

THE STUDY AND TREATMENT OF CANCER BY PROTEOLYTIC ENZYMES:
A PRELIMINARY REPORT*

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PART I. EXPERIMENTAL

ANYONE who has been actively engaged in eye work will be aware of the rapid absorption of cataractous lens protein following the needling of congenital cataract. The varying and ultimate degree of absorption of these intraocular proteins in the adult is also a constant clinical finding. It was with a desire to know something of the biochemical factors concerned in this process that I undertook my research in the September of 1930. In the February number of the *Canadian Medical Association Journal*, 1934, I published an article which seemed to throw some light on these biochemical changes.

Hydrolysis of protein is carried out by active substances called enzymes, which act as catalysts. In the normal human body there are many enzymes. Those chiefly concerned with the hydrolysis of proteins foreign to the body are three in number, namely, leukoprotease, an active protein ferment associated with the polymorphonuclear leukocytes; lymphoprotease, contained in the large mononuclear lymphocytes; and globuloprotease, an enzyme which has been shown to be associated with the globulin fraction of the blood serum. It is a combination of the action of these three enzymes that is chiefly responsible for the process known as autolysis when this takes place *in vivo*.

Active extracts of these enzymes may be obtained and may be made to hydrolyse cataractous lens protein *in vitro*. A glycerine suspension of a mixture of these body enzymes was introduced into the lens in an attempt to hasten the absorption of cataractous lens protein in rabbits. Hydrolysis occurred very rapidly, but there was no control of the reaction. Invariably these eyes would go phthisic, or, in other words, there was no specificity, as all the intraocular structures were attacked.

At this point it became apparent that if any satisfactory results were to be obtained some

source of enzyme possessing specificity must be found. The possibility of using the proteolytic microorganisms presented itself. After a careful and extensive examination of the literature I found that, although a considerable amount of work had been done, the present knowledge of the production and action of these enzymes was in a very confused state. It occurred to me that possibly the specificity might rest in the type of stimulation received by the microorganism. In other words that, if we grew these organisms on a medium containing one type or group of proteins, the living cell would secrete only the type of enzyme or enzymes necessary to break down these particular proteins. In the *Journal of Infectious Diseases*, (1919, 24: 347), Diehl was able to prove that a degree of specificity of this nature existed.

After a considerable effort we found that we were able to procure a solution containing a specific type of enzyme, if we grew these organisms on a medium containing no other source of nitrogen except the insoluble lens protein which we wished to attack. We found that this enzyme solution would digest fresh insoluble lens protein *in vitro*, but would not digest gelatine or caseine. As a matter of convenience this solution was called "Ensol", from the first two syllables of the two words enzyme and solution.

Examining in a broad way our research at this point, it is easy to see why we applied this principle to the cancer problem. If we could do this with insoluble lens protein, why could we not do the same thing with foreign protein of any sort, provided that we could get the proteolytic microorganisms to grow on the protein we wished to attack?

We procured a piece of human scirrhus breast carcinoma tissue under sterile conditions, and, after removing from it all normal tissue as far as possible, put up sections in tubes containing 0.85 per cent NaCl. We inoculated each of these tubes with pure cultures of proteolytic

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microorganisms. We found that *B. histolyticus* in pure culture grew rapidly and that we had left in our tubes after four to six days incubation nothing but the fats of the tumour tissue and the fibrous tissue stroma of the growth. The actual cancer cells themselves had been digested by the enzymes secreted by *B. histolyticus*. The fluid in the tube contained a large proportion of the active enzyme. We filtered this fluid through a Berkefeld candle and obtained a sterile filtrate which when placed on fresh sterile carcinoma tissue showed much more rapid lysis of the cancer cells than took place in control tubes undergoing sterile autolysis.

Here then we had a sterile fluid containing an active substance which would cause lysis of the carcinoma cells. Could it be possible that we had found an antibody or active substance specific for the cells which had stimulated its production by the living *B. histolyticus*? If so, could it be used in the body without harmful effects and, finally, would it remain active in the blood stream or be neutralized by other body fluids?

