survival rate in the node-involved cases is reduced to 48%, but here again only four patients died of cancer, and here also there were no local recurrences. Many of these operations were extremely difficult, and this is reflected in the high operative mortality. However, of the nine patients with deep pelvic node involvement two survived and are well, one at 10½ years and one at 6½ years. This may suggest that the removal of the deep nodes is not an important step in the operation.

At the time these cases were treated we had little knowledge about the incidence and pattern of deep node involvement and no way of knowing if this step in the operation was vital. As a result of a far larger series we now know that the anatomical spread of cancer of the vulva in the lymphatics is fairly regular, and that involvement of the deep nodes is seen in only about 15% of all cases. As a result of this and the development by Dr. Ruth Dearing (1952) of her rapid node-smear technique we now modify this part of the operation by exposing the external iliac nodes and removing the lowest medial node (the node of Cloquet) and the lowest lateral external iliac node. These are smeared and stained (this takes no longer than seven minutes) whilst the superficial nodes are removed. If the deep nodes are negative the inguinal ligament is not divided and no further dissection of the iliac region is carried out. If they are involved then we proceed as we did with all the cases in this series. The greatest advance of this technique is undoubtedly the wide excision of the vulval area, because we have had no local recurrences in this series up to five years.

Discussion

The results really speak for themselves. The operation is more complicated than difficult and does require constant practice. The nursing is very complex, and the technique requires a fair amount of ancillary help and experience, especially in cytology since the introduction of the modification described above. The experiment—it has long since ceased to be one so far as I am concerned—may be said to have paid a handsome dividend, and the results are more than gratifying. It would seem well within the scope of any large centre which is prepared to concentrate its material and study the pathological and anatomical features of this disease.

Summary

Owing to the comparative rarity of carcinoma of the vulva few people see sufficient cases to become very familiar with the problems concerned in its treatment.

After research into the causes of failure to cure the disease an experiment was tried in which all the cases in a wide area were referred to one surgeon, who applied a more extensive operation based on the lessons of the preliminary research.

The results of the treatment of 79 cases seen before March 31, 1949, are reviewed.

One patient refused treatment and 13 were considered unfit. The operability rate was 83%. The absolute five-year survival rate was 61% and the relative five-year survival rate—that is, the survival of all cases operated on—was 74%. When the lymph nodes were involved the five-year survival rate was 48% and when they were not involved it was 86%.

These figures are a great improvement on other published figures and it is believed that they are well within the reach of any centre which decides to pool its cases into the hands of a special team which will carry out a radical approach to the disease.

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TREATMENT OF GOUT WITH H.P.C.

BY

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One feature of the revival of interest in the rheumatic diseases following the introduction of cortisone and A.C.T.H. has been the screening of a great variety of substances for evidence of a cortisone-like action on the collagen group of diseases. Among the therapeutic agents, old and new, which have been examined is a cinchoninic acid derivative—namely, 3-hydroxy-2-phenylcinchoninic acid (H.P.C.). In the U.S.A. Blanchard *et al.* (1950) reported promising results with H.P.C. in cases of acute rheumatic fever, chronic rheumatoid arthritis, and disseminated lupus erythematosus. In this country Rennie *et al.* (1951) found the drug of value in a small group of cases of rheumatic fever and scleroderma. This preliminary report suggested that a further investigation was justifiable, and in the summer of 1951 a small supply of H.P.C. was obtained for trial and was used in a few early cases of rheumatoid arthritis. The results were not dramatic, and it was felt that H.P.C., being a derivative of cinchophen, might be of greater value in the treatment of gout. Accordingly, the small supply was hoarded until suitable cases were seen, but, as often happens, no patient with typical gout attended for many months; then several cropped up within a few weeks.

To date, 12 cases have been treated with H.P.C., a bitter yellow powder compressed into white-coated tablets containing 250 mg. The initial dosage recommended by Blanchard *et al.* (1950) was 20 mg. per kg. of body weight daily, in divided doses, by mouth, with an equal amount of sodium bicarbonate to prevent gastric upset. The amounts used in the trial, and the results, are described in the case abstracts.

