existence of the tumour. It did so, however, in Grawitz's first case, though the indications were susceptible of misinterpretation.

Result of Operation.—This is unusually fatal. Madelung's 3 cases reported by Lubarsch died, without uræmia or peritonitis to account for the fatal termination. Askanazy's case died from recurrence. One of our Mater cases (Mr. Coppinger's) is still alive, three years and a-half after operation, and is one of the very few recorded cases in which the patient was cured by the operation.

Metastases.—These were found 20 times out of 29, a fact which proves the malignant tendency of these suprarenal neoplasms. One of our cases having recovered, and the necropsy of the other having been refused, I am not in a position to say anything on this head. Generalisation is usually ushered in by rupture of a tumour mass into the renal vein. The lung is a favourite seat of the secondary growths. They have also occurred in the liver, pancreas, heart, thyroid, etc.

British Cases and Literature.—In the debate¹¹ on the case of a kidney tumour, which seems to belong to this class, and which was operated on by Mr. Walsham, Dr. Newton Pitt expressed the opinion that some renal tumours were possibly related to aberrant suprarenal bodies. The patient in this instance was a child aged 9 months. If my suspicion as to the true nature of this malignant growth, which recurred and caused the patient's death eleven months after Mr. Walsham's successful operation, prove correct, this will be, perhaps, the earliest known instance in point of age. On the same occasion, Dr. Snow spoke of a collection of 60 tumours derived from the Wolffian bodies having been made by Mr. Windle. I do not know where the account of this collection is to be found. Mr. Shattock¹² suggests the Wolffian origin of many kidney growths. Hamilton¹³ calls tumours of this kind "hæmorrhagic sarcoma." Cases recorded by Morris,¹⁴ Sharkey,¹⁵ Paul,¹⁶ and others may possibly prove to belong to this category, as most certainly does Bell and Johnston's case.¹⁷ In Mr. Bland Sutton's work on tumours, there is no mention made of the relation of epithelial kidney tumours to suprarenal "rests." I heartily agree with the author when he says (p. 257) that "it is impossible to write an account of carcinoma of the kidney until surgeons are more alive to the interest of the question, and take steps to place malignant tumours of the kidney whilst still fresh in the hands of experienced pathological histologists." Enough has been said to show that the English literature of surgical pathology is almost a blank on this important and interesting subject; and the object of this paper is to attract the attention of British pathologists to these little known tumours, and to do something towards placing our knowledge of them on the same level as that of most other neoplasms. My best thanks are due to my colleagues at the Mater, Messrs. Coppinger and Lentaigne, for kind permission to utilise their specimens and clinical notes.

[The paper was illustrated with microscopic preparations and lantern slides by the author and Mr. A. Pringle.]

REFERENCES.