In order to answer such questions, at least partially, some mouse experiments were undertaken with what appeared to be startling results. The "ensol" solution in this case was made from the mouse carcinoma tissue. Biopsies on these animal tumours before and after treatment by intramuscular injections of ensol showed the tumour cells in various degrees of destruction. The nuclei in many cells were powdered and the cytoplasm showed vacuolation, with increased fibrous tissue formation. Not being familiar with this type of investigation from the cytological point of view, I decided to place this work in more experienced hands. It has been referred to Dr. Murray, Director of the Imperial Cancer Research Institute, London, England.

During the progress of the animal experiments several cases of carcinoma were under my care with eye conditions. They had been pronounced incurable and sent home to die, after all forms of recognized modern treatment had been applied. These were given human carcinoma ensol intramuscularly. There was no inflammatory or other systemic reaction. These cases are reported in part two of this paper and are mentioned in the order in which they were taken on. The immediate effects were most remarkable and quite unlike anything previously observed. To verify and confirm these results

I naturally sought other cases which could only be secured by announcing the discovery to my colleagues and soliciting their cooperation and assistance. This has been most generously rendered. As one would expect, the type of cases which we felt justified in treating were only those considered hopeless from the point of view of all recognized forms of treatment. In spite of this severe test the treatment has produced results which, we feel, confirm our earlier observations.

PART II. CLINICAL

Cancer Research carried on from the initial point of view as a search for the cause of the disease, or rather this group of diseases, seems, on the surface, to be a logical point of attack. Usually, if we know the cause we are in a favourable position for treatment.

In the August number of the *Canadian Medical Association Journal* of this year (p. 125) there appeared an article by Dr. James Ewing, Director of the Memorial Hospital of New York City, whose views on the cancer problem are widely accepted. Dr. Ewing concludes his article with the following sentence: "The secret of malignancy seems still to remain enshrouded in the obscurities of intracellular life, where it will probably long remain".

Let us think of the malignant cell as a biological unicellular unit and forget for the moment its various morphological characteristics. When the first malignant cell is formed in the body it must be looked upon at once as a living unit. It possesses life, and, along with this attribute, the urge to reproduce. In order that life may continue and reproduction take place its metabolic processes must be maintained. It is undoubtedly placed in favourable soil, and, much to the detriment of humanity, lives its prolific existence, finally exterminating its host. If we consider these factors of malignancy, we must concede that this abnormal body cell, no matter where it came from or of what chemical composition it is, can be looked upon as a parasitic microorganism. The only difference is in the cell's chemical composition.

With this established fact before us the problem of controlling malignancy may logically be approached in much the same way as some of the known successful methods of treating infectious diseases. The most successful of all attempts to control infectious diseases has been

the use of antidiphtheritic horse-serum. In this particular case we have been fortunate in finding a source of production of an antibody whose actual chemical composition is unknown.

The problem of cancer control then crystallizes itself into but two questions. First, where can we find a source of specific antibody against these proliferating abnormal body cells? Secondly, if we do, can it be used in the human body without harmful effects? When these two paramount problems have been satisfactorily solved most of us will agree that we have taken a very decisive step toward the control of this scourge.

PRODUCTION OF THE "ENSOL" SOLUTION

About 10 grm. of malignant tissue are removed at operation under sterile conditions, kept sterile, and dissected free from all normal tissue in the laboratory. The material is then placed in a large test tube containing 1 grm. of tissue to 10 c.c. of normal saline solution. The tube is then inoculated with pure culture of *B. histolyticus* and incubated at 37.5° C. under anaerobic conditions for from four to six days, or until the fluid contents of the tube have settled out. When this has occurred the contents of the tube are centrifuged and the supernatant fluid filtered through a Berkefeld candle. Viability tests on this filtrate are done and if it is found sterile the enzyme solution is then ready to use.