Case 1

A farm worker aged 58 had his first attack of gouty arthritis in 1947, when his left hand, feet, and ankles were affected; subsequent acute attacks led to progressive involvement of the knees, elbows, and shoulders. He was admitted to Harrogate Royal Bath Hospital for a course of physical treatment in 1950 and had colchicine therapy during several acute episodes, with moderate benefit. At home he experienced general deterioration and was readmitted in January, 1952, when he joined a test group of cases which were given A.C.T.H. by intravenous infusion. The first infusion contained 10 mg. of A.C.T.H., and his condition improved during the next seven days; the second infusion contained 20 mg. of A.C.T.H., and his arthritis was appreciably relieved for 24 hours. The following day he relapsed to his original state, and the next day he developed a typical acute attack of gout with extremely painful tender joints and constitutional upset with pyrexia. At this stage H.P.C. was given in daily doses of 2 g., and he improved rapidly, being able to walk within 24 hours; after six days he had made such good progress that the dose was halved, and he continued to do well on 1 g. daily for another eight days. At this point he developed a recurrence of pain in his knees when walking, and began to complain of some nausea and looseness of the bowels. These symptoms became more severe next day, but treatment had to be interrupted in any event, as the available supplies of H.P.C. had been used.

During the next 12 days he deteriorated very much, until a fresh supply of H.P.C. enabled treatment to be resumed.

Improvement was almost immediate, and he continued to do well for three weeks, after which recurrence of the mild diarrhoea with pruritus and the appearance of an itching facial erythema caused treatment to be interrupted.

A third course was begun, but this led to a recurrence of a more widespread rash, and treatment was again stopped. His skin condition cleared up quickly, but his gout returned in a moderately severe form and he was most anxious to continue with H.P.C., in spite of the risk of skin complications. In an attempt to uncover any psychological bias, he was given inert tablets similar in appearance to H.P.C. for a few days, but at the end of this time he was having an attack of acute gout with a plasma uric acid level of 11.5 mg. per 100 ml. Although this setback weakened his faith in H.P.C., he responded at once to genuine treatment, and after a three-weeks course he was fit enough to go home, very much improved in general.

Subsequent Progress.—During the next six months he had great difficulty in obtaining supplies of H.P.C., and his clinical condition varied accordingly. He was recommended to take 0.75 g. daily as a maintenance dose for periods of three or four weeks, with intervals as his clinical condition suggested; in fact, some intervals were longer, and he then deteriorated rapidly, but he always derived immediate benefit when treatment was resumed.

Over the complete trial period of nine months he had at least 210 g. of the drug without serious toxic reaction, and laboratory tests showed no disturbance of liver function, no progressive rise in his blood urea level, and a recurrent sharp depression of his plasma uric acid curve after the initiation or resumption of medication. He regarded the occasional diarrhoea and rash as trivialities compared with the great benefit which the drug produced, and he was convinced that for him it was superior to colchicine.

Case 2

A labourer aged 40 had his first attack of gout in 1940, when his left big toe became painful and swollen; later the left ankle was affected. Since then he has had recurrent bouts in the feet, ankles, and right shoulder. Previous treatment with colchicine had relieved his acute symptoms in a few days.

He was admitted to the Royal Bath Hospital with less acute but more constant pain in the feet, ankles, and right shoulder. There was no swelling, redness, or warmth in the affected joints, and movement was restricted only by pain. During the first month he improved steadily with physical treatment, but biochemical tests suggested that he might be heading for a flare-up of the classical type. Within the next few days this did in fact occur; the right ankle became acutely painful, swollen, and tender. H.P.C. therapy was begun at once with 1.5 g. daily; dramatic improvement occurred in the first 12 hours, and continued steadily during the next five days, at the end of which he was completely free from pain when at rest but still had some pain on movement of the affected joint. At this time he complained of an itching psoriasiform lesion of the neck and shoulders; he stated that this rash always broke out during an acute attack of gout. After seven more days' treatment he felt very fit in general and was entirely free from pain, both at rest and on movement. The daily dose was then reduced to 0.75 g. for a further five days, by which time he was perfectly fit and up and about all day. He had never before made such a rapid recovery. He felt that H.P.C. was much superior to colchicine.

Case 3

A male clerk aged 23 developed acute arthritis at the age of 17 and was treated for rheumatoid arthritis with gold injections, which had no effect. In 1949 he was admitted to the Royal Bath Hospital, where clinical and laboratory investigations established the diagnosis of "chronic tophaceous gout" with chronic nephritis and hypogonadism. He benefited to some extent from treatment and was able to

go home, where he kept fairly well during the next two years. At the end of 1951 his condition deteriorated rapidly and he was readmitted for a course of physical treatment.

