So it was shown that spontaneous mammary cancer in mice usually resulted from the interaction of three causative factors: hormonal stimulation, inherited susceptibility, and the milk-borne mammary tumour agent.

Bittner also contributed to the discovery of an inherited hormonal influence. In 1944, when reciprocal matings were made between animals of the cancer-susceptible *A* (low incidence in virgins) and *C3H* (high incidence in virgins) strains, it was demonstrated that the hormonal pattern associated with the genesis of mammary cancer in virgin females was transmitted to the *F*₁ females, maintained as virgins, which had high incidences of mammary cancer. Bittner (1945) termed the hormonal mechanism responsible for the induction of mammary cancer in virgins "the inherited hormonal influence".

"The inherited hormonal influence . . . is probably the result of the action of multiple genes. The same genes probably do not produce the inherited susceptibility and the inherited hormonal influence."

Apart from these contributions, which opened entirely new fields, he wrote many other papers—245 in all—which made valuable contributions to the knowledge of mouse mammary tumours.

As may be expected, Bittner was the recipient of many honours and he was much sought after as a lecturer: among these were the Alvaranga Prize, College of Physicians of Philadelphia (1941); Comfort Crookshank Award and Lecture, London (1951); Bertner Award and Lecture, University of Texas (1957); honorary D.Sc. from Bard College (St. Stephen's) (1950).

In 1957 Bittner visited Perugia to participate in the Second International Symposium on Mammary Cancer. It was a great satisfaction to him to be the recipient (together with Alexander Haddow and Leonell C. Strong) of an honorary degree in medicine and surgery, from the University of Perugia, on July 29 of that year.

On February 23, 1961, when Dr. O. Meredith Wilson was inaugurated president of the University of Minnesota, Bittner was in a position of honour. In fact, he participated on behalf of one of the two oldest institutions represented, leading the academic group by wearing the gown of the Perugia University Medical School, incidentally with a colleague dressed in an Oxford (England) robe. On Thursday, February 16, 1961, *The Minneapolis Star* published a three-column article illustrated with coloured photographs of Bittner and other doctors in their academic gowns as they would appear at the inauguration.

Bittner returned to Perugia in June 1961 to participate in the Ciba Foundation Symposium on Tumour Viruses of Murine Origin (June 21–23) and the International Conference on the Morphological Precursors of Cancer (June 26–30), and to attend the centenary celebrations of the chair of morbid anatomy in the University of Perugia, as the representative of the University of Minnesota.

I would like also to recall the exceptional brightness and intelligence of his eyes and his inimitable charm. He was fond of his house and garden and was an enthusiastic photographer.

He is survived by his wife, formerly Mary Esther Mahaffy, two daughters, Mary Margaret (Mrs. Merlyn C. Bowker) and Elizabeth Ann (Mrs. Edwin H. Loague), two sisters, Katherine (Mrs. Leonell C. Strong) and Josephine (Mrs. George E. Turnbull) and a brother, Mr. Guy C. Bittner, to all of whom their many friends extend their deepest sympathy.

LUCIO SEVERI

His family, his numerous professional associates and friends, others who liked him personally, and many more who were stimulated by his writings learned with sorrow that Prof. John J. Bittner had died on December 14, 1961. Some of Bittner's fundamental contributions to

cancer research and his background have already been summarized by Dr. Leonell C. Strong in the April 1962 issue of *Cancer Research*. Added emphasis of deserved international scope is placed on Bittner's contributions to cancer research by Prof. Lucio Severi in the preceding obituary.

To-day's investigators in cancer biology must realize indeed that the foundations of their discipline were laid by a few gifted researchers, such as Bittner, making a series of basic discoveries with keen intuition and painstaking observation. Bittner's important findings do not depend on the extensive instrumentation now so much used in oncology. His achievements demonstrate the pioneering application of uncomplicated experimental technique to clearly formulated problems, even in a field as complex as is the inquiry into the nature of cancer. The impact of Bittner's findings cannot be positively correlated with the cost of his instrumentation or with his laboratory space in square feet.

Bittner's long series of studies on the development of mammary tumours in mice has probably stimulated cancer research on a world-wide scale as much as any other single series of observations. His long-continued and scarcely fashionable insistence, particularly during the past decade, on a mammary tumour 'agent' rather than a 'virus' reflected his sound caution when faced with tempting premature extrapolation. While documenting painstakingly, throughout a lifetime, the part played by what we now call the Bittner agent, he also devoted careful observation to the factors interacting with his agent.

In a virus-conscious era of oncology, it is scarcely surprising that the question whether the Bittner agent is indeed a virus or a cytoplasmic 'gene' or 'particle' is often posed. Such semantic controversy revolving around as yet inconclusive data must not detract, however, from Bittner's important disclosure of the part played by an infective agent in the genesis of a mammalian neoplasm.

We may remember, further, that the Bittner of Bittner-agent fame consistently concerned himself with the part played by endocrine and metabolic factors in mammalian carcinogenesis. Two points are particularly pertinent. First, he emphasized that mammary cancer in the mouse can develop in the absence of a demonstrable agent, and that the burden of proof for assuming that the presence of an infective agent constitutes a *sine qua non* for mammary carcinogenesis in the mouse rests with those who make this claim. Secondly, he devoted much research to the question as to whether the agent exerted its effect via the endocrine.

Basic contributions by Huseby and Bittner related in this connexion to endocrine mechanisms of breast cancer in the mouse. Many others, too many to name, are indebted to Bittner for the opportunity to co-operate with him, as I am.

Bittner's scholarship in the field of inquiry into the nature of cancer was indeed an invaluable asset not only to those privileged to work with him, but also to many others who came or wrote for his advice. He was open-minded to new approaches and willing to lend his unreserved support to explorations of unconventional fields. The resolution of several temporal parameters of physiology and pathology at different levels of mammalian organization would not have been possible without his guidance and help. In later years, Bittner's activities also included the support of the work of others by making available his inbred strains of mice. He kept up with the literature in a rapidly developing field which he had so greatly stimulated and remained active in the laboratory for seven years following a first coronary occlusion, which preceded the second, fatal one. He died on his way to work. He lives in the history of biology and medicine with those endeavouring to understand organisms and their diseases by dint of painstaking observation.

FRANZ HALBERG