A technical discussion of this fluid and its constituents is of biochemical interest only and should not rightly be included here. It is sufficient to say that this germ-free filtrate contains an active substance which seems to attack the tumour cells by which it was produced. Again it is only of biochemical and bacteriological interest to discuss the factors of lytic and synthetic processes which occur in these tubes. What is of vital interest is what happens in the cancer patient when such a solution is injected into the system. This will be best told by accurate case histories of a few of the earliest cases, taken in the order in which they presented themselves for treatment, as shown by their case number.

CASE 1

Mr. S.L., aged 49 years. Epidermoid carcinoma, proved by biopsy, originating in the left posterior nasopharynx and spreading to the frontal sinus, ethmoids, left antrum, anterior clinoid process and the frontal bone. Metastases had occurred in the cervical glands,

but these had been treated with radium and surgery. The primary lesion had disappeared following deep radiation, but had recurred. The condition was of 1½ years' duration. While under observation this patient had been treated for syphilis, also for duodenal ulcer, requiring a gastro-enterostomy in 1934.

The case was referred as hopeless on May 10th, 1935. The patient complained of intense pain on the left side of the face and temple; marked bulging of the left eye; ptosis and loss of vision in the left eye (p. l. only); deafness in the left ear; marked cachexia.

Treatment with "ensol" was commenced on May 10, 1935. The dose was empirically set at 2 c.c., which at first caused some general malaise. After ten days' treatment the bulging eyelid showed some skin wrinkles. Vision was 20/100. Hearing in the ear had improved from C. V. 2 ft. to C. V. 18 ft. The patient became slightly upset and treatment was discontinued for a week. It was recommenced on May 28th. By June 7th the single daily dose had been increased to 4.5 c.c. He again became upset. When this upset cleared the dosage was changed to 0.5 - 1 c.c., alternating daily. On July 8th he had a typical bilious attack and treatment was discontinued entirely.

On September 7th the proptosis had completely disappeared. Except for a paralysis of the left levator palpebri, the left eye was as normal as the right. The pain had eased completely.

CASE 2

Mrs. E.M., aged 45 years. The left ovary was removed on August 7, 1934, and found to contain papillomatous cysts which had involved the peritoneum. She was treated extensively with deep radiation following the operation.

On February 14, 1935, she was admitted to hospital complaining of severe crampy pelvic pain, constipation, bladder irritation, general cachexia and loss of weight.

Exploratory operation showed that the pelvis was matted with growth which had bound down the lower small intestine. Section of the growth was reported on as "secondary columnar cell carcinoma".

After discharge she was sent home to die. Morphina, to grs. iv daily, was required to ease the pain. The bowels were very constipated and required enemata.

Treatment with ensol was commenced May 14th as an experiment. An empirical dose of 2 c.c. was given every third day.

The patient steadily gained in weight, the bowels became normal, the appetite good. Opiates were reduced to heroin, gr. 1/12, which has since been discontinued entirely.

On September 7th the patient appears a normal healthy individual. She is doing her own housework, going on picnics and swimming. No opiates are used; weight gain, 32 lbs. since May. The bowels are normal, no laxatives being necessary.

CASE 3

Mr. M.J.V., aged 40 years. Obstructing carcinoma of pylorus. Duration of symptoms 9 months. Diagnosed by x-ray and at operation, when a posterior gastro-enterostomy was performed. No biopsy was made, but surgeon's report reads "Scirrhus growth involving 3½ inches of the pyloric antrum, with evidence of peritoneal spread. Glands along lesser curvature extending down to cœliac axis. Liver appeared normal". The operation was on May 31, 1935.

The patient was referred on June 14th for treatment with ensol. He had no appetite, and cachexia was very marked. There was no pain. An x-ray plate, July 2, 1935, made for record, showed the stoma functioning well. Treatment continued until July 14th when the patient was allowed to go to Montreal on business. He returned on July 30th. At this date (September 7th) he is being carried on a small biweekly dose. His weight gain from June 14th is 18½ lbs. His colour is

clear and fresh. Appetite is good. X-ray report of the examination on July 2nd shows the stoma to be working well. The pylorus could not be filled. X-ray examination, August 10, 1935; stoma working well. The pylorus at the screening was filled in part; the stomach was also emptying through the pylorus. X-ray examination, September 7, 1935; stomach shadow was larger in area than at last examination; not emptying through pylorus. The stoma was functioning well.