At this stage it was thought that he might benefit from H.P.C., and 2 g. was given daily. After two days he developed an itching erythema on the neck and forearms, which had been exposed to bright sunlight, but this cleared spontaneously within an hour. This complication recurred the next day, but the reaction to sunlight was noticed and thereafter he avoided direct sunshine. After eight days' medication, during which time the plasma uric acid concentration had fallen from 9.6 to 6.8 mg. per 100 ml., the dose of H.P.C. was reduced to 1 g. daily. Treatment was interrupted on the eleventh day because of a recurrence of itching of the skin. During this first phase his previous general improvement had continued, but when H.P.C. was withheld he began to deteriorate steadily. After a 10-day interval his plasma uric acid level had risen to 8.5 mg., so H.P.C., 2 g. daily, was resumed. After only three days, during which the blood urea increased from 77 to 110 mg. per 100 ml., the drug was withdrawn because of the patient's known impairment of renal function and the reported tendency of H.P.C. to produce azotaemia in some cases.

Case 4

A gardener aged 74 had suffered from recurrent attacks of gouty arthritis for 14 years but had been able to keep working as a gardener for most of the time.

He was admitted to the Royal Bath Hospital on March 6, 1952, with subacute arthritis affecting the hands and feet, which had multiple tophaceous deposits, and he seemed a suitable case for trial. H.P.C., 1.5 g. daily, was given and improvement began almost at once. After 12 days he developed some looseness of the bowels, associated with pruritus, and the drug was withheld for one day, being then resumed with a dosage of 0.75 g. During the next fortnight his condition deteriorated slightly, which suggested that he might not be getting quite enough of the drug. However, a return of the mild diarrhoea led to the treatment being interrupted for 10 days. He then had a general relapse, with a return of joint pain and tenderness, and H.P.C. therapy was resumed. Unfortunately, only two doses produced a recurrence of his diarrhoea, and the treatment was then stopped finally.

During this period the patient had a total of 30 g. of H.P.C. and his plasma uric acid levels ranged from 9.9 to 4.2 mg. The drug produced much improvement in his arthritic symptoms, but his alimentary tract was too intolerant of it to allow treatment to continue any longer.

Case 5

A farmer now aged 56 had sudden onset of pain, swelling, and redness of the metatarso-phalangeal joint of the left big toe in 1941. The condition settled down, but he had occasional recurrences during the next seven years. In 1948 he had an acute polyarthritis affecting the elbows, wrists, hands, and feet; this was improved by a course of physical treatment. Thereafter transient attacks of pain occurred in the hands until January, 1952, when he had another attack of acute polyarthritis, in which the shoulders, hands, knees, and right foot were involved.

This acute phase was still present when he was admitted to the Royal Bath Hospital, and in view of his history, the presence of a large tophus, and the biochemical findings a course of H.P.C. was started. He was given 1.5 g. daily for nine days, the dose then being halved because of a slight looseness of the bowels; this cleared up in three days and the larger dose was resumed. However, after two days' treatment a moderately severe diarrhoea with vague abdominal pain recurred, and, although these responded to symptomatic treatment, the dose of H.P.C. was reduced to 1 g. daily, on which he continued for another 25 days. Clinically, he made a steady improvement, and at the end

of the course of treatment he was up and about all day, with no joint pain or tenderness, and felt well enough to return to his farm.

Subsequent Progress.—During his first few days at home he developed a marked vesicular rash on his face, following exposure to bright sunshine, which would suggest some cumulative effect of H.P.C. administration. The rash cleared up spontaneously and his improvement was maintained during the next three months.

Case 6

A publican aged 58, who reported a family history of gout, had himself suffered from the condition for 11 years, with recurrent acute attacks about four times a year which responded favourably to colchicine. He was admitted to the Royal Bath Hospital at the beginning of an acute attack of gout in the left ankle, associated with a more chronic arthritis affecting the knees and the elbow, wrist, and fingers of the right arm. H.P.C. treatment was started at once with 1.5 g. daily. This brought a dramatic improvement within 24 hours, with great diminution of pain, tenderness, and swelling of the ankle, and less marked, but none the less definite, improvement in the condition of the other affected joints. After 10 days he developed an itching erythema of the face and hands, following exposure to bright sunlight for about half an hour. As he still had some pain in the feet when walking, it was thought desirable to continue with H.P.C., but the dose was reduced to 0.75 g. daily; however, this was not quite sufficient to suppress his symptoms, because he developed slight pain and tenderness of the affected ankle within a week. The dose was then increased to 1.5 g. daily, on which he improved and continued to make excellent progress during the next month. By this time his condition was so good that the dose was reduced to 1 g. daily, on which he continued to do well.

