concentrated by vacuum distillation, and no haematopoietic activity had been demonstrated. It was therefore assumed that the material in the gastric juice that could be made active by vacuum distillation was held back by the ultrafilters. To test this, Case 12 was injected with fresh gastric juice first concentrated by ultrafiltration, then diluted with 0.3 per cent. hydrochloric acid, and re-concentrated by vacuum distillation. The patient had a severe reaction, a decrease in red blood cells, and an increase in icterus following the injection. Chart IV

CHART IV.—This shows the prolonged reticulocyte response of Case 12 following the intramuscular injection of normal human gastric juice first concentrated by ultrafiltration, then diluted and re-concentrated by vacuum distillation, and the response of the blood to three intramuscular injections of the amount of concentrated liver extract (3 c.cm.) derived from 100 grams of whole liver.

shows the prolonged reticulocytosis, the peak (345,000 per c.mm.) being reached on the thirty-fifth day after the injection. A definite clinical response and rise in red blood cells had occurred by then, although the rise in red blood cells was markedly delayed. There was a subsequent increase in reticulocytes following the intramuscular injection of liver extract.

This showed conclusively that the material in the gastric juice which could be made active was held back by the ultrafilters used. It also demonstrated that the gastric juice concentrated by ultrafiltration and re-concentrated by vacuum distillation was haematopoietically active, whereas on three occasions (Group 2) the gastric juice concentrated by ultrafiltration only had been inactive. The results obtained in Group 3 and in Case 12 indicated that after concentration by vacuum distillation a goodly percentage of the activity passed through the ultrafilters, although practically all of the material that could be released or made active by concentration by vacuum distillation was held back by the ultrafilters. It would seem, therefore, that during the process of vacuum distillation a haematopoietically active substance was obtained that was smaller in size than the material from which it was formed or released.

SUMMARY

The results of these studies indicate that some change in fresh human gastric juice must take place before a haematopoietically active material can be demonstrated by the intramuscular injection into patients with pernicious anaemia. At the present time the actual mechanism of this change is not known. Any of at least three explanations might account for this change. The first is that, during the process of vacuum distillation the intrinsic factor acts upon an extrinsic factor present

in the gastric juice in too small amounts to be active when fed by the mouth. The intrinsic factor is known to be present in fresh human gastric juice, and has been demonstrated by us in another group of experiments to be present at the onset of the vacuum distillation in all the preparations which were made active by this procedure, and in none of those that were not so made active. The second is that during the process of concentration by vacuum distillation, a material irritating or toxic to the haematopoietic system is produced. The prolonged and delayed reticulocyte response, marked bone marrow irritation, the delayed rise in red blood cells, and the fact that each patient who responded to the injection of the concentrated gastric juice had a more or less severe reaction, suggest this possibility. Case 12 is of especial interest in this connexion. After the injection the temperature rose to 106° F., the red blood cell count decreased 0.55 million, and there was an increase in icterus. There was no rise in red blood cells until after a prolonged reticulocytosis. The third possibility is that during the concentration by vacuum distillation a hormone is released or activated.

In our opinion the haematopoietically active substance must be formed by the action of the intrinsic factor on an extrinsic factor in the gastric juice, or by the production of a substance irritating or toxic to the haematopoietic system.

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ADDITIONAL SYMPTOMATOLOGY IN SIMPLE ACHLORHYDRIC ANAEMIA

BY

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Although its recognition has been slow, its nomenclature varied, and its features diverse, unequal, and inconstant, a type of non-haemolytic primary anaemia, associated with a relative gastric achlorhydria, has of recent years been admitted a separate clinical entity since its distinctive pathology was made clear by Witts¹ in the Goulstonian Lectures of 1932. The object of this communication is to indicate two additional features of the symptomatology, believed not to have been hitherto recorded, which occurred in patients admitted to St. Thomas's Hospital Medical Unit during 1932. These are: (1) acne rosacea, and (2) thinning of the hair. It must be admitted in each case that a single example of such a symptom might appear at first sight to have occurred fortuitously, in spite of the diversity of symptoms—more especially abdominal—which are known to occur; but it is considered justifiable to record them, if only because they might be expected on pathological grounds.

ACNE ROSACEA

The skin condition was observed in a woman with most of the usual features of simple achlorhydric anaemia.

Mrs. G., aged 60, complained of palpitations and shortness of breath for six months, accompanied by pain in the epigastrium, chiefly post-prandial. She had long come to

recognize that meat in any form particularly aggravated the pain, and for some weeks she had been subsisting mainly upon carbohydrates. On examination there was slight oedema of the ankles and moderate enlargement of the spleen. The blood contained 4.3 million red cells per c.mm., but only 32 per cent. haemoglobin, and the stained films showed poikilocytes and occasional pessary forms. Gastric content analysis revealed no free HCl to histamine stimulation in half-hourly specimens up to two and a half hours. Considered together, the symptoms gave no doubt as to the clinical condition. But in marked contrast to the considerable pallor of the rest of the skin, that of the nose and cheeks was blotchy and hyperaemic, with a downward spread also on to the lower lip. This blotchy area consisted of confluent papules, which were not, however, surmounted with comedones, and even a casual inspection made it certain that the condition was typical acne rosacea.