- ¹ *Handbuch der allg. Path.*, Bd. ii. ² *Cit. in Beneke, Ueb. d. Versprengung von Nebennierenkeimen in der Niere, Ziegler's Beitr.*, ix, p. 451. ³ *Path. Trans.*, xlv, p. 141, 1894. ⁴ *BRITISH MEDICAL JOURNAL*, 1895, vol. i, p. 630.
- ⁵ *BRITISH MEDICAL JOURNAL*, January 7th, 1895. ⁶ *Beitrag zur Kenntniss d. primären Angiosarkome d. Niere, Ziegler's Beitr.*, viii, p. 146. ⁷ *Unters. d. glykogenreiche Endotheliome, Ziegler's Beitr.*, xii, p. 65. ⁸ *Ueb. d. Structur d. Nierenadenome: Ihre Stellung zu d. Strumae suprarenales aberrate (Grawitz), Virch. Arch.*, Bd. cxxxiii, p. 405. ⁹ *Virch. Arch.*, Bd. lv. ¹⁰ *Der Epitheliakrebs, Leipzig*, 1865. ¹¹ *Quart. Jour. Microscop. Science*, xxii, 1882, p. 17. ¹² *Bau u. Entwicklung d. Nebennieren bei Reptilien, Arbeiten a. d. Zoolom. Inst. Würzburg*, Bd. iv, 1877. ¹³ *Arch. f. mikroskop. Anat.*, xxii, 1883. ¹⁴ *Quart. Jour. Microscop. Science*, 1884. ¹⁵ *Unters. ü. d. Entw. des Harn-u. Geschlechts-Apparates d. Amniven, Internat. Monats. f. Anat. u. Histol.*, Bd. ii, 1885. ¹⁶ *Textbook of Embryology, English ed.*, 1882, p. 404. ¹⁷ *Beitr. z. Kenntn. d. norm. u. path. Anat. d. Glandula carotica u. Nebenniere, Virch. Festschrift*, Bd. i. ¹⁸ *Ueb. die morphol. Bedeutung der Niere in ihrem Verhältniss zur Vorniere und Nebenniere, etc., Anat. Anzeiger*, v, 1890, and *Studien ü. d. Bauplan d. Urogenitalsystems d. Wirbelthiere*, Jena, 1891, pp. 67 and 68. ¹⁹ *Sammlung klin. Vorträge*, No. 33, Ueb. den Krebs, p. 176. ²⁰ *Ueb. direkte Betheiligung des Ektoderms an der Bildung der Urnierenanlage, Arch. f. Anat. u. Physiol., Anat. Abth.*, 1884. ²¹ *Journal of Anatomy and Physiology*, October, 1892. ²² *Zur Anat. der Nebenniere, Stzber. Wiener Akad. d. Wissensch.*, Bd. ci, Abth. 3, November, 1892. ²³ *Loc. cit.* ²⁴ *Studien ü. die Spezifität des Altruismus u. die Anaplasie der Zellen, Berlin*, 1893. ²⁵ *Virch. Arch.*, Bd. cxxxv, p. 124. ²⁶ *Virch. Arch.*, Bd. xciii, 1883. ²⁷ *Deutsche Arch. f. klin. Med.*, Bd. xliii, 1883. ²⁸ *Ztschr. f. Chirurg.*, Bd. xxviii. ²⁹ *Zur Lehre von der Versprengung von*

Nebennierenkeimen in der Niere, Ziegler's Beitr., Bd. ix. ³⁰ *Dissert.*, Marburg, 1891. ³¹ *Virch. Arch.*, Bd. cxxvi. ³² *Loc. cit.*, i, p. 616. ³³ *Arch. d. Heilkunde*, 1875, Heft. 3. ³⁴ *Wiener med. Jahrbücher*, 1883, p. 213. ³⁵ *Arch. d. Phys.*, 1882; *Revue de Méd.*, 1884, 1885. ³⁶ *Loc. cit.* ³⁷ *Geschwülste der in der Niere Eingeschlossenen Nebennierenkeime, Ziegler's Beitr.*, Bd. xiv. ³⁸ *Loc. cit.* ³⁹ *Loc. cit.* ⁴⁰ *Loc. cit.* ⁴¹ *BRITISH MEDICAL JOURNAL*, April 1st, 1893, and November 10th, 1894. ⁴² *Path. Trans.*, xxxvii, 287, and *BRITISH MEDICAL JOURNAL*, November 29th, 1894. ⁴³ *Textbook of Pathology*, vol. ii, Part. I, p. 306. ⁴⁴ *Loc. cit.* ⁴⁵ *Path. Trans.*, xxxv, p. 235. ⁴⁶ *BRITISH MEDICAL JOURNAL*, June 12th, 1886. ⁴⁷ *Montreal Medical Journal*, February, 1891; *Ref. in Centralbl. f. allg. Path. u. path. Anat.*, iii, p. 424.

THE PATHOLOGY OF PERNICIOUS ANÆMIA.¹

By WILLIAM HUNTER, M.D., M.R.C.P.,

Pathologist and Curator of Museum, Charing Cross Hospital; Senior Assistant-Physician, London Fever Hospital; Assistant-Physician, West London Hospital.

IN undertaking the duty imposed upon me by our Secretaries of opening this discussion I deem the moment not inopportune to review our present position with regard to this subject. Personally I welcome this opportunity because, since the publication of my first investigation, now seven years ago, my own published work has been confined almost exclusively to special observations, for example, excretion of urinary pigment, of iron, of blood pigment, of aromatic sulphates, and of ptomaines—fitted to throw any light on the nature of the disease.

Avoiding then going into details, I propose, on the present occasion, to confine my attention to discussion of the broad question, the relation of pernicious anæmia with other forms of anæmia.

THE RELATION OF PERNICIOUS ANÆMIA WITH OTHER FORMS OF ANÆMIA.