He was discharged home a week later, and continued to take 1 g. daily for the next two months. During this time he had occasional recurrences of the facial erythema on exposure to bright sunlight when gardening, but he himself decided to do his gardening when the sunshine was less intense. He had no difficulty with the rash until the third month, which was in midsummer, when he complained of some increased tingling of the skin of the face, irritated by shaving; on account of this the dose was reduced to 0.5 g., which he took at night. He continued to keep very well during the next two months, but the skin irritation then became rather troublesome and it was felt wise to stop the drug. He had had six months' continuous medication, with a total of 150 g. of H.P.C. During that time there was no recurrence of gout or of the more chronic arthritic symptoms, and he declared spontaneously that he had enjoyed better health than for many years; he also thought that H.P.C. relieved his gout much more quickly and effectively than colchicine had done.

Case 7

A commercial traveller aged 43, who had been a heavy beer-drinker for many years, developed his first attack of gout in 1943 and had recurrences of varying severity in the succeeding years. In 1949 he had an unusually severe attack, and was admitted to a hospital where colchicine treatment was given with good effect. He was prescribed a "rigid diet" and advised to give up beer-drinking. On this regime he had only minor recurrences for three years, but intercurrently suffered a coronary occlusion with posterior cardiac infarction, which left him subject to anginal attacks on minimal exertion.

In 1952 he had another acute attack of gout, with general constitutional upset and fever, and involvement of the left foot and ankle. After a week's home treatment, which brought only slight improvement, he was admitted to hospital, where 1.5 g. of H.P.C. was given daily. Improvement was immediate: within 48 hours he had no pain when at

rest, and in a week he could walk freely within the limits of his cardiac disability. After another 10 days the dose was reduced to 1 g. daily, and his improvement continued; however, he developed a facial rash which became so irritating that the drug was stopped after a month. He remained well for about a fortnight, during which time his skin cleared; but thereafter he began to feel rather depressed and thought that "the gout was starting up again."

A typical flare-up in the left foot followed, and 1.5 g. of H.P.C. was given daily with dramatic improvement; three days later the dose was reduced to 1 g. daily, and was kept at that level for a month, with no further complication. The daily dose was then reduced to 0.5 g., and the patient went on holiday for a month in high spirits. At the end of this period he was seen as an out-patient, and reported favourably, but 14 days later he had a mild recurrence in spite of the continued administration of H.P.C. It was then presumed that the maintenance dose was too low, but in view of our experience with other cases it was felt desirable to prescribe higher doses only on the occurrence of an acute attack or when premonitory symptoms appeared.

Case 8

This patient was a company director aged 67. There was a strong history of gout on both sides of the family: his mother had severe gout and so had his father's brother; in addition, a deceased brother of the patient had also suffered from the disorder. The patient had a 30-years history of the disease, with attacks of varying frequency and increasing severity.

He was admitted to hospital with acute arthritis of the left elbow and wrist, and was ill and feverish. H.P.C. therapy was begun with 2 g., and improvement occurred in 12 hours. The dose was reduced to 1.5 g. daily for the next seven days, during which time his improvement was remarkable in comparison with his previous experience, and then it was again reduced to 1 g. daily. After a few days he felt so well that he was allowed to go home to see to some urgent matters of business; he reported as an out-patient a week later, when he stated that his progress had been excellent. On this occasion, however, a slight facial erythema was observed, although he had not noticed it. He was anxious to continue on treatment, as he found that he was able to carry on his business without impediment, and the daily dose was not altered. When seen again in 10 days he had remained very well, but the facial rash had become vesicular and irritating, so continuous treatment was stopped.

During the next three months he was seen regularly, and remained well. He reported that he had had several "warnings" of impending gouty attacks, but he had found that two to four days of intensive treatment with H.P.C., in doses of 1.5 g. daily, prevented these from developing into major episodes. He was able to continue an active business life, and felt that he had an effective remedy for his gout, which previously had incapacitated him for weeks at a time.

