

i.e., 1.26 lb. (570 g.) per child per week. If the rate of contamination was 1 p.p.m., a meal containing 100 g. of groundnuts would result in a dose of 0.1 mg. which would be 0.0025 mg. per kg. body-weight in a 40 kg. (88 lb.) child. The lethal dose (L.D.₅₀) in 50% of ducklings is 0.4 mg. per kg.; to attain this a 40 kg. child would need to eat 16 kg. of nuts, which is unthinkable. However, if the nuts contained 10 p.p.m. it would require little more than 2 weeks for a child to total an L.D.₅₀ duckling dose. From the data presented here on the state of the nuts in relation to aflatoxin content (tables II, III, and IV) it would seem difficult for a level of contamination of 10 p.p.m. or more to escape unnoticed; many would discard groundnuts if there was an obvious growth of mould. However, at a level of 1 p.p.m. the fungal growth may not be sufficient to make it obvious to casual observation (fig. 1). At this concentration the description of the nuts was predominantly "many with broken testa".

There is, however, a real danger that the mould may grow on the nuts during a damp period followed by an arrest in growth with a change in climate or storage conditions. The nuts may then appear relatively free from mould, although they may be dirty. This may well have been the case in sample 25 which was classified as in a fair condition, but had a high aflatoxin content. With this last reservation, it is probable that groundnuts could be regularly eaten with an aflatoxin content of up to 1 p.p.m. Whilst on the one hand it would take a considerable period of time for an L.D.₅₀ dose to be consumed, it should also be pointed out that no sample examined by us was free of *A. flavus* spores. It is difficult to predict the cumulative effect at such levels, particularly as the effect of aflatoxin is so species-dependent. Insufficient is known about the cumulative effects of low doses to reach a conclusion regarding the implications to human hepatoma in Uganda except to say that if it does play a role it is most likely to be intermittent and chronic. The probability of a toxic dose being consumed at one meal is almost negligible, and at 1 p.p.m. it would require something like 6 months to total such a toxic dose.

An analogy with current views on radiation hazards may provide some guidance to the situation. The maximum accepted safe cumulative dose throughout any given year is approximately 1/100th of a single lethal dose (Adrian Committee 1966). If the analogy is valid, it might provide a basis for considering the possible harmful effects of aflatoxin in foodstuffs.

The obvious speed with which the aflatoxin can accumulate in groundnuts, given the right conditions, the nature of cropping, length of storage, humidity, and rainfall in areas where the groundnuts are grown, recommends a more detailed inquiry than was possible here. Furthermore, the report by Coady (1965) on the isolation of toxin-producing fungi from other food sources in Ethiopia indicates that attention should not be confined to groundnuts.

We thank Dr. J. Nabney for supplying us with details of his method for estimation of aflatoxins before publication; the British Empire Cancer Campaign and the East African Medical Research Council for supporting this research; and Dr. Y. M. Clayton for assisting us with the identification of the species of fungi.

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Before Our Time

SOME ASPECTS OF THE FIRST RECORDED CASE OF MULTIPLE MYELOMA

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IN an important series of papers published between 1846 and 1850, John Dalrymple,¹ Henry Bence Jones,²⁻⁴ and William MacIntyre⁵ described all the essential features of the disease now known as multiple myeloma. These papers covered the clinical aspects of the disease, the properties of Bence Jones protein, the postmortem findings, and the histological appearances, and left no doubt that the authors considered this a hitherto undescribed disease "essentially malignant in nature... affecting the "osseous system".

WILLIAM MACINTYRE

William MacIntyre was perhaps the most remarkable member of this outstanding trio. He was, at the time he saw the patient in 1845, 53 years of age and physician to the Metropolitan Convalescent Institution and to the Western General Dispensary, St. Marylebone. On Friday, Oct. 30, 1845, he was called from his rooms at 84 Harley Street, to see a patient who had been under the care of Dr. Thomas Watson for several months. From the history and examination, MacIntyre noted many important clinical features of the disease, including the severe bone pains and could later assess the significance of the pathological fractures. Equally remarkable was the care with which he observed the effect of heat on the urine. In view of the history of oedema, one of his first acts when he saw the patient had been to carry out this examination. He thereby noted and later described all the important characteristics of the protein that subsequently and with little justice became known as Bence Jones protein. The ability of the precipitated protein to redissolve with a rise in temperature of the urine, only to reprecipitate as the urine cooled, was clearly described. MacIntyre was also aware of the other property of this protein—namely, its tendency to precipitate at temperatures considerably lower than those of other proteins. Thus, he noticed that the protein redissolved at the "coagulating point" of albumin, namely, 160–170°F (71–77°C)—the inference being that the protein had precipitated at a temperature well below this.

