more effective than testosterone in the treatment of hypopituitarism, and that the only additional effect obtained when the two drugs were given together was an increase in growth of body hair. Whittaker and Whitehead (1954) gave additional testosterone to the maintenance treatment with cortisone in two male patients, and found increase in libido was produced. No change, however, was noticed in two female patients on the addition of testosterone to their treatment. In this series there was no conclusive proof that testosterone had any effect except to produce unwanted facial hair in one patient, and any general improvement in strength and energy or in libido with combined therapy appeared to be adequately maintained on cortisone alone. From these findings we suggest giving testosterone only to those female patients complaining of loss of libido who fail to improve with a combination of cortisone and thyroid. In male patients, routine testosterone is probably advisable, especially those in the younger age groups.

No definite conclusions regarding the value of stilboestrol can be drawn from this investigation because no detailed gynaecological studies were carried out. It was our impression, however, that stilboestrol made little, if any, difference, and its withdrawal caused no noticeable effect. As a method of treatment, therefore, we would not advise its routine use unless genital atrophy is so severe as to cause symptoms or unless oestrogen-withdrawal bleeding is desired for psychological reasons.

Summary and Conclusions

A clinical trial in which four patients with post-partum pituitary insufficiency were treated for varying periods on combined treatment consisting of D.C.A., sodium chloride, testosterone, stilboestrol, thyroid, and cortisone, and on cortisone alone, is described.

Three patients continued in good health on cortisone alone, while one patient relapsed and had to continue with thyroid.

Cortisone alone was thought to be inferior to combined therapy in respect of minor changes in skin in two patients, regression of the electrocardiogram in two, and return of cold-intolerance in one. It appeared that these changes were related to the withdrawal of thyroid, as they quickly improved when this drug was restarted.

From the study of these four patients and others treated since the trial ended, we regard cortisone and thyroid as the essential drugs to maintain good health in hypopituitarism. While cortisone alone seems to be little inferior to combined therapy, the effect of thyroid on the skin, electrocardiograms, and in some cases (which are apparently often unpredictable) intolerance to cold makes its routine use desirable. D.C.A. and salt therapy are unnecessary and complicate treatment, while testosterone is not advocated as routine therapy in female patients unless libido remains deficient without it.

We thank Professor G. M. Bull for allowing us to treat one of his patients and for his advice; Dr. R. S. Allison, who allowed us to study Case 4; Dr. J. A. Smyth and Mr. D. W. Neill for carrying out the biochemical estimations referred to in this study; and Mr R. G. Wood for the illustration.

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ASPIRIN INTOLERANCE A COMPARATIVE TRIAL OF TWO MODIFIED ASPIRIN PRODUCTS

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The use of aspirin preparations in rheumatic conditions is often attended by side-effects which preclude full relief of pain. These are gastric symptoms (nausea, heartburn, epigastric pain); salicylism (deafness, vertigo, tinnitus); and allergy (rash, bronchospasm).

Numerous aspirin preparations have been devised to reduce gastric intolerance, which is not without danger (Douthwaite and Lintott, 1938; Hurst and Lintott, 1939; Kelly, 1956) and which is reported to be commoner in rheumatic patients than in others. Femont-Smith (1955) compares the incidence of 26% of 200 rheumatoid cases being intolerant with two other series (Paul, 1943; Tebrock, 1951) where the incidence in non-rheumatic cases varied from 3 to 10%. It is, however, unsatisfactory to compare series of cases from different centres and with different assessors.

In this series an aspirin and glycine preparation ("paynocil") was compared with a citrated preparation ("disprin") in rheumatic patients intolerant of plain aspirin; intolerance in this context being defined as inability because of gastric symptoms to take doses of aspirin sufficient to relieve the rheumatic pain.

Design

The following categories were excluded from the trial: patients receiving cortisone, corticotrophin, phenylbutazone, or colchicine; those allergic to aspirin; and those whose response to treatment was so modified by psychological factors that a reliable assessment was impossible.

The conditions treated included all types of rheumatic disease, with rheumatoid arthritis predominating in both sexes; but most cases of gout and the severest cases of rheumatoid and collagen disease fell into the excluded category requiring more specific treatment.

With these exceptions all patients admitted to research unit beds were given aspirin, 50 gr. (3.2 g.) daily in divided doses, and this dosage was adjusted as necessary until pain relief was adequate, the final dose ranging from 20 to 100 gr. (1.3 to 6.5 g.) daily. Appropriate physical treatment was also prescribed.

Patients showing intolerance were changed to disprin or paynocil, in doses equivalent to the last dose of aspirin, the drugs being chosen alternately on each ward. After further dose adjustment, if necessary, the other product was then substituted for a week (the dose again being altered if necessary), after which the original choice was resumed. Patients were asked for their preference, with reasons. Salicylism was rarely encountered and did not in itself cause us to change the drug; any changes made (for other indications) did not appear to influence this group of side-effects.

Results

Results in men and women are shown separately, but no attempt is made to isolate the conditions treated.

Table I shows that 25% of patients in the series were intolerant to plain aspirin; this agrees with previous reports. The incidence in men and women was similar.

TABLE I

	Men	Women	Total
No. of patients	71	107	178
„ intolerant to aspirin ..	19	26	45

Table II shows results obtained in the aspirin-intolerant cases. Of 23 given disprin first, 5 preferred it, 10 preferred paynocil, and 8 were indifferent; all the men who made a choice preferred paynocil. Among 22 given paynocil first, opinion was more evenly divided—8 for paynocil, 9 for disprin, and 6 abstaining.