This patient had a mild degree of impairment of renal function, and his blood urea level rose during the first week of treatment from 58 to 72 mg. per 100 ml.; at the end of the second week, when the dose of H.P.C. was lower, the reading was 46 mg. per 100 ml.; in the succeeding months, when he had no continuous therapy, his blood urea levels were 52 and 60 mg. per 100 ml.—probably his "normal" figures.

Case 9

A publican aged 51 had 20 years' history of typical gout, beginning in the great-toe joints; attacks occurred about once a year at first, gradually becoming more frequent and more severe, and extending to other joints. In the past five years the bouts had become much worse, lasted longer, and left chronic arthritic symptoms.

He was admitted to hospital with acute gouty arthritis of both feet, the right ankle, and both knees; H.P.C.

therapy was begun at once with 1.5 g. daily, which produced considerable improvement within 24 hours. After 48 hours he developed diarrhoea and the dosage was reduced to 0.75 g. daily, on which he continued to improve during the next fortnight. At this stage he had a slight irritation of the face after shaving, and the dose was reduced to 0.5 g. daily for another fortnight. He then developed a mild attack of gout—at a time when I was absent on holiday, so that no alteration in dosage was made. This was much less severe than his "usual attack," lasting only four days, compared with the previous average duration of 10 to 14 days. When I saw him again 14 days after the attack the skin lesion had become more serious, with vesiculation and pustulation. In view of his improved clinical condition H.P.C. treatment was stopped and he went home 10 days later, fully ambulant and completely free from pain. He had been treated previously with colchicine, and was convinced that H.P.C. was a more effective rapid remedy. Although he had a chronic renal lesion, his blood urea level did not exceed 28 mg. per 100 ml. at any time during treatment, and there was no evidence of hepatic dysfunction in spite of the fact that his bowel and skin were irritated early and severely by the drug.

Case 10

A business man aged 61 had his first attack of gout 12 years previously, when both great toes were affected. In the intervening period he had recurrences at varying intervals, and in the past two years his left knee and right wrist were involved, particularly after strenuous exercise in which these joints were in play. When first seen he had acute arthritis of the right wrist and was prescribed H.P.C. in daily doses of 1.5 g., which produced much improvement in two days. After another week he felt so well that he resumed active work in his garden, but this provoked some pain and swelling of the feet, in spite of continuous medication. His feet improved during the next five days, but he then developed an itching erythema of the face and hands, so the daily dose was reduced to 1 g. This level was inadequate, for he had a mild attack of gout in the succeeding week, and although this cleared up much more quickly than usual he was unable to walk for a few days. After 14 days on the reduced dose he had a recurrence of the facial rash, with vesiculation, and treatment was interrupted.

At this stage he was advised to take H.P.C. only when he felt that an attack was coming on, and to limit the dose to 1.5 g. daily for two or three days. In the following year he acted on this advice with good effect and was able to avoid any major episodes. After six months, however, he found that he had to take the drug for three days, whereas previously two days' treatment was sufficient.

In the period of continuous therapy he had 35 g. of H.P.C., but there was no evidence of hepatic disturbance as a result, although he had a history of "catarrhal jaundice" in 1928, which might have predisposed to liver damage if H.P.C. were hepatotoxic.

Two Further Cases

The following two cases were treated in Professor Hartfall's clinic at Leeds, and the summaries were kindly supplied by his senior registrar, Dr. Chandler.

Case 11.—A man aged 60 had his first attack 29 years ago, with recurrences every year or so, affecting the feet primarily but more recently involving the knees and wrists. He had very little chronic disability, but there was associated radiological evidence of Paget's disease, which caused him some pain, although the current symptoms were articular and undoubtedly the expression of gout. On admission his blood uric acid reading was 7.2 mg. per 100 ml., and he was given 2 g. of H.P.C. daily. His blood uric acid levels were estimated daily and showed a rapid fall under the influence of treatment, and by the fifth day the reading was 4 mg. per 100 ml., associated with complete

relief of symptoms. He was sent home on a daily dose of 1.5 g., and this was maintained for two months, when it had to be interrupted because of a vesicular facial rash. During the next three months his condition deteriorated in spite of colchicine therapy, and in January, 1953, H.P.C. treatment was resumed with daily doses of 1.5 g., which gave complete symptomatic relief.