Thanks to the many valuable contributions made within recent years by a number of observers—Russell, Mott, Garrod, MacMunn, Hale White, Gowland Hopkins, Stockman, and others—the material available for such a discussion has been greatly increased. So far as my own view is concerned I see no reason to change the opinion I expressed seven years ago—namely, that there are very strong pathological grounds for regarding this form of anæmia as a special variety of anæmia, if indeed, it be not a special disease. In particular from no form of anæmia is it, in my view, more easily distinguishable by its pathological characters than from anæmia resulting from loss of blood or from the anæmia of wasting disease. The grounds on which I base this conclusion are, as determined in my earlier work, briefly as follows:

HÆMOLYTIC NATURE OF PERNICIOUS ANÆMIA.

1. The extreme degree of blood change which pernicious anæmia invariably presents (and which I may add is not at all invariable in the case of many conditions whose anæmia is regarded as identical with pernicious anæmia) is always marked by certain pathological changes, characteristic either as regards their nature, their degree, or their peculiar association. These changes are constantly met with in the liver, and not infrequently in the kidneys and spleen.

2. These changes according to my observations are characteristically absent in traumatic anæmia and in wasting anæmia.

3. They consist for the most part of deposits of blood pigment, with corresponding increased richness in iron in the liver, preferably in the liver cells of the outer two-thirds of the hepatic lobule, frequently also the capillaries of the liver, and within the cells of the convoluted tubules of the kidneys.

4. This pigment is not the result of extravasation, and is distinguishable from such by important differences affecting both its character and its distribution.

5. From its character and its amount it denotes an excessive destruction of blood as the prominent and most constant and characteristic feature of the disease.

SPECIAL CHARACTER OF THE HÆMOLYSIS.

As regards the nature of this destruction I concluded from my experiments further, (1) that it differs in important respects from, and is no mere exaggeration of, the ordinary blood destruction of health (*vide postea*).

¹ Read in the Section of Pathology at the annual meeting of the British Medical Association, held in London, July-August, 1895.

2. It has, however, this in common with the latter, that it occurs within the area of the portal circulation, notably within the spleen, to a less extent within the capillaries of the gastrointestinal area, and to a still less extent within the capillaries of the liver itself.

3. It differs also in what appear to me essential respects from the blood destruction characterising two well-known and dissimilar forms of blood disease—namely, malaria, in which the red corpuscles are individually attacked and become the seat of disease, and paroxysmal hæmoglobinuria, in which a great dissolution of red corpuscles with liberation of hæmoglobin takes place in the general circulation. On the one hand, there is no evidence that in pernicious anæmia, as in malaria, the red corpuscles are individually diseased, and the distribution of the pigment in the two diseases presents accordingly important points of difference. On the other hand, there is no evidence that any extensive general dissolution of red corpuscles takes place in the general circulation in pernicious anæmia, such as undoubtedly occurs in paroxysmal hæmoglobinuria. Hæmoglobinuria does not occur in pernicious anæmia as under such circumstances it would. The excessive destruction of pernicious anæmia appears, then, by process of exclusion, to be a special process, requiring for its initiation the operation of special factors, and not an exaggeration of the ordinary destructive processes in health.

Inasmuch as the destruction is confined to the portal circulation (destruction in the general circulation would, as I showed, be attended by hæmoglobinuria), and the gastrointestinal tract is even in health the chief area by whose activity the degree of blood destruction is influenced, it appears reasonable to conclude that in pernicious anæmia the source of the poison which affects the blood injuriously is also this area.

RÔLE OF EXTRAVASATION AS A FACTOR IN CAUSING THE FEATURES OF PERNICIOUS ANÆMIA.

Another view has been put forward and ably advocated by my friend Dr. Stockman, of Edinburgh; and inasmuch as it constitutes a sort of compromise between the view which regards pernicious anæmia as an essentially hæmolytic variety of anæmia, and that which regards it only as an extreme form of anæmia, Dr. Stockman's view seems to me to call for special notice.²

Dr. Stockman, in his studies of the disease, has been greatly impressed by the frequency of occurrence of bleedings and extravasations of blood in the variety of anæmia we term pernicious; and he has come to the conclusion that it is the occurrence of such extravasations that constitutes the difference between ordinary severe anæmia and pernicious anæmia. The latter, in his view, is not a special form of anæmia. The large quantity of pigment found in various organs, especially the liver, is not, he considers, an evidence of a special destructive process, but is merely the result of absorption of blood from a host of minute extravasations occurring from time to time in various parts of the body. In support of this view he finds that an increase of pigment in the liver can be produced by injecting blood subcutaneously into rabbits.

