Harvey Cushing's Influence on Norman Dott's Work on Acromegaly: Pituitary Research, Treatment Modalities, and Research Dissemination c.1900–c.1960

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OBJECTIVE: **To review Dr. Harvey Cushing's influence on Mr. Norman Dott's work on acromegaly and other subjects surrounding the pituitary gland such as pituitary research, treatment modalities, and research dissemination. Dott was the first Professor of Neurosurgery in Scotland during 1947 and was considered a pioneer of the understanding and treatment modalities for pituitary disorders such as acromegaly. During 1923, he published an article regarding pituitary physiology that won him the award for the Rockefeller Fellowship Trust, to travel to Boston Massachusetts, giving him the opportunity to train under Cushing's supervision for the years of 1923–1924. However, similarities can be seen between Dott's physiology project that was completed before he ever met Cushing, as well as his treatment suggestions for acromegaly, after he had finished his training under Cushing's supervision.**

METHODS: **This was a historical perspective based on literature review. We reviewed Norman Dott's archives held by University of Edinburgh Library or online sources and we compared these with the work Cushing had previously performed in a chronological fashion. Cushing's work on the pituitary gland and acromegaly can be largely found online, in biographical books, and in other secondary sources. The search included words such as "trans-sphenoidal surgery," "x-ray," "Harvey Cushing," "Norman Dott," "Acromegaly," "Annual Meetings," and "Pituitary physiology." We excluded any primary sources that were not published between 1900 and 1960 regarding either pituitary physiology or the treatments for acromegaly.**

CONCLUSIONS: **Sir Norman Dott was the first Professor of Neurosurgery in Scotland during 1947 and is well known for his pioneering work on intracranial aneurysms. Although less well known for his contribution to pituitary pathologies, we would like to share his contribution in this regard and correlate it with Cushing's influence.**

INTRODUCTION

Acromegaly is a compound word derived from the Greek words *akro* and *megalo*, meaning extremity and big, respectively, first defined by French doctor Pierre Marie in 1886. This pathology is caused by pituitary tumors secreting greater than normal levels of growth hormone, leading to the progressive somatic enlargement mainly affecting the face and extremities.[1]

An important and perhaps less-recognized contributor to the understanding and treatment of pituitary disorders was Sir Norman McOmish Dott (1897–1973), who was the founder of Surgical Neurology in Scotland (Figure 1). Dott was born on August 26, 1897, in Edinburgh and was of Scottish Huguenot descent. As a teenager, Dott pursued an engineering career; however, after a terrible accident in 1913, which resulted in a permanent hip injury and an extended hospital stay, Dott realized his true calling was a career in medicine. By 1919, Dott received the MBcHB from the University of Edinburgh and in 1923 he became a Fellow of the Royal College of Surgeons in Edinburgh.

From 1917 to 1922, Dott worked as a research assistant at the Histology and Experimental Physiology Department of the University of Edinburgh under the supervision of Sir Sharpley Shäfer. The experiments on pituitary physiology during 1922 were highly appraised, winning him the award of the Rockefeller Fellowship, where he traveled to Boston, Massachusetts. There he met Dr. Harvey Cushing, considered at that time to be the father of

Key words
- Harvey Cushing
- Norman Dott
- Pituitary adenoma
- Trans-sphenoidal

Abbreviations and Acronyms
PA: Pituitary adenoma
r: Roentgen unit
RIE: Royal Infirmary of Edinburgh

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Figure 1. Photograph of Norman Dott, in front of the steps leading to the Royal Infirmary of Edinburgh. Copyright permission provided by the Lothian Health Services Archives. Dott, Norman M, in front of steps, "The Royal Infirmary Of Edinburgh" LHB1CC24-PR1.1536, 1937, Lothian Health Service Archives, Edinburgh.

neurosurgery, with whom he worked from 1923 to 1924. At the time, Cushing was a forerunner in the research, diagnosis, and treatment of pituitary disorders at John Hopkins hospital and was one of the first to have ever successfully surgically operate a patient with acromegaly.[2]

By 1947, Dott became the professor of Surgical Neurology at the University of Edinburgh, the first one to obtain this title in Scotland. In July 1962 Dott received "the freedom of the City of Edinburgh," which is the highest award a citizen of the city of Edinburgh can obtain.[3]

EXPLORING PITUITARY PHYSIOLOGY WITH PUPPIES AND DOGS

On March 20, 1923, Dott published an article regarding the physiological functions of the pituitary gland. During that time, he was working in the Department of Physiology at the University of Edinburgh under Sir Schäfer Sharpley's supervision.[3]

