Robert Costello – The Prophet of Pituitary Adenomas

a report by

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In the 1930s a young investigator at the Mayo Clinic in Rochester, Minnesota, had a unique opportunity. Robert Costello conducted a careful and systematic analysis of pituitary glands obtained at *post mortem* examination from patients who had no obvious symptoms of endocrine disorders. The results were published in 1936.[1] In this study of 1,000 human pituitary glands he discovered more than 200 benign tumours, most of them quite small. This unexpected finding went relatively unnoticed by the general medical community at the time. This may have been because it was published in a pathology journal, or because it came at a time when tumours and cysts of other endocrine glands were being recognised and reported. At that time, the recognition of acromegaly occurred quite rarely and cases of Cushing's disease were few and far between. Most of the pituitary adenomas being diagnosed and treated in the era before magnetic resonance imaging (MRI) scans and sophisticated endocrine laboratory tests were macroadenomas that produced headache and progressive visual loss. In those days it was thought that pituitary adenomas accounted for only about 6% of primary brain tumours.

It was not until the 1970s that the current 'explosion' in the diagnosis and treatment of pituitary tumours began and the importance of Dr Costello's study was validated. The factors that have led to our current state of knowledge include advances in a number of areas. The revival of the trans-sphenoidal microsurgical approach provided a new, safe way of approaching the sellar area where these tumours begin. The concept of the microadenoma, a small benign tumour that could cause disease because of its endocrine hyperactivity, was critical.

The pituitary microadenoma was a lesion that could be removed selectively using microsurgical techniques while preserving normal pituitary function. The advent of accurate hormone testing allowed these tumours to be diagnosed at a relatively early stage, and the actual incidence of pituitary tumours began to be recognised. Over the past 100 years systematic attempts were gradually made to link hormonal excess or deficiency to symptoms and patient complaints. The most common symptoms were enlarged extremities (acromegaly) and obesity/striae (Cushing's). Important related symptoms such as mood swings, infertility, psychological problems, high blood pressure, arthritis, depression and apathy were often attributed to health issues unconnected to hormonal disorders Between 30 and 40% of the population experiences sexual dysfunction – an important symptom of pituitary disease. Obesity is a major national health concern, along with osteoporosis and diabetes mellitus. All are unmistakably linked to hormonal issues.

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The pioneering neurosurgeon and pituitary physiologist Harvey Cushing produced a clear, compelling and decisive exposition of the findings in patients with pituitary adenomas. The true significance of these findings, and the extent of the prevalence and importance of pituitary disease, has yet to be fully appreciated. The total number of pituitary adenomas has probably not changed over the 70 years since Dr Costello's initial discovery of the prevalence of pituitary adenomas.

A recent meta-analysis of this prevalence was conducted on behalf of the Pituitary Network Association (PNA) by a multidisciplinary team of quality researchers.[2] Their examination of series of both autopsy and imaging studies from Dr Costello's time to today essentially confirmed his numbers. Therefore, the surprise is not the high number of

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adenomas found, but that the medical community has been generally unaware of the true prevalence of these lesions. The discovery of advanced pituitary imaging, first with computed tomography (CT) and then with MRI, allowed for the detection of pituitary tumours of all sizes and for the development of effective medical, surgical and radiotherapeutic treatments. Furthermore, the results of treatment could be thoroughly evaluated with imaging and laboratory follow-up. It is likely that Dr Costello would be pleased to see the current state of the diagnosis and treatment of pituitary adenomas that derived from the findings of his laborious studies.

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We now have data showing that pituitary adenomas account for 20% of surgically treated primary brain tumours. A large number of these adenomas are treated with medication alone or with surgery and radiosurgery. In some cases they are not treated at all. Doctors can recommend continued observation of the tumours and follow them with a 'wait and see' attitude, anticipating that neither tumour growth nor possible infarct or haemorrhage will interfere with the patient's survival or quality of life. This conservative philosophy demands rigorous and frequent follow-up imaging and visual and laboratory testing.

New cases of pituitary tumours are diagnosed in about 17 people per million in the general population per year. At any given time, as many as 100 people per 100,000 are living with pituitary tumours. It is distinctly possible that a similar number of cases go unreported or undiagnosed every year, even though the characteristic symptoms may be evident to a practised endocrine professional or pituitary surgeon. There is a legitimate concern about the large number of pituitary tumours that remain undiagnosed and untreated. The symptoms of these tumours include some of the most common complaints that individuals may experience. Putting them together in an accurate diagnosis is a major challenge for many physicians. Raising awareness among the public, medical practitioners, public health authorities and federal health agencies (e.g. the National Institutes of Health [NIH] and National Communicable Disease Center [NCDC]) is an inescapable need and remains an important goal.[3]

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Four very important segments of society are in dire need of pituitary/endocrine/hormonal education. The first segment is the general medical community; this means the medical professionals (nurses, nurse practicioners, physicians' assistants and doctors) who usually see the patient first. This is the critical 'tipping point' for most patients. They wonder: 'Will I be believed, tested, diagnosed and referred to an expert for confirming the diagnosis and recommending expert treatment?' If so, the patient is among the lucky few. Too often, the answer is 'no'. Doctors tell them that their symptoms do not match the classic criteria for clinical symptoms. If the patient's symptoms do not match the doctor's knowledge and experience of pituitary disease, they may wrongly be attributed to other conditions.

The second segment of society that needs education on hormonal issues is the mental health community. This is where patients turn for solutions to sexual failure (lack of libido), mood swings, inability to concentrate or focus on the task at hand, workplace insubordination and other psychological problems. The correct diagnosis is often not forthcoming because the mental health practitioner is trained to look for signs of a difficult family background, environmental factors, workplace stress and other correlates of behavioural difficulties, rather than hormonal imbalance. Hormonal failure (excess or insufficiency) is rarely suspected or discussed. Hence, another treatment opportunity is often lost.

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The third segment comprises the patient and the patient's family. They can easily identify a host of symptoms and complaints, yet the very significant symptoms – the results of a malfunctioning master gland – are rarely recognised or considered in the search for a diagnosis. Finally, society at large is undereducated on the subject of hormonal health.

Only recently have we begun to understand the many types of diabetes and thyroid problems, to mention but two recognisable issues. Most other hormonal problems, of equal value to the patient's wellbeing, are sadly neither diagnosed nor treated in a satisfactory fashion. ■

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