Case 12.—A man aged 77 had 10 years' history of gout, which began in the ankles and gradually became more active and generalized. He was seen with acute arthritis of the hands and ankles, and H.P.C. therapy was started with a daily dose of 2 g. with considerable benefit. He was sent home on a daily dose of 1.5 g., on which he continued to do well during the next two months: thereafter he was given 0.75 g. daily on alternate weeks, and remained well during the subsequent four months.

Commentary

In the early cases H.P.C. was given in fractions at 0, 1, and 2 hours after breakfast, as recommended by the American workers. However, the incidence of diarrhoea shortly after the ingestion of the tablets led us to try more normal hospital methods. The drug was then given in divided doses after the main meals, two, three, or four times daily according to the total amount, and this system caused less alimentary upset.

In their pharmacological studies, based on animal experiments, Marshall and Dearborn (1950) conclude that "neither acutely nor chronically does H.P.C. appear to be a very toxic substance." In our series of cases, summarized in the table, there was no major toxic incident, but minor reactions were frequent. Alimentary upsets, in the form of vague nausea or diarrhoea, were largely avoided by

H.P.C. Therapy: Summary of Dosage and Toxic Reactions

Case No.	Duration of Treatment (Days)	Total Dose of H.P.C. (g.)	Plasma Uric Acid: Range during Period (mg./100 ml.)	Toxic Reactions		
				Skin	Alimentary	Renal
1	270	210	14.4-4.8	Erythema. Vesiculation	Nausea. Diarrhoea. Pruritus ani	Azotaemia
2	17	22	7.8-5.1	Psoriasis	Diarrhoea. Pruritus ani	
3	24	25	9.6-6.8	Erythema		
4	36	30	9.9-4.2			
5	40	44	6.9-3.8	Vesiculation	Diarrhoea	(?) Azotaemia
6	180	150	7.5-2.8	Erythema		
7	120	95	7.0-1.8			
8	27	32	6.1-2.1	Erythema. Vesiculation		
9	44	28	8.3-4.7	Erythema. Vesiculation. Pustulation	Diarrhoea	(?) Azotaemia
10	28	35	6.5-2.4	Erythema. Vesiculation		
11	66	99	7.2-4.0	Vesiculation		
12	190	155	Initially 6.0	Vesiculation		

giving the drug in divided doses throughout the day, always with an equal amount of sodium bicarbonate. Skin reactions were very troublesome and there was an element of photosensitivity in the early appearance of the usual erythema: the later reactions, characterized by vesiculation and sometimes pustulation, were probably due to excretion of the drug in the sweat, and were most severe in warm weather. (Incidentally, it was noticed that in the warm weather, when there was increased sweating and diminished output of urine, acute attacks of gout were more frequent.) Renal disturbances were not serious, with the exception of Case 3, which was unusually severe and complex, and the frequency of micturition reported by Simson and Bunim (1951) and Ehrlich *et al.* (1952) was not complained of by any patient. However, it would seem wise to have frequent estimations of the blood urea level of any patient receiving medication for a long period. Liver dysfunction was not found in any case in the group and,

although the limitations of liver function tests are realized, it seems reasonable to conclude that the absence of any hepatic complication, in patients treated 12 to 18 months previously, suggests that H.P.C. has no marked hepatotoxic effect, in spite of its relationship to cinchophen. In fact, a careful and critical review by Hueper (1948) mentions that cinchophen, when used in the treatment of gout, was much less toxic than was commonly supposed.

Conclusions

As the case summaries show, H.P.C. is an effective agent for the treatment of acute gout, and patients who had been treated earlier with colchicine were convinced that the new drug was more effective, in that it relieved their symptoms more quickly and more completely. In cases of the more chronic type of gouty arthritis, H.P.C. again proved effective, but its action was slower and less dramatic: it would appear that about a month's treatment is necessary in such cases before appreciable improvement occurs, but that, thereafter, acute episodes may be treated or prevented by a few days' intensive therapy. Although continuous treatment may be given for longer periods without major complications, the frequent occurrence of skin lesions makes any form of maintenance therapy impracticable, in spite of the fact that a severely affected patient may prefer an irritating rash to acutely painful joints.

