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The efforts of William van Mildert, last Prince Bishop of Durham, and of the Dean and Chapter led in 1832 to the passage through Parliament of "an Act to enable the Dean and Chapter of Durham to appropriate part of the property of their church to the establishment of a University in connection therewith". Temporary accommodation was provided in the house known as Archdeacon's Inn on Palace Green and the first students came into residence in 1833. On 1 June 1837 a Royal Charter was issued recognising and confirming the constitution of the University. Seven days later the first Durham degrees were conferred under the authority of this Charter. An Order of the Queen in Council of 8 August 1837 appropriated Durham Castle, previously a palace of the Palatinate See, to the uses of the University. One of the objectives of the founders was to establish in the North of England "an Institution which should secure to its inhabitants the advantage of a sound yet not expensive academical education".

Two similar schemes in earlier centuries had failed. When Henry VIII seized the property of the monasteries a scheme was proposed for the establishment of a college at Durham, but nothing came of it. During the Commonwealth, in May 1657, letters patent were issued for the foundation of a corporate body to be known as "the Provost, Fellows and Scholars of the College in Durham of the Foundation of Oliver, Lord Protector", and the Provost and Fellows were actually nominated. A proposal that the College should have power to grant degrees roused the opposition of Oxford and Cambridge, and Richard Cromwell promised that nothing should be done to the prejudice of the two ancient universities. This scheme died with the Protectorate.

The new University in 1832 was Collegiate, although initially there was only one college, now University College situated in Durham Castle. In 1846 this was followed by Hatfield Hall, where expenses were reduced by providing all meals in common at a fixed charge and by letting the rooms furnished. Unattached, later known as non-collegiate students, were first admitted in 1871. They themselves established a St Cuthbert's Society in 1888. In 1947 St Cuthbert's Society became the recognised designation of the non-collegiate students. Its current relationship with Council was adopted in 1948. Bede College, established independently for men in 1839, took University degree students from 1892. In 1975 it was merged with its women's counterpart, St Hild's College, which had been founded independently in 1858 and brought into connection with the University in 1896. Two private halls, St Chad's and St John's founded in 1904 and 1909 took the style and title of an Independent College in 1919.

Women have been admitted to Durham since the 1890s. In 1895 Senate petitioned the Crown for a supplementary charter enabling degrees to be conferred on women and in the Michaelmas Term, 1896, the first four women students matriculated, all of them members of St Hild's College. In 1899 Abbey House on Palace Green was opened as a Women's Hostel. By resolution of the Council of the Durham Colleges in 1919, the Women's Hostel became known as St Mary's College. Women students residing at home had first been admitted in 1895 and in 1947 this body of women students became known as St Aidan's Society, with its own Principal. It became St Aidan's College in 1961. The following Colleges were subsequently established in Durham: Grey (1959), the Graduate Society (1965) (renamed Ustinov College in 2003), Van Mildert (1966), Trevelyan (1967), Collingwood (1972) and Josephine Butler (2006). In 1968 Ushaw College was recognised as a Licensed Hall of Residence in the University. All the Colleges now admit both men and women students, although St Mary's College has retained an area of accommodation for women only.

During the nineteenth and early twentieth centuries the numbers of students in Durham itself remained small. The University's original endowment was insufficient to maintain the country's first university course for engineers instituted in 1837 and, with the exception of Mathematics, science also declined. Student numbers in related institutions in Newcastle soon exceeded those in Durham. In 1852, the Medical School in Newcastle became "the Newcastle upon Tyne College of Medicine in connection with the University of Durham" and the University began to award medical qualifications. A College of Science in Newcastle upon Tyne was founded in 1871, under the aegis of the University. From this developed Armstrong College which offered a wide range of pure and applied science as well as Arts courses.

The original constitution of the University, which placed its government under the control of the Dean and Chapter of Durham, was modified in 1908 to create a federal institution. This provided an organisation at University level functioning equally in Durham and Newcastle and wholly responsible for examining and granting degrees. The students, however, were members of the University by virtue of their membership of its largely autonomous, constituent parts in Durham and in Newcastle. A Royal Commission of 1935 led to further constitutional changes which took effect in 1937. Under the new arrangements the Durham Colleges continued as the Durham Division, but in Newcastle the College of Medicine and Armstrong College were merged to form a unified Newcastle Division named King's College. Two full-time appointments were established to lead the two Divisions, the Warden of the Durham Colleges and the Rector of King's College

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who served alternately as Vice-Chancellor and Deputy Vice-Chancellor of the University until the Act of 1963.

After the 1939-45 war both Divisions expanded rapidly and the federal organisation was soon rendered out of date. The various governing bodies within the University concluded that there should be a separate University of Newcastle. The Universities of Durham and Newcastle upon Tyne Act of 1963 provided for the establishment of the University of Newcastle upon Tyne with the former Durham Colleges continuing as the University of Durham. Pure science teaching within Durham had been re-established in 1924 at the same time as the Department of Education was opened. Both developments were the result of collaboration between the Durham Colleges and the County Council and for many years were in large part funded by a special rate levied by the latter. The original range of pure science departments was extended after 1945 and applied science and engineering were introduced in 1960 and 1965 respectively. Large scale development in the Social Sciences came after 1960 and the range of Arts departments was also expanded in the 1960s. The present academic departments at Durham are organised into eight Schools, including the Durham Business School, and seventeen other Boards of Studies, all contained within the three Faculties of Arts and Humanities, Science, and Social Sciences and Health.

University College, Stockton on Tees, opened to students in October 1992 offering joint qualifications of the Universities of Durham and of Teesside. It was established in partnership with the University of Teesside and the Teesside Development Corporation. In 1994 the Privy Council approved its status as a residential and teaching college of the University of Durham. Since 1996, by agreement between the two Universities, the students have been studying for University of Durham degrees. In 2001 John Snow College and George Stephenson College were established. In recognition of Her Majesty Queen Elizabeth II's Golden Jubilee in 2002 and the tenth anniversary of the Stockton campus, Her Majesty gave permission for the University to change the title of the campus from University of Durham Stockton Campus to Queen's Campus.