In the published article titled "An Investigation into the Functions of the Pituitary and Thyroid Glands. Part. I. Technique of Their Experimental Surgery and Summary of Results," Dott was investigating the effects of increased and reduced function of the pituitary gland on different organs within dogs and cats.[4]

Dott's methodology for inducing hyperpituitarism (increased pituitary function) was either by injection or feeding the test subjects with powdered substance of the anterior lobe of oxen. For the induction of hypopituitarism (reduced pituitary function), Dott chose 3 ways of creating that state. For puppies and dogs, he performed craniectomies. This was a complicated procedure where the temporal bone of the skull was removed, creating a pathway from above to reach the pituitary. Then he would either remove part of the gland (first method) or insert a platinum plate that stopped blood flow to the pituitary, thereby causing a similar effect (second method).

The third method, which was suggested to Dott by Schäfer, was performed on cats due to their different skull anatomy from dogs. This procedure involved the insertion of a hollow tube through the eye socket into the pituitary area, which was then used as a conduit for an electrode to pass through to electrically ablate the pituitary gland.

The analysis of Dott's unpublished experimental notes that led to the publication of the article concerning pituitary physiology is crucial for the understanding of his experimental attributes. In this part of the investigation he used 3 puppies from the same litter, 1 male and 2 female.[5] Daily observations were compiled into a diary with a postmortem analysis for each puppy based on their pituitary state. The organs assessed included the skin, thyroid, omentum, and epiphyseal growth plate, which were then compared with a control, in this case a healthy dog.

His results showed that for hyperpituitarism there was an increase in epiphyseal cartilage growth (elongation of bone), increased internal temperature, increase in the rate of maturation of the gonads, hyperactivity, and a reduction in fat deposits. The opposite happened when he induced the state of hypopituitarism.[5]

Striking similarities can be seen when comparing Dott's work with previous experiments other researchers had made on the pituitary, especially Cushing. At the start of the published article, Dott appreciates the contribution of previous researchers to the literature of the pituitary, but most recognized is Cushing who, according to Dott "made the largest contribution to the knowledge of the pituitary body."[4] Not only did Dott praise Cushing's modifications on previous experimental methods, but he also claimed to have used one of Cushing's surgical equipment called the "special hooked knife (Cushing)." The existence of this knife is confirmed from Cushing's reference in 1910, to the "knife hook,"[4] which was used to open the dura lying under the pituitary.

In the same publication Cushing gives credit to a colleague by the name of Emil Goetsch with whom they performed animal experiments in the Hunterian Laboratory. The experiment is described as follows: "For example, three terrier puppies from the same litter were selected for a growth test. A, the largest of the three, was hypophysectomised… B was fed daily upon whole gland extract… C selected as the control."[6]

The experimental methods used by Dott in 1922 are strikingly familiar to those used by Goetsch and Cushing. Even though Dott

recognized both Goetsch's and Cushing's work in the review section of the article, he does not mention that a similar experimental method had been previously performed in 1910 but, on the contrary, exposes their failure to replicate the state of hyperpituitarism.[4]

Cushing's concepts of the physiology of the pituitary gland significantly influenced Dott's experiment, a secondary source revealed, which indicates that Cushing had significantly impacted Dott's research on the pituitary, even though they had never met before.[3] One could argue that Dott was able to use the information from preceding research and modified the available techniques to succeed where his predecessors had failed.

The examples of the innovative modifications Dott made were the use of platinum plate, which cut the blood supply to the anterior pituitary lobe, and use of electrical ablation of the pituitary and successfully inducing hyperpituitarism by feeding animal subjects with pure anterior lobe extracts.[4] By inducing hyperpituitarism Dott achieved what Cushing admittedly said he could not, "Feeding…Our results with the canine have been largely negative,"[6] which could be considered a significant addition to the literature surrounding the pituitary gland.

TREATMENT MODALITIES FOR ACROMEGALY

Trans-sphenoidal Surgery

An important aspect of the treatment of acromegaly that Dott mentioned on several occasions was the use of the trans-sphenoidal route for surgery. However, numerous sources revealed that Cushing taught the technique to Dott during his training in 1923–1924.[7] An analysis of Cushing's impact on Dott's surgical treatment for acromegaly will be examined in this section.

