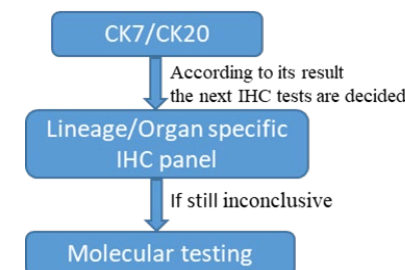


“Role of Immunohistochemistry in Differentiating Carcinomas of Unknown Primary”



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Introduction:

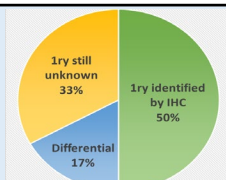
Carcinoma of unknown primary (CUP) accounts for **2–5%** of all malignancies and is the **6th leading cause of cancer-related death in the UK**. Despite advances in imaging and histopathology, about **one-third** of malignancies of uncertain origin (MUO) remain unclassified as CUP after extensive investigations. Accurate primary site identification guides therapy; **immunohistochemistry (IHC)** is central to this work-up.

Methods

Focused literature review (PubMed, 2010–2025) on IHC and molecular profiling in CUP

Result:

- IHC resolved ~49–50% of CUPs
- IHC Provided a differential in ~17%
- CUPs remained unresolved in ~30–35%
- Algorithm of IHC:**



CK7/CK20 Pattern	Common associations	Next specific marker
CK7+ / CK20–	Suggests adenocarcinoma of lung, breast, ovary, endometrium	Lung: TTF-1, Napsin A Breast: ER/PR, GATA3 Ovary/Endometrium: PAX8
CK7– / CK20+	Colorectal carcinoma	CDX2, SATB2
CK7+ / CK20+	Pancreatic, Gastric or urothelial carcinoma	Pancreas: CK19 –SMAD4 Gastric: MUC5AC Urothelial: GATA3 – P63
CK7– / CK20–	Suggests prostate, renal, hepatocellular carcinoma	Prostate: PSA, NKX3.1 Renal: PAX8, RCC marker Liver: HepPar-1, Arginase-1

- CK7-/CK20+ is highly specific for colorectal origin (~96.7%)
- Molecular assay improve origin identification to ~70–90%+; Epigenetic profiling validated at **97.7% sensitivity** and **99.7% specificity**.

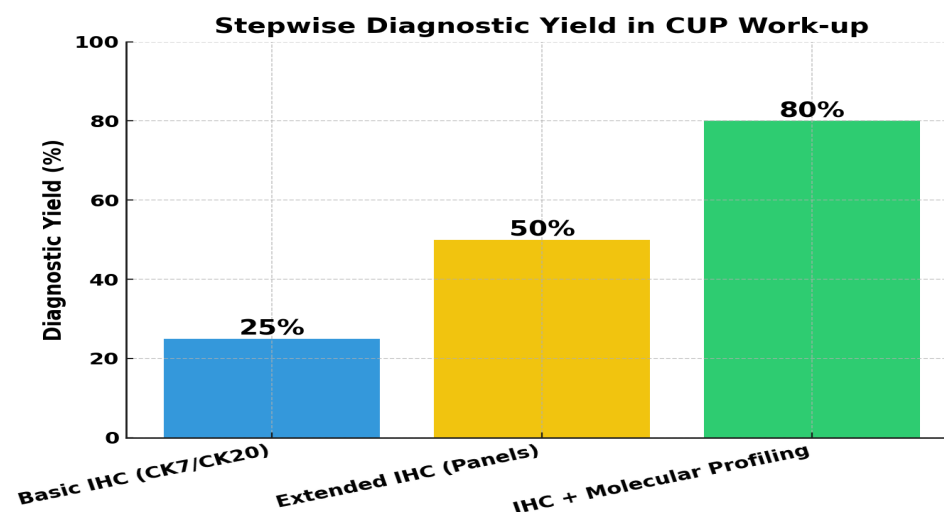
Discussion:

IHC offers a stepwise, cost-effective approach but is limited by antigen loss in poorly differentiated tumours and overlapping expression. When inconclusive, **molecular assays** add diagnostic resolution.

Conclusion

IHC remains the first-line tool in CUP. A practical algorithm (CK7/CK20 → lineage/organ-specific markers) narrows differentials. **Integrating molecular profiling** yields the highest diagnostic accuracy and improves patient outcomes.

Study	Patients number	1ry Identified by IHC	IHC gives differential only	1ry remains Unknown
Ren et al. (2023)	625	49.3%		50.7%
Omar et al. (2021)	141	49.6%	17.7%	32.6%
Lalchita et al. (2023)	40	50%	12.5%	37.5%
Horlings et al. (2008)	38	42.1%	31.5%	26.3%



Reference:
Scan here