CASE 4

Mr. R.H., aged 60 years. Epithelioma, proved by biopsy, of the inside of the right cheek, with secondary masses in the cheek and neck. The growth began as a small ulcer in June, 1932. Extensive treatment with radium and deep radiation was given.

He was referred as hopeless on July 2, 1935. On examination there was an ulcerated area on the buccal surface of the cheek and lower alveolar margin down to the bare bone. The ulcer had a raised, rolled beaded edge. The skin of the cheek was puckered in an area corresponding to the location of the ulcer. A hard indurated mass extended up the cheek to within 1 inch of the line of the external auditory canal and cantlus, and down the neck to a point half way between the angle of the jaw and the clavicle, and spreading up behind the ear. The swelling was localized to the right side of the mid-line.

The patient complained of post-auricular pain and deafness in the right ear; intense pain in the buccal ulcer; inability to open his mouth because of the mass. His general condition was poor. He was using codeine freely for pain.

Treatment with ensol was commenced on July 3rd. The first change noticed was cessation of the post-auricular pain and improved hearing after the second treatment. Softening of the growth first began in the upper margin and then in the post-auricular mass. An œdema occurred in the right eyelid and on the right half of the lower lip. By July 30th the whole growth had softened. The upper margin had receded so that the upper alveolar border could be felt. The ulcer edges were sloping. The œdema was still present in the two areas.

Treatment was discontinued on July 30th. On August 3rd a small fistula opened on the site of the original lesion and his pain completely disappeared. For over a week he improved and the growth became almost fluid. Large veins began to appear at the posterior margin.

About August 12th it became apparent that secondary infection was present in the mouth. On August 21st he had recurrent severe hæmorrhages from the external maxillary artery and died.

CASE 5

Miss M.H., aged 67 years. Skin recurrence of scirrhous carcinoma in the incision after operation on the left breast, 1933. Two nodules and a large mass appeared in the autumn of 1934. These were treated by radium in February, 1935. The nodules disappeared. The large mass decreased in size but began to grow again. Also one of the small nodules recurred.

Referred on July 2nd. Biopsy for proof and a small portion removed for autogenous ensol. At this date the main mass was deep red in colour, lobulated, with some undercut edges. Measurements: 6.0 cm. in length, 4.8 cm. in width, and 1.5 cm. at the highest point from the skin surface. It was fixed to the chest wall, of very hard consistency and bled easily.

Treatment with ensol was commenced on July 4th and continued until August 2nd, when treatment was discontinued in order to observe any further changes which might occur.

On September 7th the main mass measures 4.4 cm. in length, 3.9 cm. in width, and its height is 1.1 cm. above the chest wall. The edges are sloping and the

epithelium has grown in over all the edges, preceded by well-defined blood vessels. The growth is now distinctly lobulated and each lobule is soft on palpation. The small nodule has diminished to approximately one-third of the original size. The growth is painless and can be moved easily over the chest wall.

CASE 6

Mrs. C.C., aged 70 years. Mixed cell sarcoma, proved by biopsy, over the right scapula extending into the axilla, with a second mass along the 9th, 10th, and 11th ribs in the posterior axillary fold.

The growth began in 1931. Extensive surgery, radium, and x-ray therapy have been used without lasting effect.

Referred on July 14th, when a biopsy was done for tissue to be used for producing autogenous ensol.

The main mass was fungating and was fixed tightly to the scapula. The second mass was ill defined, subcutaneous and hard as a rib. Pain was continuous over the mass, in the axilla and in the forearm. The patient was using opiates freely.