TABLE II

	Disprin Tried First			Paynocil Tried First			All Cases		
	M	F	Total	M	F	Total	M	F	Total
No. of patients ..	9	14	23	10	12	22	19	26	45
Disprin preferred ..	0	5	5	5	4	9	5	9	14
Paynocil ..	5	5	10	3	4	7	8	9	17
Equally satisfactory ..	1	3	4	1	1	2	2	4	6
„ unsatisfactory	3	1	4	1	3	4	4	4	8

The relative efficacy of the three drugs sometimes differed; four patients found the buffered preparations less effective than plain aspirin, and two found the opposite. Disprin was judged more effective than paynocil in three cases and less effective in one. In this connexion (remembering that the efficacy of salicylates is diminished by alkalis such as sodium bicarbonate, which accelerates excretion) it is noteworthy that two patients in the “unsatisfactory” group experienced improved tolerance without apparent loss of analgesia when every dose (of paynocil in one case and of aspirin in the other) was accompanied by magnesium trisilicate.

One patient who reported that she never took aspirin because of her duodenal ulcer was given paynocil from admission; unfortunately her ulcer symptoms reappeared in a few days, and analgesics had to be withdrawn.

Conclusions and Comment

In this series 45 out of 178 rheumatic patients (25%) could not take adequate doses of aspirin. Of these 45 patients, 37 (82%) responded well to paynocil, disprin, or both. There was a slight majority (17 to 14) in favour of paynocil, but the numbers are too small for this to be significant. Most of those who expressed a preference for one product did so because of marked inability to stomach the other, demonstrating that “one man’s meat is another man’s poison,” and that there is a place for both preparations in the treatment of rheumatism, since one may succeed where the other fails.

Summary

The freedom from gastric side-effects and the analgesic efficacy of two modified aspirin preparations—paynocil and disprin—have been compared in rheumatic patients intolerant of aspirin. Four-fifths of these patients benefited, and two-thirds expressed a definite preference for one or other of these drugs, the preferences being fairly evenly divided between the two. Differences in the analgesic effect were encountered, but no definite pattern emerged. The high incidence of aspirin intolerance in rheumatic patients was confirmed.

Acknowledgment is made to Messrs. Bencard Ltd. for the supply of the aspirin-glycine compound.

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Medical Memoranda

Abdominal Periarteritis Nodosa

It is extremely rare for periarteritis nodosa to present as an acute abdominal emergency. However, several cases have been reported which conform to the pattern of gradually increasing abdominal symptoms culminating in an attack of peritonitis, at which stage laparotomy has been performed. The ultimate diagnosis has usually come from the histologist, but three cases are recorded (Manges and Baehr, 1921; Logue and Mullins, 1946) in which the nodules of periarteritis were visible to the naked eye within the peritoneal cavity. We wish to describe a fourth case in which these nodules were visible at laparotomy. Obviously the visibility of the periarteritic nodules depends on their size, and this in turn on the degree of necrosis in the arterial wall, which is one of the variable factors in this disease.

CASE REPORT

A young man of 20 was admitted to St. Mary's Hospital, Portsmouth, on May 13, 1955, with severe epigastric pain. At the age of 9 he had an attack of anterior poliomyelitis which left some residual wasting of the right thigh and leg; in the past year he had had attacks of asthma. For the preceding three weeks he had suffered from intermittent epigastric pain, diarrhoea, and aching pains in the right leg. During this period he had been on a “gastric diet,” which had given him some relief. For the 18 hours before admission his epigastric pain had been severe, and he had acute nausea but had not vomited; his bowels had been open normally during that time.

He was thin, pale, and over-anxious. His temperature was 100° F. (37.8° C.), pulse 120, respirations 20. His tongue was clean and moist. The abdomen was tender in the epigastrium and the right hypochondrium; there was widespread moderate abdominal rigidity, with very marked rebound tenderness in the lower abdomen and faint bowel sounds on auscultation. Rectal examination did not reveal any peritoneal tenderness. The respiratory and cardiovascular systems were normal apart from a blood pressure of 148/110 mm. Hg. The urine contained no albumin. An abdominal radiograph showed there was no gas under the diaphragm. His leucocyte count was 17,000 per c.mm., of which 90% were neutrophils and 3% eosinophils.

It was thought that the patient had peritonitis, probably due to a perforated peptic ulcer, and laparotomy was therefore performed, the abdomen being opened through a right paramedian incision (Mr. J. D. Youngusband). There was no free fluid. The first striking finding was that the greater part of the small intestine, and especially the ileum, showed a blotchy, purplish discoloration which was maximal about 2 in. (5 cm.) from the ileo-caecal valve and extended throughout the small intestine with the exception of the upper 2 in. (5 cm.) of the jejunum. Two small round yellow sloughs about half an inch (12.5 mm.) in diameter were present in the bowel wall, indicating imminent perforation. There was little or no fibrinous reaction. The colon was mildly thickened, with generalized faint inflammatory changes. The mesentery, surface of the bowel, and parietal peritoneum were extensively studded with whitish pinpoint nodules; these were best seen in the mesentery of the small intestine and along the peripheral vascular arcades of the mesenteric vessels. Most of the abdominal contents felt gritty because of these nodules. The spleen was not enlarged or affected by the nodules; the liver also was normal. The appendix was not inflamed. The nature of the nodules and the condition affecting the bowel was obscure. The two areas of threatened perforation were carefully oversewn and specimens of the nodules removed for biopsy; the abdomen was then closed. The histological report (Dr. R. D. Clay) stated: “Serial sections of a nodule reveal it to contain a small artery with focal necrosis of the whole thickness of its wall