Cushing's book written in 1910 described the trans-sphenoidal procedure where the pathway through the nasal cavity was followed to reach the sphenoid bone.[8] The sphenoid bone lies superior-posteriorly to the nose and is located deep within the cranial vault. Part of it consists of the orifice where the pituitary gland sits, which serves as a route for surgeons to reach pituitary tumors. Cushing gave a detailed description of how he performed the operation and suggested that this operation would be the preferred option for the treatment of acromegaly.[8]

The surgical technique of the trans-sphenoidal surgery had been passed from Cushing to Dott in 1923, sources suggest. Surprisingly, Cushing in 1929 decided to use the trans-frontal over the trans-sphenoidal approach for the treatment of pituitary disorders because of significant delay deciding which of the 2 operations should be used and the slightly increased risk of meningitis the trans-sphenoidal approach imposed.[9]

Despite Cushing's decision, Dott persisted with this surgical approach. Using his engineering background, Dott added a light source on the nasal speculum instead of relying primarily on the head lamp as suggested by Cushing, leading to better illumination and visualization of the pituitary gland.[10] By 1956, Dott performed 120 trans-sphenoidal surgeries, with the last 80 having 0 mortality, whereas in the review article of Cushing's case notes in 1923, the reported mortality rates was set at 8.6%.[11] Moreover, Dott was promoting his alternative method to people like the French Neurosurgeon Gerrard Guiot. During 1956, Guiot visited Dott for 2 weeks to observe the trans-sphenoidal approach for 2 patients with pituitary tumors, which left Guiot so impressed by Dott's techniques that he bought his equipment and started using the same method later that year in France.[10] Dott's success at maintaining and modifying his Cushing's methods achieved improved outcomes compared with his predecessor. Out of posthumous respect of Cushing, Dott never published his results on the treatment of pituitary tumors, thus avoiding any contradictions to his predecessor's work. Another secondary source also claims that Cushing told Dott after showing him how to perform the trans-sphenoidal surgery that he should not teach this procedure to anyone else.[12] This shows how Cushing's influence might have limited the extent Dott could spread his research regarding the treatment of acromegaly.

