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Galton D A G, Goldman J M, Wiltshaw E, Catovsky D, Henry K & Goldenberg G J. Prolymphocytic leukaemia. *Brit. J. Haematol.* 27:7-23, 1974.
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This paper gave the first description of a rare form of lymphoid leukaemia distinguished from classical chronic lymphocytic leukaemia by its clinical features: high leucocyte count, short course, and distinctive cytomorphology (a lymphoid cell with condensed chromatin and a prominent vesicular nucleolus). [The *SCI*® indicates that this paper has been cited in over 225 publications since 1974.]

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In 1956 an elderly patient was referred to the Royal Marsden Hospital, London, with a diagnosis of acute lymphoblastic leukaemia. The spleen was greatly enlarged and the leucocyte count very high, both due to large lymphoid cells with a prominent nucleolus but coarsely clumped hyperchromatic chromatin resembling that of a mature lymphocyte and quite unlike that of a lymphoblast. Similar cells infiltrated the bone marrow. Suspecting a variant of chronic lymphocytic leukaemia (CLL), I administered alkylating agents, but the patient did not respond, became thrombocytopenic, and died.

By 1963 Eve Wiltshaw and I had treated nine similar patients at the Royal Marsden and Hammersmith Hospitals. The spleen was greatly enlarged and the leucocyte count very high in all; the key cell was the bizarre form noted in the first case. In contrast to CLL, enlarged lymph nodes were conspicuously absent, and the survival was of short duration in the nine patients who presented with systemic symptoms (although, in one otherwise fit man, splenic infarction unmasked the disease at an earlier stage, and he survived 18 months). We named the condition prolymphocytic leukaemia (PLL) from the characteristic cell morphology.

I showed the blood films to Maxwell Wintrobe, who recalled the film of a seemingly fit man whose referral letter recommended urgent treatment for acute leukaemia; the letter had been written three years earlier! I had encouraged Gerry Goldenberg, our research fellow from Winnipeg, to prepare the case reports for publication, but suspecting the course of PLL to be more protracted than we had thought, I deferred publication. Ten more years brought only five more cases, but in two we had the opportunity to observe a prolonged symptomless phase. The clinical and haematological features in all 15 cases were remarkably similar and distinct from those of classical CLL.

This paper has been highly cited because PLL has been recognized more often since the recent general revival of interest in cytomorphology and, more especially, because Daniel Catovsky and his colleagues have carried out detailed studies on the electron microscopy,[1] immunological phenotype,[2,3] enzyme cytochemistry,[4] cell-volume measurements,[5] and cytogenetics[6] of PLL cells. They have shown that both B- and T-forms exist and that both forms are distinct from the related chronic B- and T-cell leukaemias. This work adds to the accumulating knowledge on the phenotypic heterogeneity of the lymphoid leukaemias. Such detailed analysis of leukaemia cells will throw light on the large family of lymphocytes because it is probable that leukaemia-cell populations are expansions of normal lymphocyte subsets, some of which may exist in numbers below the limit of detection. Thus immunology will be enriched along with the understanding of cell differentiation and maturation.

1. **Costello C, Catovsky D, O'Brien M & Galton D A G.** Prolymphocytic leukemia: an ultrastructural study of 22 cases. *Brit. J. Haematol.* 44:389-94, 1980.
2. **Catovsky D.** Prolymphocytic and hairy cell leukemias. (Gunz F W & Henderson E S, eds.) *Leukemia.* New York: Grune & Stratton, 1982. p. 759-81.
3. **Catovsky D, Melo J V & Matutes E.** Biological markers in lymphoproliferative disorders. (Bloomfield C D, ed.) *Chronic and acute leukemias in adults.* Boston: Martinus Nijhoff, 1985. p. 69-112.
4. **Crockard A, Chalmers D, Matutes E & Catovsky D.** Cytochemistry of acid hydrolases in chronic B- and T-cell leukemias. *Amer. J. Clin. Pathol.* 78:437-44, 1982.
5. **Costello C, Wardle J & Catovsky D.** Cell volume studies in B-cell leukaemia. *Brit. J. Haematol.* 45:209-14, 1980.
6. **Pittman S & Catovsky D.** Chromosome abnormalities in B-cell prolymphocytic leukemia: a study of 9 cases. *Cancer Genet. Cytogenet.* 9:355-65, 1983.

