

of the growth for microscopical section. He quotes Naegele as having a similar death two days following biopsy for sarcoma of the tongue. Cirillo states that he does not believe that the cause of death in either case was pneumonia, although in both there were some indications of lung involvement.

Prognosis

On this subject I shall confine myself to saying that from the published cases the prognosis is not so gloomy as might be expected, especially as the operative treatment of many of these has been restricted and inadequate. Of twenty-four cases quoted by Fripp and Swan, eleven patients were alive and well at periods varying from six months to thirteen years from the time of operation. The condition in the remaining thirteen recurred early, either locally or in the cervical nodes.

Treatment

I could find no record of any sarcoma of the anterior two-thirds being treated with radium. Numerous cases are recorded, as that of Simons,¹⁴ in which x-ray therapy and radium had been used in the treatment of lymphosarcoma of the base of the tongue. In the past a wide removal of either the whole or half the tongue was recommended, sometimes followed by a bloc dissection of the cervical glands. I followed the latter teaching in my own case. I did not use radium for the tongue, mainly because the cut surface of the tumour appeared firm, fibrous, and relatively avascular when a small wedge was removed for biopsy. The microscopical appearance confirmed this relative avascularity. With regard to the neck, I performed a bloc dissection of the cervical glands on the same side, since I cannot help feeling that this procedure is more efficacious than superficial or interstitial irradiation in cases of secondary malignant glands.

Case Report

A male, aged 44, healthy in other respects, attended the out-patient department complaining of the rapid onset of a swelling of the tongue. He had no pain of any description, and there was no history of injury. On examination there was a swelling one inch in diameter and firm in consistence situated near the tip of the tongue on the left side (see figure). The swelling was intraglossal, and there was no ulceration of the covering epithelium, which was a little stretched over the convexity of the tumour. Protrusion was full, and there was no fixation. The cervical nodes were not palpable.

A small wedge-shaped piece of the tumour was taken for microscopical examination, and was reported by the pathologist as a round-celled sarcoma. Clinical and x-ray examination of the chest revealed no secondaries. Whitehead's operation was undertaken, the left half of the tongue, including part of the right half in the vicinity of the tumour, being removed. Three weeks later I performed a bloc dissection of the glands on the left side of the neck, and this was followed up by a course of x-ray therapy. The glands removed at operation were not sarcomatous when sectioned.

The patient is well and free from local and glandular recurrences at the time of writing, which is a year and a half after the operation.

Conclusions

1. Sarcoma of the tongue is a rare disease.
2. There are, however, several characteristic symptoms and signs which help to distinguish sarcoma from the nodular type of carcinoma.
3. Attention is drawn to the fact that small round-celled sarcoma occurs sometimes in the anterior two-thirds, suggesting that this type of growth is not, as has been frequently stated, a lymphosarcoma.
5. The prognosis appears to be less gloomy than might be anticipated.

I am indebted to Dr. T. B. Davie and Dr. Hugh Smith for examining and reporting on the microscopical sections.

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TREATMENT OF CHOLERA WITH A NEW ANTI-CHOLERA SERUM

PRELIMINARY NOTE

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Since the introduction of saline transfusion by Sir Leonard Rogers little progress has been made in the treatment of cholera. The mortality rate is still very high; in the recent epidemics in the Central Provinces and Ganjam Districts it was over 50 per cent. Saline transfusion is only a means mechanically to replace the loss of fluid, but up to this time nothing has been found to counteract the toxic condition or the fatal vasomotor paralysis. During the height of an epidemic of cholera, when the mortality is high, death has been due mostly to vasomotor paralysis. The saline transfusion has often only a transitory effect; the pulse gradually sinks, and no stimulant can improve it. Excess of saline produces oedema of the lungs. Unless the toxin which produces the fatal vasomotor paralysis can be neutralized, further advance is not likely to be made in treating successfully the more severe cases of cholera. I thought that a potent anti-cholera serum might achieve this, and I accordingly began, three years ago, to try to isolate the toxin which is responsible for the acute symptoms.

Isolation of a Toxin

For long the attempt to isolate the real toxin which produced the acute diarrhoea and vasomotor paralysis in cholera was unsuccessful. I was trying to isolate the toxin while in charge of the biological laboratory of the Bengal Chemical and Pharmaceutical Works. In December, 1932, I made a communication on the "Nature of Cholera Toxin and Symptoms of Cholera" to the Scientific Section of the All-India Medical Conference.¹ In this I showed that by anaerobic culture of the cholera vibrio in a special broth a toxin could be obtained which, when injected in small doses intravenously in rabbits, produced cholera-like diarrhoea. I obtained sufficient corroborative evidence of the presence of a toxin in this medium by experimentally producing cholera-like diarrhoea in laboratory animals. The result was published in the *Comptes Rendus des Séances de la Société de Biologie* of Paris,² in which the technique of preparation of the toxin and experimental pathogenic action were described.

Preparation of Serum and Trial

This toxin was prepared from only one strain of cholera vibrio, as it was found to produce uniform toxin provided the medium was prepared exactly according to our formula. Conservation of the virulence of the strain was found to be as difficult as that of *B. diphtheriae*, and the production of toxin depended upon conservation of

the virulence. Our toxin is a filtrate of eighteen hours' broth culture. When injected intravenously into rabbits in repeated small doses it produced intense thirst and restlessness within a few minutes, and subsequently diarrhoea-like stool. With this toxin I attempted to immunize horses, the highest dose injected being 500 c.cm. At the end of the process of immunization I was astonished to find that the agglutinating titre of the serum was 1 in 8,000. This serum was then concentrated, and the agglutinating titre of the concentrated and purified serum was 1 in 12,000 of H agglutinin, and 1 in 1,600 of O agglutinin. I had no opportunity, however, of verifying the curative value of this serum except in laboratory animals. A previous injection of serum prevented experimental production of choleric diarrhoea with the toxin in laboratory animals.