Summary

Clinical trials of H.P.C. (3-hydroxy-2-phenyl-cinchoninic acid), a derivative of cinchophen, in 12 cases of acute gout or chronic gouty arthritis have given satisfactory results. No major toxic effects complicated treatment, but minor reactions were common, involving particularly the skin: for this reason, it is recommended that this form of medication should be reserved for short-duration treatment of acute episodes, or for prophylactic treatment in patients in whom premonitory symptoms occur.

This investigation was conducted during my tenure of a Research Fellowship in Rheumatism of the University of Leeds and Royal Bath Hospital, Harrogate, and I am indebted to the physicians of the latter institution for access to the cases described, and to Professor S. J. Hartfall for facilities at his clinic in the General Infirmary at Leeds. It is a pleasure to record my thanks to Mr. R. Moffett, chief laboratory technician of the Rheumatism Research Unit of the University, for the many necessary biochemical investigations which he carried out so carefully and willingly. Generous samples of H.P.C. were provided by Herts Pharmaceuticals Ltd., through the good offices of Dr. D. McAnally.

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The *Yearbook of the Universities of the Commonwealth*, 1954, is 111 pages larger than the 1953 issue. It covers all the university institutions in the Commonwealth, giving general information and listing the academic staff and number of students. In this issue an attempt has been made for the first time to give for each university a statistical note of the number of its students who come from other countries. The statement of the history and functions of the Association of Universities of the British Commonwealth has been amplified. The alphabetical index of staff of the university institutions now comprises over 30,000 names. The *Yearbook* is published by the association at 36-37, Gordon Square, London, W.C.1, price £3 3s.

CAROTID-CAVERNOUS FISTULA

FIVE CASES WITH "SPONTANEOUS" RECOVERY

BY

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Of the 15 cases of carotid-cavernous fistula recorded at the Radcliffe Infirmary, Oxford, during the years 1938-53, a spontaneous cure has occurred in five. Compared with other published series this is a high proportion, but in the three most recent cases the cures were not strictly spontaneous. These have been specially noted, as there were factors associated with their recovery—namely, carotid arteriography and hypotension—which might be called upon in future to encourage similarly satisfactory results. In three of the cases (two young men and a young woman) the cause was a severe head injury, but in two elderly women there was no apparent precipitating factor in the onset of symptoms. Particularly gratifying has been the absence of serious visual disturbance after recovery.

Case 1

A married woman aged 36 fell from her bicycle on October 19, 1944, and sustained a severe head injury. Her retrograde amnesia was 12 hours and post-traumatic amnesia four to five days. No definite skull fracture was seen on x-ray examination, but a right third nerve palsy with diplopia persisted and slight nominal dysphasia and continuing frontal headache were present. A month later she had an attack of vomiting, the headache was worse, the left eye protruded, the conjunctival vessels were distended, and considerable chemosis developed. The right eye soon followed suit. Visual acuity fell on the right from J 10 to J 18, and on the left from J 1 to J 12 (uncorrected). There was complete paralysis of the third and sixth cranial nerves on the right, and of the sixth on the left. A loud bruit was heard, particularly over the left fronto-temporal region, and this could be abolished by compressing the left common carotid artery. The degree of proptosis necessitated a left tarsorrhaphy two months after its onset. With rest in bed and sedation, some improvement in the proptosis and chemosis occurred, and the vision improved to J 4 on the right and J 6 on the left. The right third and sixth cranial nerve palsies also improved. During the period in hospital, digital compression of the left common carotid was attempted on several occasions but produced a feeling of faintness and paraesthesiae in the limbs. Ligation was therefore considered to be unwise. She was discharged from hospital five months after the injury with improvement both in the proptosis and of the bruit, which, although still present, was not very troublesome to her.

She continued much the same until July 20, 1945 (nine months after injury), when she felt faint while driving her car, and, after stopping it, did in fact lose consciousness. On recovering, she was given several alcoholic drinks and remembered little until she awoke the next day to find that the bruit had disappeared; the eyes had become very swollen again and she had a very bad headache. Examination revealed gross oedema and proptosis, on the right more than the left, and bilateral ophthalmoplegia which was almost complete. No bruit could be heard and the eyeballs did not pulsate. Steady improvement occurred, however, and she left hospital again two months after this episode, by which time the proptosis had almost subsided and her visual acuity, which had again been reduced, had improved to J 2 on the left and J 6 on the right. The right pupil was a little sluggish and there remained a complete