Treatment with ensol was commenced on July 15th. After ten days it was possible to ease the pain in all but the forearm. On July 29th the skin around the growth was irritated by a disinfecting solution and for a week no change in the pain was noticed. From August 5th to date the pain has been completely controlled. This is the first time since February, 1935, that the patient has been completely free from pain. She is taking no opiates at all.

Both growths show a marked change. The upper mass is puffy at the edges and can be moved slightly over the scapula. The lower mass has centred into a well-defined lump which is quite doughy. It also can be moved over the rib.

CASE 7

Mrs. A.R., aged 52 years. Carcinoma of the cervix with extension laterally; masses being palpable through the abdominal wall in the right iliac fossa and in the right lumbar region. The primary lesion was diagnosed one and a half years ago. Referred for treatment on July 15, 1935.

The patient was very cachectic. She suffered intense spasmodic pain. The masses in the abdomen were nodular, irregular in outline and extremely tender. There was extensive ulceration of posterior vaginal wall, but no fistula. Narcotics were being used freely for the relief of pain.

Treatment with ensol commenced on July 16, 1935. No improvement was noted up to July 27th and intravenous ensol was given. After four doses she felt slightly easier, but her general condition was so bad that treatment was discontinued. After ten days, during which she became no worse, the treatment was begun again and she began to respond. At present the pain can be fairly well controlled. The abdominal masses are still tender, but their outline is less nodular and the growths appear to be of softer consistency.

CASE 8

Mr. W.C., aged 80 years. Carcinoma of the pylorus of the stomach—diagnosed by clinical finding and x-ray, which showed a 24 hour retention. No exploratory operation could be done because of patient's poor general condition.

Referred for treatment on July 18th. The patient was vomiting three to four times daily; he had no appetite; was very weak; and had a constant dull sense of weight in the epigastrium.

Treatment with ensol was commenced July 20th. After one week it was noticed that the patient was not vomiting and was eating small but normal meals. As his memory was vague, no optimum dose could be ascertained and after ten days' cumulative dosage he had a gastric upset. Treatment was discontinued for three

days. He has improved slightly since, but has periodic upsets about once a week.

CASE 9

Mrs. E.G., aged 39 years. An ulcerating scirrhous carcinoma of the right breast, proved by biopsy, serpiginous in outline, 6 by 5 inches at the longest and widest points and extending down so that the pectoral muscles were visible in the base. Five small outlying ulcers up to 1 inch in circumference. Secondary metastases in the bones and a pathological fracture of the left hip. The right arm was œdematous down to the finger tips. Duration of the ulcer, 8 months; of the original tumour, one year.

Referred for treatment on July 21, 1935.

Her general condition was poor, she appeared toxic and had pyrexia.

Treatment with ensol was commenced on July 21, 1935. The œdema in the arm showed the first change after the third dose. On July 28th the two larger secondary ulcers were dry and scaly. On July 30th the patient had an attack of acute gastritis, which was caused by overeating, as she had been feeling so much better. For three days, only liquids could be retained and the toxæmia increased. Treatment was discontinued. On August 4th she was improved but still toxic. On August 8th she died suddenly at breakfast. No autopsy could be obtained, but sections of the breast tissue were made.

CASE 10

Mrs. M., aged 61 years. Secondary carcinoma (proved at original operation) in both lungs, with osteoplastic and osteolytic changes in the upper lumbar vertebrae and suggestive changes in both hip bones and femurs. The original growth was in the left breast. Radical mastectomy in March, 1932, followed by routine deep radiation. She reported for treatment on July 21, 1935.

The patient was markedly breathless, even when at rest and had to be propped up in bed. On auscultation, there were marked changes in both lungs and fluid in both bases. This was later confirmed by x-ray. The heart was relatively normal. Her general condition was fair.

Treatment with ensol was commenced on July 22, 1935. By the end of the first week the breathing had improved, so that patient could be comfortable when at rest. Improvement continued slowly until July 31st, when, after treatment, she had a sensation in the left chest and coughed up some dark phlegm. From this point on improvement was marked. On August 8th she was allowed to leave hospital and receive treatment as an out-patient. Breathlessness is apparent now only on exertion. She is taking gentle exercise and her general condition is improving.