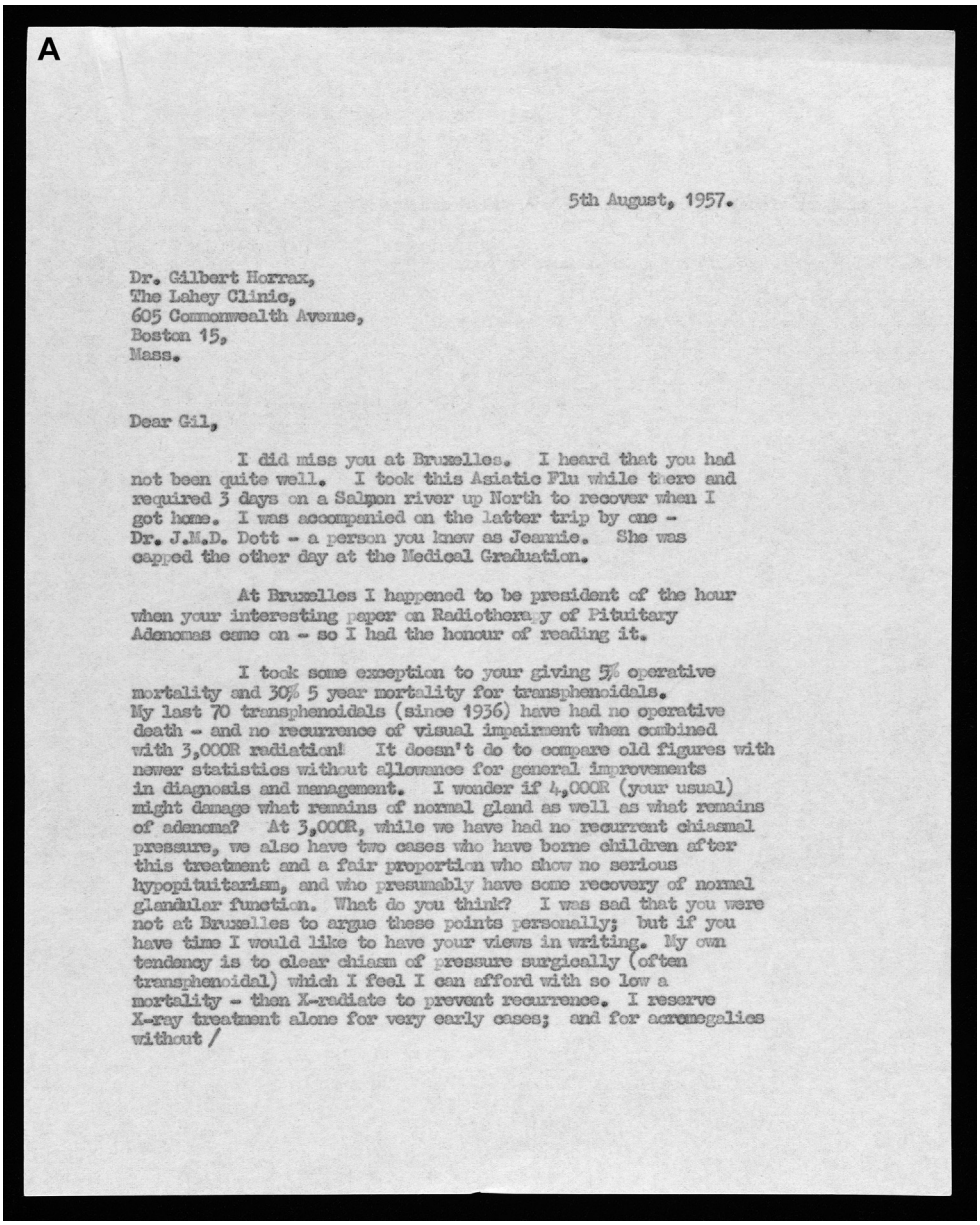
Radiotherapy

Radiotherapy for acromegaly was first introduced by the French radiologist Antoine Béclère in 1909, who was able to show that repeated X-ray exposure improved the symptoms of patients with pituitary disorders.[13] The use of X-ray was suggested by Dott for both the treatment and diagnosis of pituitary tumors years after Cushing gave similar suggestions.

Cushing was one of the first few to implement X-rays for the treatment of pituitary disorders. During 1923–1924, Cushing persuaded Dott and Dr Percival Bailey to review a series of patients with pituitary disorders, which resulted in the publication titled "A Consideration of Hypophysial Adenomata."[3] Standing out from these cases is a report regarding a male patient from Ohio, 1923, who was diagnosed with acromegaly, presenting with headaches and who 3 years before had temporary vision loss in the temporal aspect of his left eye.[11] The reasons this particular case is important are the use of X-ray for the treatment, diagnosis of acromegaly patients, and the related complications. Cushing diagnosed this patient with the use of X-ray and preoperatively treated the patient with 4 rounds of radiation. After the fourth round of radiotherapy, the patient experienced headaches and complete loss of vision. Upon surgical exploration of the patient, Cushing realized that the tumor was "liquid tissue" and necrosed. Within the same article, Cushing admits that the use of X-ray was a risky practice that affected local structures and, in some cases, exacerbate symptoms.[3]

The biggest evidence of Dott's radiologic interest for pituitary disorder management came from a speech he gave in Newcastle in 1957, where he suggested specific X-ray intensity levels for the treatment of patients with pituitary adenomas (PAs).[14] The requirements he suggested for X-ray adjuvant therapy were 3000 roentgen (r) units for 3 weeks using 250 kV. The Roentgen unit measures the exposure quantity of X-radiation by the electricity produced per cm^3 and was named after Wilhelm Conrad Roentgen, who was the first to discover X-rays.[15]

Specifying the quantity of exposure was crucial for Dott, since 2 of his patients experienced fatal brain injury after being exposed to radiation levels greater than 3000r during the 1930s.[14] The letter correspondence between Dott and Dr. Gilbert Horrax (Cushing's successor and right-hand man) from Boston, Massachusetts, during 1957 shows the importance of specifying the X-ray exposure for the treatment of pituitary tumors (**Figure 2**).[16] In the letter, Dott asked Horrax whether the X-ray therapy of 4000r is causing collateral damage to the healthy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5th August, 1957.

Dr. Gilbert Horrax,
The Lahey Clinic,
605 Commonwealth Avenue,
Boston 15,
Mass.

Dear Gil,

I did miss you at Bruxelles. I heard that you had not been quite well. I took this Asiatic Flu while there and required 3 days on a Salmon river up North to recover when I got home. I was accompanied on the latter trip by one - Dr. J.M.D. Dott - a person you knew as Jeannie. She was capped the other day at the Medical Graduation.