Dr. Watson had evidently not examined the urine during the time that the patient had been under his care. But he appears to have been present during the discovery of this unusual protein or else MacIntyre discussed his perplexing findings with him, since both physicians quite

1. Dalrymple, J. *Dublin J. med. Sci.* 1846, ii, 85.
2. Bence Jones, H. *Lancet*, 1847, ii, 88.
3. Bence Jones, H. *Proc. R. Soc.* 1847, 5, 673.
4. Bence Jones, H. *Phil. Trans. R. Soc.* 1848, p. 55.
5. MacIntyre, W. *Med. Chit. Trans.* 1850, 33, 211.

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independently sent a specimen of urine to Bence Jones. It was customary then for the specialist services to be provided by practising physicians and surgeons, and Bence Jones had already established a reputation as a chemical pathologist.

BENCE JONES

Henry Bence Jones, of 50 Lower Grosvenor Street, was at this time only 31 years of age and was physician to St. George's Hospital. He was able to confirm MacIntyre's findings and then proceeded to examine the urinary protein in some detail. His papers were therefore concerned with the properties, analysis, and significance of this protein, whereas the paper by MacIntyre dealt mainly with the clinical features of the disease. For this reason, Bence Jones became credited with the discovery of the protein. Further confusion arose over the part played by Dr. Thomas Watson, since Bence Jones quotes the letter from Dr. Watson which accompanied the urine: "The rube contains urine of very high specific gravity. When boiled it becomes highly opaque. On the addition of nitric acid it effervesces, assumes a reddish hue and becomes quite clear; but as it cools assumes the consistence and appearance which you see. Heat reliquefies it. What is it?" Nevertheless, the fact that the urine specimens were sent on Saturday, Nov. 1, 1845—that is, the day after Dr. MacIntyre had been called in for consultation—supports MacIntyre's claim to the discovery, and this is established by the statements made by Bence Jones in his papers. In the first² he writes: "On the last day of October, a peculiar state of urine was discovered, through the carefulness of Dr. MacIntyre", and in the second, "He [Dr. MacIntyre] being in attendance on the case with Dr. Watson, had two days previously first observed the peculiar reactions of the urine."

DALRYMPLE

MacIntyre³ also described the postmortem examination carried out by Mr. Alexander Shaw, surgeon to the Middlesex Hospital. The significant findings were in the bones, particularly the ribs and sternum, and the cervical, thoracic, and lumbar vertebrae. The affected bones were softened, fragile, and easily cut, with the interior replaced with a soft, "gelatiniform", blood-red substance. Some of this material taken from two of the lumbar vertebrae and a rib was referred for histological examination to John Dalrymple, surgeon to the Royal Ophthalmic Hospital, Moorfields, and a member of the Microscopical Society. He described the nucleated cells which were present in great numbers and which formed the bulk of this gelatiniform mass. These cells were said to vary in size and shape but the majority were round or oval with the smaller cells "one and a half to twice larger than the average blood cell or blood disc" (red blood-cells).

TABLE I—DETAILS OF PATIENT WITH MULTIPLE MYELOMA DESCRIBED BY WILLIAM MACINTYRE AND HENRY BENCE JONES

	MacIntyre ³	Bence Jones ^{1,4}
Name	Mr. M—	No details.
Address	London	London.
Age at death	45	45 ¹ 47 ⁴
Date of death	Jan. 1, 1846	Jan. 2, 1846.
Occupation	Tradesman	Tradesman ² Grocer ⁴
Social details	Married early Numerous offspring "Holiday in Scotland"	Wealthy.