Due to unavoidable reasons I could not proceed further with the experiment until the cholera epidemic broke out in Calcutta in the middle of March, 1934. The trial was made in the cholera ward of the Chittaranjan Hospital. In the beginning of the epidemic no serum was given to any patient, and the mortality was as high as 34 per cent. In the second week of April I injected this serum subcutaneously in a few toxic cases, but no appreciable result could be obtained with 20 c.cm. At that time I also tried ordinary polyvalent serum (prepared by different manufacturers of this country), both subcutaneously and intravenously, in doses up to 40 c.cm. The result was not only unsatisfactory, but there was distinct evidence of early setting in of uraemia.

Dosage Employed

I then began to inject my serum intravenously in doses of 20 c.cm. The result, though encouraging in mild cases having a specific gravity of 1060 or below, was not up to my satisfaction in highly toxic cases with higher specific gravity. I had then been thinking of intraperitoneal injection of my serum, in order to get the maximum amount absorbed through the same route as the toxin in the shortest possible time. At first, due to certain natural apprehension, the serum was not given intraperitoneally until the condition of the patient was hopeless. In one patient, admitted in a collapsed condition with a specific gravity of 1064, the result of the serum was so evident that I became more hopeful of success. When I was satisfied that the intraperitoneal injection was absolutely harmless, and could be easily given by a fine trocar and cannula specially made for the purpose, I began to inject 20 c.cm. after the first intravenous saline transfusion in all patients admitted in a collapsed condition. I am glad to say that some of the highly toxic cases were saved in this way. Control cases without serum, treated with calomel, ol. ricini, kaolin, etc., were maintained to compare the result of the serum treatment.

As my stock of serum was not adequate, and due to apprehension of uraemia, I was giving only 20 c.cm. of serum in the beginning, but I found, subsequently, that I might have saved a larger number of patients had I given sufficiently higher doses of serum. Such apprehension of causing damage to kidney by the sudden introduction of a large amount of albumin is natural in the beginning of experiments. The apprehension, however, was found to be baseless. In the latter part of the serum treatment a single saline transfusion and a single intraperitoneal injection of 30 to 40 c.cm. of serum, according to the severity of the symptoms, diluted with 200 c.cm. of normal saline, diminished the frequency of stool within two or three hours, and the patient usually passed urine within four to five hours.

In the beginning of our trial with serum calomel and menthol pill was administered to patients who vomited frequently; later the only treatment was one saline trans-

fusion on admission and the serum. In Chittaranjan Hospital the highest mortality was found to be during the latter part of April and the first three weeks of May, and then the death rate declined up to the end of the third week of June. During the last week of June and the first week of July the mortality again increased. Out of thirty-two cases treated during the second exacerbation of the epidemic, as evidenced from the increase in the rate of mortality in control cases, only four patients died, of whom one was admitted to hospital three days after the onset of the disease, one died of excessive purging following administration by mistake of high doses of sodium phosphate, which I was giving in the beginning of the epidemic, and the other two died within two hours of admission before the serum could be absorbed. The results of the serum treatment are given in the following tables.

TABLE I

Control cases	211
Deaths	73 (34.1 %)
Serum-treated series	198
Deaths	40 (20.2 %)

TABLE II

Cases treated with 30 to 40 c.cm. of serum...	32
Deaths	4 (12.5 %)
Control cases treated without serum	57
Deaths	15 (26.3 %)

The intraperitoneal injection appeared to us to be the route through which our serum acted best. The rationale of intraperitoneal absorption of serum cannot be easily disputed in cases of cholera, and I propose to discuss it further at some future time. The dilution of the serum with warm normal saline seemed to me to be important. I tried different quantities of saline, from 25 c.cm. to 500 c.cm., but 200 c.cm. was found to give the best results.

This method is quite easy with a trocar and cannula of small calibre. After a small injection of novocain on the left side of the lower abdomen 1½ inches from the median line and 1 inch below the navel, the trocar with the cannula is introduced to pierce the skin and the muscle; the trocar is then withdrawn, and with a little twist the cannula easily pierces the parietal peritoneum and enters the abdominal cavity.

The results, though not entirely successful, were sufficiently convincing to indicate that a solution of this problem is likely to be reached by improving the potency of the serum. I am sure, from what I saw in those cases in which a larger amount of serum was given, that had I used a sufficiently large quantity in the beginning the results would have been entirely convincing. Unfortunately my stock of serum was exhausted before I could try it in another epidemic. I hope, however, to be able to prepare a sufficient quantity before the next epidemic breaks out in Calcutta.

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The German Association for Internal Medicine will hold its forty-seventh congress at Wiesbaden from April 8th to 11th, under the presidency of Professor Schottmüller of Hamburg. The first day will be devoted to a joint session with the German Association for Research into the Circulation, and the last day to a joint session with the German Association for Balneotherapy and Climatotherapy. Topics to be discussed include: medical problems relating to aeronautics; blood diseases associated with the myeloid systems; serological diagnosis from the points of view of the clinic and the general practitioner; and gastroscopy, with special reference to gastritis. Inquiries about the congress should be addressed to Professor Schottmüller, Alsterufer 33, Hamburg 36.