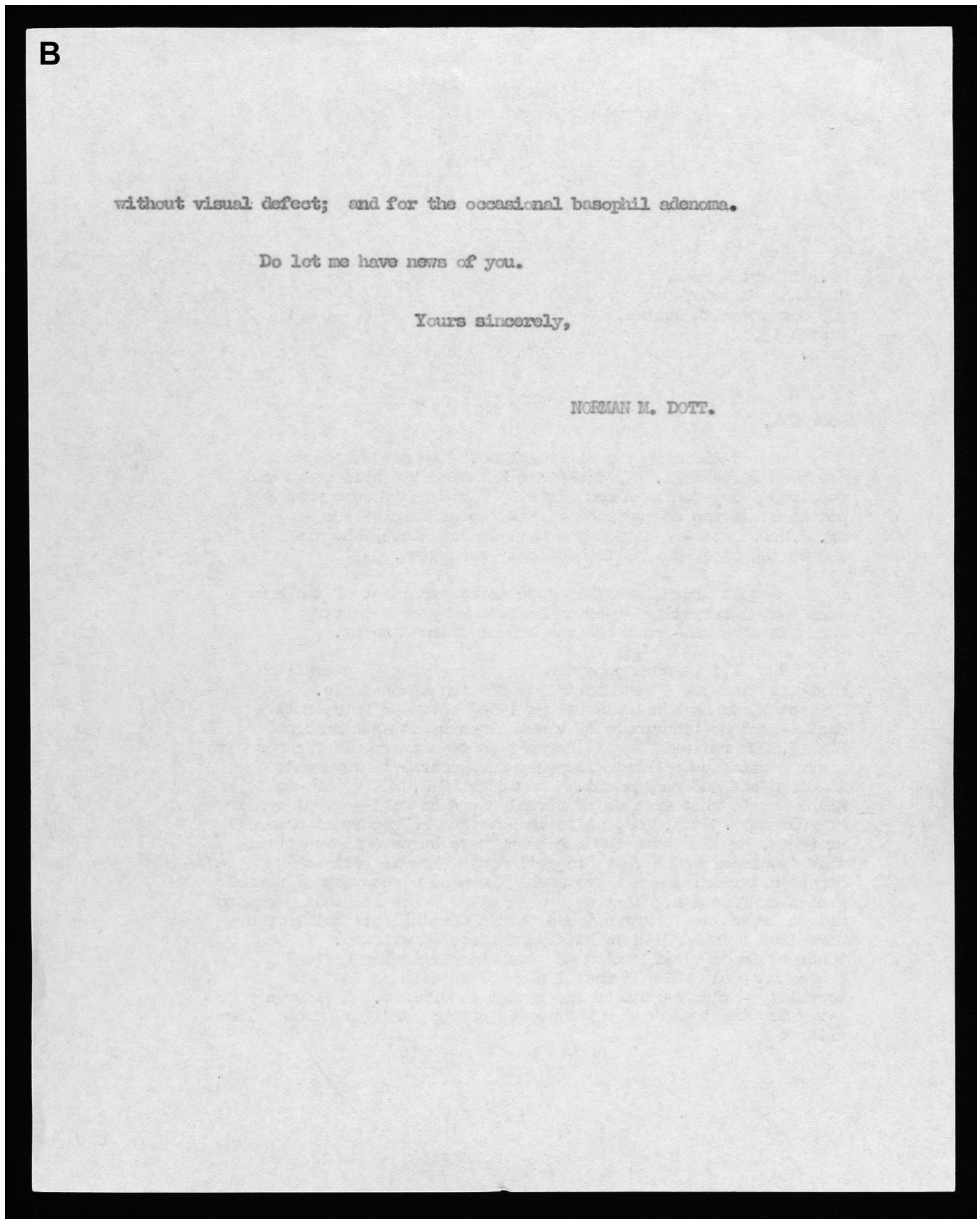
At Bruxelles I happened to be president of the hour when your interesting paper on Radiotherapy of Pituitary Adenomas came on - so I had the honour of reading it.

I took some exception to your giving 5% operative mortality and 30% 5 year mortality for transphenoidals. My last 70 transphenoidals (since 1936) have had no operative death - and no recurrence of visual impairment when combined with 3,000R radiation! It doesn't do to compare old figures with newer statistics without allowance for general improvements in diagnosis and management. I wonder if 4,000R (your usual) might damage what remains of normal gland as well as what remains of adenoma? At 3,000R, while we have had no recurrent chiasmal pressure, we also have two cases who have borne children after this treatment and a fair proportion who show no serious hypopituitarism, and who presumably have some recovery of normal glandular function. What do you think? I was sad that you were not at Bruxelles to argue these points personally; but if you have time I would like to have your views in writing. My own tendency is to clear chiasm of pressure surgically (often transphenoidal) which I feel I can afford with so low a mortality - then X-radiate to prevent recurrence. I reserve X-ray treatment alone for very early cases; and for acromegalics without /

Figure 2. Dott's letter to Dr. Gilbert Horrax, 1956–1957, with regards to the new results achieved using trans-sphenoidal approach and the better outcomes seen using radiotherapy at 3000r compared with 4000. This letter comes after the Newcastle meeting in 1957, where Horrax did not attend because of his new diagnosis of lung cancer. Copyright permission provided by the Centre for Research Collections, Edinburgh University Library.[16] (Continues)

aspects of the pituitary glands of his patients and suggested exposure to radiation as high as 3000r as adjuvant therapy to trans-sphenoidal surgery. Furthermore, Horrax's report on the trans-sphenoidal having 5-year mortality rates of 30% was challenged by Dott, as his method had 0% mortality rates in the previous 20 years.