Dalrymple also noted that the larger and more irregular cells frequently contained two and often three nuclei. These descriptions would be consistent with malignant plasma cells with some multinucleated forms. Dalrymple's paper was illustrated by two woodcuts which were credible drawings of these cells. Both Dalrymple and MacIntyre believed that this disorder was principally a malignant disease of bone. They were puzzled because the tumour had not extended outside the bone, and this they explained by the limited duration of life of the nucleated cells and therefore limited production of bulk by the tumour.

THE PATIENT

The identity of the patient has so far been unknown. It would also be interesting to know the cause of death that appeared on the death certificate of this first recorded case of multiple myeloma. In order to trace this case therefore, the personal details of the patient were taken from the various papers (table 1). Unfortunately, the index of deaths for the first quarter of 1846 gives only the names in alphabetical order, the district of registration, and the volume and page number of the entry in the Register of Deaths. The initial step in the search was therefore to extract from the index the names beginning with M, of all males who died in the London area. In the first quarter of 1846, of the 45,941 males who died in England and Wales, 7259 had names beginning with M, and of these 437 died in the London area. These names were then arranged according to volume and page number to facilitate the search of the Register of Deaths by officers of the General Register Office. The search instructions were to note all names of men aged 45, 46, or 47 years, who died on Jan. 1 or 2, 1846. The expected number of such men can be calculated. Thus, 437 names will represent all deaths from birth onwards, and from the figures in the Annual Report of the Registrar General for that year about 20 of these would be aged 45 to 49 years. Assuming that the death-rate is equal over this age-span, then only about 12 of these men would be aged 45, 46, or 47. These 12 men would have died over the period from Jan. 1 to March 31, and therefore no more than one of these can be expected to have died on Jan. 1 or Jan. 2.

TABLE II—DETAILS OF DEATH CERTIFICATE

When and where died	Name and Surname	Sex	Age	Occupation	Cause of death	Signature, description and residence of informant	When registered	Signature of Registrar
First of January 1846 at No. 37 Devonshire Street	Thomas Alexander McBean	Male	45 years	Grocer	Atrophy from Albuminuria Certified	Mary Davidaon present at death No. 22 Devonshire Street	Eighth of January 1846	William Registrar

The search agreed with this prediction, since only one man was found who fulfilled all the particulars and this person must therefore be the patient seen by Watson, MacIntyre, and Bence Jones (table II). It is gratifying to find that the death certificate is consistent with the known personal details, including the holiday in Scotland! Not unexpectedly, the details of the patient given in MacIntyre's paper are correct, in contrast to some of the details given by Bence Jones. The cause of death is given as "atrophy from albuminuria". This was a reasonable diagnosis, since the term albuminuria was used in those days quite non-specifically to mean proteinuria. Alternatively, the cause of death might have been given as "McBean's disease with MacIntyre's proteinuria".

I should like to thank the officers of the General Register Office for their kind cooperation.

Round the World

U.S.A.

The growth of the Citizens League Against the Sonic Boom, based in Cambridge, Massachusetts, has been striking. Founded only nine months ago (March 9, 1967) by nine charter members, it has today over 2000 members from the U.S.A., Canada, the United Kingdom, and Sweden. The director, Dr. W. A. Shurcliff, is a physicist at Harvard University, and the deputy director, Prof. J. T. Edsall, is a biochemist, also at Harvard. The League includes many other eminent professional men— aeronautical and acoustical engineers, biologists, doctors, lawyers, economists, architects, teachers, and musicians.

The League takes up no position about military planes and their sonic booms, but vigorously opposes the development of commercial—i.e., civilian—supersonic transport planes (S.S.T.s). Using facts gleaned from deep within Government reports on sonic-boom tests, and some wrung from the U.S. Federal Aviation Administration (monolithically for the S.S.T.) the League has prepared an impressive array of moderately written fact-sheets, recording firm evidence that sonic booms of intensity 1 lb. per sq. ft. are intolerable—both to people and to property—and concluding that the 2 lb. per sq. ft. booms predicted for the S.S.T.s would be "doubly intolerable".

The League has moved fast. It has collected a library of technical reports and clippings about sonic booms, drafted and published advertisements in many magazines and newspapers, including several half-page advertisements in the *New York Times*, and raised more than \$20,000 through voluntary contributions. It has created a national committee; it has taken part in many TV and radio programmes; it is in touch with conservation groups in several countries, including the Anti-Concorde Project (give or take an e) in the United Kingdom.

