyposis. Dis Colon Rectum. 1988;31:253–257. (4) Leggett, B, Poplawski B, Pachter N, Rosty C, Norton I, Rosty, C. Cancer Council Australia Colorectal Cancer Guidelines. Colorectal cancer/familial adenomatous polyposis: clinical practice guidelines for the prevention, early detection and management of colorectal cancer. [Internet]. Sydney: Cancer Council Australia, 2017.