Horrax apologetically replied in September 1957 with, "I am extremely ashamed to say that I did not know about your recent experiences with trans-sphenoidal operations… Certainly, with your experience of no deaths and no recurrence of visual impairment, when combined 3000r radiation, there can be no question but that would be the procedure of choice."[16] Unfortunately, within the letter Horrax exposed that he had been on treatment for lung cancer, which lead to his death only days after, thereby failing to disseminate or implement this information to the neurosurgical unit in America.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without visual defect; and for the occasional basophil adenoma.

Do let me have news of you.

Yours sincerely,

NORMAN M. DOTT.

Figure 2. (Continued)

Concerns regarding the effects of radiation exposure was a major topic for Dott and his staff. In 1951, a letter between Dr. W. S. Shearer, the Director of the radio-diagnostic department at the Royal Infirmary of Edinburgh (RIE), and Dott, shows the concern Dott's staff shared because of the exposure they were facing from X-rays.[17] Shearer's opinion was based on previous literature saying that the maximum X-ray skin exposure should be 300r units per exposure. However, no research evidence was available on recurrent X-ray exposure and its cumulative effects, therefore he suggested to Dott that his staff members should take 20 films a week (180r), 30 films a month (270r), or 60 films in a year (540r).[17]

Operators had specific regulations recommended by the X-ray and radium exposure committee, which included wearing lead rubber aprons during work; however, the same did not apply for Dott's nursing staff. As a result, in 1952, Dott complained on behalf of his nursing staff that they also should be protected from

X-ray exposure and urged that they should wear lead aprons as well. Shearer declined the request on the basis that the nurses were working at a safe distance from the X-ray machines.

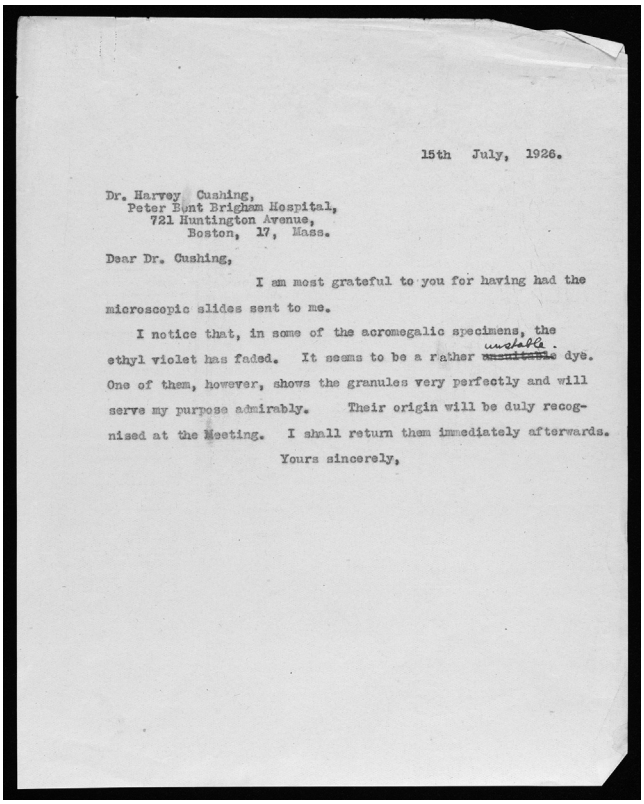
By 1957, a memorandum was issued by the Medical Research Council named "Radiation Hazards in Diagnostic X-ray examinations," which was received the same year by Dott.[17] As a result of this publication on the hazards to man from nuclear and allied radiation, radiologists decided during a meeting on March 21, 1957, to agree on a policy regarding X-ray exposure. Having explained the genetic harm X-rays cause, they conclude that this investigation should not be performed on the "abdomen and pelvis in pregnant women" and other organs like the genitalia. Fear of legal action from patients for unnecessary excessive use of X-ray was one of the reasons why the memorandum included the need for substantial clinical examination of the patient before any X-ray investigations, to reduce the exposure to radiation hazards. It should be mentioned that during this period cinema also popularized the concept of the public fear of radiation. The film produced in 1936, titled "The invisible X-ray," starring Boris Karloff was the first movie which emphasized the theme of harmful radiation, showing how popular radiation had become because of its hazards.[18]