The following twenty cases are briefly summarized.

CASE 11

Mrs. L.W., aged 51 years. Carcinoma of the rectum; colostomy performed in 1931. She was fairly well until March, 1935, when a series of hæmorrhages occurred. Since then she has been going gradually down hill.

Treatment with ensol was commenced on July 22nd. After five weeks' treatment her general condition has definitely improved and the rectal pain has eased.

CASE 12

Mr. A.C., aged 57 years. A colloid carcinoma of ascending colon. An ileo-transverse colostomy was performed in June, 1935. This relieved the pain and obstructive symptoms but his general condition did not improve.

Treatment with ensol was commenced on July 24th. After six weeks' treatment the man has gained 18 lbs. and has returned to part-time work.

CASE 13

Mrs. A.H., aged 51 years. A malignant ulcer on the chest wall. The history began seven years ago. Both breasts have been removed. A recurrence in November, 1934, ulcerated and is now 8½ by 5 inches at the widest points, with a typical rolled, raised, beaded edge. A mass of glands in the right supraclavicular region had involved the plexus, causing constant pain in the right arm.

Treatment was commenced on July 26th. On September 7th the ulcer edges are flattened, the sides sloping and the base shows fresh granulation tissue. The arm pain is slightly relieved.

CASE 14

Miss G.B., aged 56 years. Secondary metastases from an original scirrhous growth in the right breast, in the head of the 8th rib and in the body of the 7th dorsal vertebra. The spine was markedly angulated and she complained of constant pain, but there was no paralysis.

Treatment with ensol was commenced on July 28th. The pain was controlled by August 7th. On August 29th the patient went home for a rest. The pain has not returned to date.

CASE 15

Mr. F.C., aged 63 years. A mass in the bowel at the pelvi-rectal junction, adherent to the right side of the sacrum. Main complaints, pain over the sacrum and small thready stools. Cachexia is marked.

The case was diagnosed on July 25, 1935 and treatment with ensol commenced on July 27th. The treatment continued to September 4th. The pain over the sacrum has lessened. The stools are larger and his colour is good. Appetite is fair and the weight has remained stationary.

CASE 16

Mr. F.D., aged 43 years. A periosteal sarcoma of the right femur. Diagnosed and treated with deep therapy in May, 1935.

Treatment with ensol was commenced on July 27th. At that date the largest circumference was 23¼ inches. After fourteen days' treatment the area was much less tense, but from that time on, no appreciable change has occurred. The latest measurement is 23 inches.

CASE 17

Mrs. D., aged 58 years. An original carcinoma of the cervix which had spread to the trigone of the bladder. Radiation had apparently checked the spread, but the patient was left with a vesico-vaginal fistula and some rectal ulceration. There was three hour control of urine in the vagina.

Treatment with ensol was commenced on July 25th and continued to August 11th. No change was noticed in the patient's condition at the time of her discharge.

CASE 18

Mr. T.W., aged 57 years. Primary carcinoma of the upper left lung. He complained of extreme weakness and dyspnoea and had lost over 100 lbs. in weight.

Treatment with ensol was commenced July 26th and continued to September 4th, when the patient was rested. He now has no effort in breathing; he is driving his own car and taking moderate exercise; his appetite is good and his weight is increasing.

CASE 19

Mr. N.Z., aged 35 years. Scirrhus carcinoma of the pylorus. A posterior gastro-enterostomy was performed in January, 1935. The patient improved until July 1st, when vomiting returned. When he reported on July 20th he was completely obstructed, but his general condition was too poor to permit of surgical intervention. After six days' intravenous treatment to combat dehydration, he was given ensol treatment until August 5th, when his general condition had improved enough to permit a laparotomy. The whole stomach, including the stoma, was involved by the growth. The patient died on August 13th. Portions of the growth obtained for microscopic study.