The response has been enormous. Before March, 1967, only a few people had spoken out against the boom; noteworthy among these was Bo Lundberg, then director general of the Aeronautical Research Institute of Sweden. Since March, more than 900 newspaper articles and 40 magazine articles against it have been published in the U.S.A. Nearly every major newspaper has carried an article expressing alarm that Governments propose to subsidise the construction of a machine that, while saving a little time for an elite few and perhaps yielding a small profit for aviation, will destroy the peace and quiet of millions of people.

The League says that its educational campaign is to be intensified until the Governments are forced to admit that the sonic boom is more than a small defect in the S.S.T. programme, more than a mere annoyance, but is an outrage to civilised living. The League is not satisfied with Government protestations that, at the start at least, the S.S.T.s would be operated only over oceans; it is convinced that, once loosed on the world, they will encroach on assured quiet until uninterrupted sleep will become a historical curiosity.

Very Speeal Articles

THE BOAT

"Well", said the Boatman, "So Yev' wakened up at last."

"Yes", I said, "where am I?"

"In a boat", said he.

"Thanks", I said, "I can see that. Where is the boat?"

"I don't rightly know", answered the Boatman. "Do you mean to tell me that you sit craft, and by the look of you, have been doing so for a long time, and don't know where we are?"

"That's what I said", he replied.

"Do you perhaps know where we are?" I asked, with a touch of sarcasm.

"No", he said.

"But . . ." I began.

"Look, young feller", he answered, "when you a-sleepin' in the bilges there, I thought ye'd the lot. I was a sensible lad wot I could have a sensible talk with. I was like all the rest of 'em, askin' a mort o' questions: nobody knows answers to. I give up askin' questions afore yew was hatched, an' I only asked one then."

"What was that?"

"Same as yew, young man. When the owner ol' boot, he say to me, 'George', he say, 'I'm hully sorry to give yew this leaky old craft ter be master of, but as yew see, I've nothin' else'. 'Where do I steer for?' sez I. He give me a queer ole look an' a wink, an' then sez he, 'steer afore yer own nose, bor, an' some day happen yew'll somewhere'. I could see he wuz a Suffolk, like me, so that wam't no use pesterin' him with talk an' questions, so I kep me mouth shut. 'Dew yew keep 'er afloat, an' into the wind, bor', sez he, 'an' yew'll find yer time well occupied', an' with that he went off, slow-like up the hard, an' I never see him since."

"There seem to be lots of people on board", I said.

"Too many. The cussedest lot yew ever did see. When they ain't fightin' each other an' lightin' fires fit to burn the bottom out of her, they're arguin' about wot none of 'em don't understand. See that lot up in the bows there?", he said, becoming more communicative, "clever dicks if ever any. Always shoutin' back that they can see lights or land or summat, and tellin' me how to run this ship. If it ain't it's them others to port and starboard—different colours and talk, but the same ideas, more or less. All on 'em my job better 'n I do, and jumpin' about sos yew can't 'er on an even keel. All the same, I'd rather 'ave them than this bunch in the starn, moanin' an' gripin' an' sayin' sinkin'—not but wot we aren't, 'alf the time. But we ain't done it yet", he finished with a note of triumph.

"Where are you from?" I asked.

"I'm out of Lowestoft", he said, "an' if ever I get back, you'll not find me at sea again, once I get this cargo of lubbers ashore. Gawd knows wot the owner wants 'em for."

"When are we supposed to arrive?" I asked.

"More bloody questions", he replied. "I've been sailin' this ole bitch of a boot some thousands of years now, young feller, an' I don't know when we're goin' to get into port, so more than when we started."

"What do you suppose I should do?" I asked him, rather diffidently.

"Yew do what yew please, young feller", he said. "I've got to steer this ol' boot till I get callouses on me backside, but yew please yourself. Some write books about the journey, some read 'em, some fight, or preach, or talk politics, or go whorin'. Not many get near an idea of wot the trip's about, an' they're usually the quiet sort wot 'ear songs in the wind an' see somethin' lovely in a gull's wing."

"Perhaps I could do something, as well as listen to the wind", I said, but the Boatman was gazing into the mist, and did not answer.

And that is roughly how I came to be a surgeon.