The changes to X-ray facilities occurring during the 1950s should be explored for their impact on Dott's treatment of pituitary adenomas. An issue the RIE faced in 1947 was, the delay of X-ray therapy extending to all patients also including those suffering from pituitary disorders. A letter from Dott to Dr. McWhirter, Deputy Director of the Radio-diagnostic centre in RIE, explained that patients' X-ray therapy was delayed for periods ranging from 7 to 14 days causing increased hospital stay.[17] In some cases, patients were being referred for a review X-ray while still waiting for their X-ray treatment to commence. When considering that the letter was related to Dott's own referrals for X-ray diagnosis and therapy and the delayed patients could be in some cases suffering from acromegaly one can see clearly Dott's influence on the clinical setting regarding the improved management of pituitary disorders.

Other letter correspondences from Dott relate to the new radiology department being built in Edinburgh during 1954. The new department had increased the number of beds, from 98 to 120 and 2 new X-ray machines, one being used for radiotherapy, an essential aspect of the treatment of pituitary disorders, whereas the other one was specifically used for research.[19] There would be a total of 7 X-ray therapy units, which would again assist with the treatment of patients with acromegaly. The memorandum published by Professor McWhirter for the new Department of Radiotherapy at the Western General Hospital, supports that research would be aimed for the treatment of PAs.[19] Since X-ray constituted a critical aspect for the diagnosis and treatment of patients with acromegaly, the new Radiology department was aiming its resources into this field of research thereby assisted with Dott's research by supplying new X-ray equipment and improved infrastructure.

Research Dissemination

Dott's knowledge of the pituitary enabled him to participate in scientific meetings where he would present his research regarding the histologic classification, symptomatology, and treatment modalities of acromegaly. Scientific meetings were on the of best modalities scientists to disseminate their knowledge to alter medical culture and allowed for celebrations within the medical community.[20]



15th July, 1926.

Dr. Harvey Cushing,
Peter Bent Brigham Hospital,
721 Huntington Avenue,
Boston, 17, Mass.

Dear Dr. Cushing,

I am most grateful to you for having had the microscopic slides sent to me.

I notice that, in some of the acromegalic specimens, the ethyl violet has faded. It seems to be a rather unstable dye. One of them, however, shows the granules very perfectly and will serve my purpose admirably. Their origin will be duly recognised at the Meeting. I shall return them immediately afterwards.

Yours sincerely,

Figure 3. A humble letter from Dott to Cushing during 1925–1926, showing his gratitude for the microscopic slides that Cushing had sent him for the presentation at the *British Medical Journal* meeting in 1926, Nottingham. Copyright permission provided by the Centre for Research Collections, Edinburgh University Library.[22]

In July 1926, Dott was invited to have a discussion on pituitary disorders during a *British Medical Journal* meeting. The article included a detailed summary of the variety of symptoms present in patients with acromegaly.[21] These symptoms had 2 aspects of analysis; one being the endocrine aspect and the other the anatomical compression caused by this tumor on adjacent structures. He explained that the endocrine manifestations of acromegaly, were created during a hyperpituitary state, produced symptoms of increased fibrous tissue in the patient's nose, fingers, ears, tongue, nerve sheaths, and internal organs. Other endocrine manifestations of acromegaly he included were bone overgrowth, metabolic rate increase, loss of sexual function, increased hair production, and increased glucose in urine. In addition, Dott named the histologic classification of the tumor-causing acromegaly, eosinophilic adenoma. Furthermore, X-ray images showing a distended sella turcica because of pituitary tumors were explained by Dott as a form of diagnostic indication. The anatomical aspect of symptom expression in acromegaly

leading to compression within the pituitary cavity was also explained. Headaches for example were due to tumor growth leading to expansion of the dura covering of the sella turcica. Visual disturbances he said were caused by the outward compression leading to cavernous sinus displacement. The symptoms of bitemporal hemianopia (visual loss of the temporal aspects of vision) Dott explained, were caused by the compression of the adenoma on the optic chiasm seating on top of the pituitary gland.[21]

Unsurprisingly, Dott's presentation in 1926 was mostly extrapolated from his previous work with Cushing. In fact, one of Dott's letter correspondence to Cushing, shows the deep appreciation Dott had for Cushing for providing him with valuable support and histological slides of pituitary adenomas for the presentation in 1926 (**Figure 3**).[22] At the start of his presentation, Dott credited Cushing as it was based on the review article, "A Consideration of Hypophysial Adenomata."[21]