CASE 20

Mr. J.B., aged 76 years. Clinical evidence of carcinoma of the stomach. X-ray examination showed a filling defect at the pylorus and 75 per cent retention of barium. He complained of constant dull pain in the epigastrium, vomiting, anorexia and increasing weakness.

Treatment with ensol was commenced on July 29th.

On September 7th he was moderately improved. No vomiting; the pain had subsided; his appetite was fair, but the weakness had not improved.

CASE 21

Mr. H.C., aged 65 years. Recurrence from carcinoma of prostate. Prostatectomy was performed in 1934. Recurrences in the site and in the abdominal incision. His general condition was very poor. Blood urea, 113 mg. The prostatic urethra was blocked by growth and a retention catheter was necessary.

Treatment with ensol was commenced on July 29th and continued until September 6th. His general condition is only fair. The catheter was discarded on August 28th. Pain over the bladder is still present.

CASE 22

Mr. B.F., aged 57 years. An adeno-carcinoma at the sigmoid. A colostomy was performed in April, 1935. The patient improved after operation but had had difficulty in keeping his bowels open and reported several attacks of jaundice.

Treatment with ensol was commenced on July 28th. On August 21st he reported a considerable amount of reddish discharge per rectum and two days later a large amount of "fleshy" material coming away. This continued for one week.

On September 7th, he was fairly comfortable. The discharge had ceased, but he complained of some constant pain in the rectum.

CASE 23

Mr. G.F., aged 62 years. A lympho-sarcoma in the right groin and secondaries in the left inguinal region.

Treatment with ensol was commenced on July 26th. In spite of comparatively heavy doses, both intramuscularly and intravenously, there has been no decrease in the size of the growth.

CASE 24

Mrs. C.S., aged 46 years. Carcinoma of the cervix with extension to the bladder and rectum. Her main complaints were pain associated with the bladder and pain in the back and hips.

Treatment with ensol was commenced on July 28th. By September 1st the pain in the back and hips had been relieved, but the bladder pain was unchanged.

CASE 25

Mrs. F.L., aged 31 years. On investigation, she proved to have a simple chronic mastitis.

CASE 26

Mrs. R.S., aged 42 years. Bone metastases from a scirrhus carcinoma of the left breast. The pelvic girdle and lower lumbar vertebrae were involved and there was a pathological fracture in the left hip.

Treatment with ensol was commenced on July 29th. By August 14th pain was well controlled and extension was applied to straighten the left leg. On August 19th x-ray examination showed that there was no evidence of further bone involvement.

CASE 27

Mrs. G.B., aged 40 years. Secondary metastases in both lungs from an original scirrhus carcinoma of the right breast. In June she had a collapse of the right lung and since that date complained of cough, chest pain, dyspnoea and weakness.

Treatment with ensol was commenced on July 31st. By August 7th the breathing had improved slightly. By September 1st she was able to take moderate exercise without dyspnoea. The pain in the chest was gone and her general condition was moderately improved.

CASE 28

Mr. S.C., aged 57 years. A post-cricoid carcinoma of the oesophagus. When he reported for treatment he was only able to swallow liquids and his weight was 116 lbs.

Treatment with ensol was commenced on July 31st. His swallowing began to improve after the first week and in two weeks had definitely improved. He had gained 6 lbs. in weight. By September 1st, he was able to swallow solids when chewed carefully.

CASE 29

Mrs. L.G., aged 57 years. Carcinoma of the cervix, extension to the bladder and rectum and metastases in the pelvic girdle. She complained of severe pelvic and bladder pain, with pains in the back and hips. Her general condition was poor.

Treatment with ensol was commenced on July 31st. She has shown some improvement in her general condition and at times improvement in the pelvic and back pains, but on the whole has not responded to treatment.

CASE 30

Mr. A.M., aged 33 years. Secondary metastases of sarcoma, involving the lower four left lumbar nerve roots and the vertebrae. On admission the patient was suffering intense pain over these roots and down the left leg. Large doses of morphia were required and on occasions chloroform inhalations and nembital, intravenously, were necessary to control the pain.