The interest of this case lies in the fact that acne rosacea has long been known to be associated with some form of alimentary disturbance. As long ago as 1920 Ryle and Barber² made gastric analyses in a series of twelve cases, in five of which there was complete achlorhydria throughout the period of the meal, while in two of the others there was marked hypochlorhydria. Although, it is believed, this observation has not been repeated, a degree of hydrochloric acid deficiency is now assumed by most dermatologists in the treatment of acne rosacea. The case recorded above at least indicates a common aetiological factor, since in one and the same patient there occurred two conditions—an anaemia and acne rosacea—both known to be associated with gastric hypochlorhydria, yet hitherto only separately encountered. A common factor is further suggested by the fact that the cutaneous and anaemic states improved *pari passu* under treatment. If, moreover, in apparently uncomplicated acne rosacea, blood counts revealed some degree of diminished red cell haemoglobin content, this common aetiological factor might be proved.

ALOPECIA

The case notes of the patient who complained of thinning of the hair were as follows.

Mrs. B., aged 45, had had flatulence and fullness after food for ten months, and latterly had noticed difficulty in swallowing. Most of the typical signs were present, including, incidentally, well-marked atrophy of the buccal and pharyngeal mucous membrane, on account of which difficulty was found in passing the stomach tube. On inquiry she stated that her finger-nails were very brittle and liable to longitudinal splitting: they were flat, short, and diamond-shaped, the pulp of the fingers projecting almost as far beyond each nail-tip as the total length of the nail itself. Finally, she volunteered that her hair had been "coming out" to a very considerable degree in the past six months. The diagnosis of simple achlorhydric anaemia was made, but as her hair was certainly thin and brittle it was at once recognized that a determination of the basal metabolic rate was indicated in view of the possibility of a superimposed early myxoedema. This, however, was found to be within normal limits.

Nail changes, well exemplified in the case above, are fairly common in this type of anaemia, but the pathology is obscure, since they are not found in other anaemic states, primary or secondary. No mention, however, is made in the literature of thinning of the hair. But as hair resembles nail substance, in consisting essentially of modified horn cells, it is suggested that the same unknown factor is responsible for both nail and hair dysfunction in the simple achlorhydric type of anaemia, presumably depending on iron deficiency.

I am indebted to Professor O. L. V. de Wesselow, under whose care they were admitted, for permission to publish these cases.

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CIRCUMCISION AND SYPHILIS

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The hygienic value of circumcision in the male infant has been generally acknowledged over a very long period. All will agree that such conditions as acute balanoposthitis and carcinoma penis are seldom, if ever, seen in the circumcised. It is also commonly believed that the incidence of syphilis is considerably lower in circumcised persons. In view of this widespread belief it is somewhat surprising that so few statistical reports bearing on the incidence of acquired syphilis in circumcised and non-circumcised males should be available.

There appears to be little information on this subject, particularly since the introduction of the more accurate methods in the diagnosis of syphilis following upon the discovery of *Spirochaeta pallida* and the utilization of the Wassermann test.

Jonathan Hutchinson,¹ on reviewing his cases for the year 1854, stated:

"Notwithstanding a gross proportion of nearly one-third to others the cases of syphilis presented by Jews are only as one to fifteen. That this difference is not to be accounted for by their superior chastity or their unwillingness to seek medical aid is conclusively proved by the fact that they furnish very nearly half the cases of gonorrhoea. The circumcised Jew is, then, very much less likely to contract syphilis than an uncircumcised person."

Hutchinson's figures are shown in Table I.

TABLE I.—Venereal Cases (1854)

Total Venereal Cases	Gonorrhoea	Syphilis	Proportion of Gonorrhoea to Syphilis
Non-Jews, 272	107	165	0.6 to 1
Jews, 58	47	11	4.3 to 1

Feldman² refers to the male venereal out-patients at the Metropolitan Hospital during the year 1882-3, among whom syphilis was present in 17.8 per cent. of the Jews and 62 per cent. of the non-Jews. Assuming that the remaining patients were suffering from gonorrhoea, these figures give the proportion of gonorrhoea to syphilis in Jews as 4.5 to 1 and in non-Jews as 0.6 to 1. These proportions are almost identical with those found by Hutchinson (Table I) at the same hospital some thirty years earlier.

Breitenstein³ reported in 1902 observations on 15,000 native circumcised soldiers and 18,000 European soldiers in the Dutch Indies. He noted a greater proportion of venereal infections in the non-circumcised, and that syphilis in particular was much more frequent in the non-circumcised troops.

Wolbarst⁴ has reported upon venereal diseases in the circumcised and non-circumcised, utilizing 800 cases under his care. He found that in 400 circumcised patients the proportion of syphilis and soft chancre combined was 22 per cent., whereas in 400 uncircumcised patients the proportion of syphilis and soft chancre was 41 per cent. Unfortunately this author does not give the separate figures for syphilis and for soft chancre.

More recent figures were given in 1928 by Berkowitsch,⁵ who recorded the incidence of venereal diseases in Jews