The Royal Society of Medicine held a meeting in London in 1929, where Dott started discussing several of his own cases.[21] One of the case reports entails the clinical presentation of a man aged 34 years who was suffering from acromegaly. The history of the patient included symptoms of acromegaly lasting for 2.5 years, sexual impotence of 3 years, and visual disturbances lasting 1 year. Dott's treatment plan was trans-sphenoidal incision of the pituitary gland and postsurgical radiotherapy. He noted that the patient, postsurgically, had improved vision within 14 days and an obvious decrease in acromegaly symptoms. Dott was one of the first to suggest that early adenomas could be treated by radiotherapy alone and adjuvant radiotherapy with trans-sphenoidal surgery should be performed only when symptoms of compression caused visual disturbances. During 1931, Dott gave another speech for the Forfarshire Medical Association in Dundee, using the same case report from 1929 on acromegaly.[23] On this occasion, the speech included the quote "A trans-sphenoidal operation 4 years ago followed by X-radiation caused visual recovery which has been preserved."[23]

Referring back to the speech in Newcastle during 1957, Dott also spoke about the issues regarding the compression of the optic chiasm.[24] During this meeting, Dott showed a different case report on a female patient, who at the age of 27 begun showing symptoms of acromegaly and lack of menstruation. After performing trans-sphenoidal resection of the pituitary and adjuvant radiotherapy, her symptoms of acromegaly were relieved in 2 years. Furthermore, Dott included that the success rate of his approach yielded him an average mortality rate of less than 2% in more than 100 consecutive operations with no mortalities in more than 70 cases.[24]

The research meetings Dott attended due to his knowledge of the pituitary gland had a socioeconomic aspect that also should be mentioned. In 1926, Dott was invited to the 94th British Medical Association annual meeting in Nottingham.[25] A variety of activities were available for the attendees, which included annual dinner, golf competitions, and an exhibition showcasing surgical equipment and X-ray apparatus. Similarly, various events were available for the meeting in Newcastle during 1957.[26] There, he had the opportunity to participate on an excursion to Farne Islands, the Roman Wall, and the Durham cathedral and Castle. Furthermore, on this occasion color televisions were available, giving the attendees the opportunity to watch new clinical skills, surgeries, and British Medical Association films regarding different medical themes. In both occasions, Dott was invited to give speeches on the diagnosis and treatment of pituitary related disorders like acromegaly.

These meetings served as a gathering point for sharing information, skills, and updating practises.[20] Undoubtedly, Dott used these medical gatherings as an opportunity to share the knowledge he gained from Cushing on the treatment of pituitary tumors and promote the trans-sphenoidal approach as the preferred method for treating acromegaly. In contrast, the book *The Neurologists: A History of a Medical Specialty in Modern Britain* indicates that neurologists were suspicious of surgeons who practiced under Cushing, thereby causing a division in ideologies.[20] Potentially, this could have led to limitations to Dott's ability to disseminate his research within these meetings because British neurologists were prejudiced at the time against innovative ideas coming from Cushing's pupils. Indeed, the trans-sphenoidal surgery remained unpopular until Dr. Jules Hardy improved the technique further, eventually becoming the established choice of treatment for pituitary disorders.

CONCLUSIONS

Norman Dott's knowledge of pituitary physiology and treatments from acromegaly during 1900–1960s had been largely contributed to Cushing's work. To begin with, the research on the pituitary physiology that Dott published was closely related to that which Cushing had performed during 1909. Dott's knowledge of the pituitary physiology was also highly influenced by his supervisor Schafer. However, Dott was able to accomplish positive results in areas in which his predecessors admittedly failed. Furthermore, the trans-sphenoidal surgical approach as well as the X-ray treatment of PAs were performed by Cushing before Dott started suggesting these as modes of treatment for this pathology.

Before his discussion for the *British Medical Journal*, in 1926, Dott admitted gaining most of his knowledge of the pituitary from Cushing, "As my experience on pituitary diseases has been acquired entirely under your [Cushing's] direction, I shall, of course, speak from this point of view."[27] This shows the significant impact Cushing firstly had on Dott's suggestions on the treatment of acromegaly and secondly the assistance Cushing gave to Dott on research dissemination. However, Dott made significant adjustments to these techniques and methodology of Cushing experiments, leading to improvements that Cushing expected from his student.

A letter from Cushing to Dr. Bailey, in 1929, reveals Cushing's expectations that his student would surpass him, "I shall expect great things of him. It's a poor pupil that does not surpass his master, as Leonardo wisely said."[27] The changes Dott made in his pituitary experiment, the equipment modifications for the trans-sphenoidal surgery, and the specification of X-ray exposure required to treat PAs were admittedly built on the knowledge passed from Cushing to him. However, still substantial credit should be given to Dott in the ways he used his training from Cushing to continue treating patients with acromegaly.

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