Treatment was commenced on July 30th but had no effect. The patient died on September 1st.

SUMMARY

Because of the very nature of this preliminary report it is impossible to discuss our clinical findings on a thoroughly scientific basis.

The cases have been treated and studied purely from the clinical point of view. Detailed biochemical examinations of the body fluids are being undertaken. Cytological studies of the cancer cells, comparing biopsy specimens before and after treatment, are being made and will be subsequently reported.

The solution has been used both intramuscularly and intravenously without any ill effects. Since but very little inert protein is present it

produces no protein shock. We have experienced no allergic reactions. The solution as a rule gives a negative biuret reaction, but always a positive xanthoproteic test.

The dosage is essentially individual. When pain is the predominating symptom the reaction dose produces a distinct increase in pain, commencing from one and a half to three hours after the intramuscular injection and lasting up to 24 hours, followed by complete disappearance. When pain is not a feature of the case the reaction dose produces a "picking", or "pulling", sensation in the growth for the same period of time.

Most cases seem to respond after ten to fourteen days' treatment. In the group of cases at present under observation the effects are consistently good. There has been a marked gain in weight, with disappearance of severe cachexia. Visible growths have shown arrest, with softening and absorption. In the cases where pain has been a prominent symptom the sedatives have been cut in half and in many cases discontinued.

In the internal growths a similar process is apparently going on, since a great deal of clinical improvement has been noted.

It is altogether too soon to assess the ultimate value of the method. Weeks to months must

elapse before we can determine if the cancer masses continue to show shrinkage and absorption till their complete disappearance. Clinical evidence so far leads us to think that such disappearance may occur.

Steps have been taken to prevent the exploitation of the public and the profession by unauthorized interests. Consequently, no supply of this solution will be made available until its value has been definitely proved.

The manufacture and therapeutic use of this enzyme solution is comparatively simple, when thoroughly understood. We can be responsible for no results obtained by investigators who have not had special training.

Much of the credit of carrying this work into the clinical field has been due to the energetic efforts of my esteemed associates, Dr. C. D. T. Mundell; Dr. W. A. Jones; Dr. Charles Elliott; Dr. John Tweddell; Dr. John Delahaye; Dr. Fred Bonnell; Dr. I. Sutton and Dr. W. A. Campbell.

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For long and tedious laboratory assistance throughout the course of this investigation, I feel that a great deal of its success is due to the devoted service rendered by my technician, Mr. Bertram Holsgrove.

There are many others, too numerous to mention, who have given kind cooperation and assistance when it was most needed. To all these I extend my most sincere appreciation.

PLEURAL SHOCK*

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THE term "pleural shock" has come to include a variety of symptoms, most of which are both sudden and alarming, occurring in connection with operations on the chest. A few fatalities are recorded. As early as 1850, Chabaud⁵ referred to "nervous accidents" occurring when the pleura or lung or both were operated upon. Certain writers seeking a more descriptive term characterized the symptoms as those of "pleural syncope", or "pleural eclampsia", or "pleural epilepsy", while Italian writers still speak of "epileptiform and apoplectiform seizures of pulmonary origin". It would seem that those who made use of these

terms regarded a pleural injury or stimulus as the origin of the subsequent phenomena described in such cases. The use of the term "pleural shock" may be regarded as inapplicable in view of the most up-to-date teaching in this connection. Based upon experiments and clinical observations "air embolism" is held to be more descriptive, and many regard this as the term of choice.

CASE 1

The patient, a girl of 10½ years, was thought to have pus in the pleura or lung following an attack of lobar pneumonia on the right side, from which she was tardily recovering. Exploratory thoracentesis was done on the morning of February 23, 1907. The first puncture with a medium-sized exploratory needle was made in the post-axillary line between the fourth and fifth ribs, the needle being directed upward toward the region affected, as indicated by physical signs and

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