A criticism of this view appears to me to divide itself under two heads: (1) Do extravasations occur with the frequency or to the extent which is here assumed? (2) Can the typical pigment changes found in the liver, spleen, and kidney in pernicious anæmia be caused by absorption of extravasated blood?

FREQUENCY OF EXTRAVASATIONS.

The first question I do not propose to discuss at any length. And for this reason, that the answer to it must naturally be a question of actual individual experience. I may only say that my own personal experience is entirely opposed to the view that the extravasations met with in pernicious anæmia are either of the frequency or the importance that such a theory presupposes.

It so happens that since the publication of Dr. Stockman's views, I have had occasion to make necropsies on two cases of pernicious anæmia, both under the care of Dr. Abercrombie, in Charing Cross Hospital. The changes in liver, kidneys, bone marrow, and spleen were those characteristic of the

disease. In one the retina showed a few hæmorrhages; and there were a considerable number of punctiform hæmorrhages in the subdural arachnoid especially over the right hemisphere. At one part there was a small collection of sero-gelatinous fluid over the right frontal lobe. Elsewhere in the body, after most careful search, I could not find the slightest evidence or sign of extravasation, small or great.

Now, that punctiform hæmorrhages are not uncommon in the retina and subdural arachnoid in the disease, as in one of the above cases, is well known. But that a degree of extravasation such as had here occurred was capable of inducing such an increase of pigment in the liver and kidney, as I found in these cases, is, in my view, quite out of the question.

PERCENTAGE OF IRON IN ORGANS.³

	Liver.	Spleen.	Kidney.
Case I	0.207	0.097	0.068
Case II (not even subdural hæmorrhages)	0.515	0.023	0.043
Case III (case of ordinary severe anæmia)*	0.093	0.029	0.004

Dr. Stockman admits that in some cases no hæmorrhages at all are to be found, and he accounts for this by assuming that the blood has been very quickly absorbed, leaving no trace behind. Even if one admits that this could be the case, evidence of this absorption would, I consider, be found in the glands through which the blood had been absorbed.

In the experiments I shall presently refer to, in which I caused large extravasations, I invariably found a large quantity of pigment in the lymphatic glands through which the blood had been absorbed. I have looked for them, but have not found any such change in the lymphatic glands in pernicious anæmia.

ABSORPTION OF EXTRAVASATED BLOOD AS A CAUSE OF PIGMENT CHANGES IN THE LIVER, KIDNEY, AND SPLEEN.

With regard to the second question, whether the typical pigment changes in liver, spleen, and kidney can possibly be caused by absorption of extravasated blood? It so happens that the very earliest experiments I performed in this relation, furnish, as it appears to me, a conclusive answer. And that answer is also in the negative.

My experiments had for their object to reproduce if possible the peculiar distribution of pigment amongst the different organs in pernicious anæmia, and more particularly to ascertain whether not merely an increase of pigment in one or other of these organs, but a similar distribution of the pigment amongst them, especially as between the liver and spleen, could be produced by absorption of large extravasations of blood. In health and all other diseases, as I showed, the rule is that the spleen contains a higher percentage of iron than the liver, namely, 0.083 per cent. for the liver and 0.171 for the spleen. In pernicious anæmia alone that order is reversed the liver containing invariably a notably increased percentage of iron while the increase in the spleen may be slight or absent (see above analyses). It was my special aim then to reproduce this reversed distribution of pigment.

The experiments I shall now record have a double interest. They not only bear very directly on the question to what extent the characteristic pigment changes in pernicious anæmia may be due to the absorption of extravasated blood. But they bear, for reasons presently to be seen, on the question already discussed: Whether the blood destruction in that disease is merely an exaggeration of that which occurs in health.

NATURE OF EXPERIMENTS.

The method by which I first attempted to reproduce the conditions was by transfusing blood from one animal into the peritoneal cavity of another of the same species. Both animals being anæsthetised, the whole of the blood of the one was transfused into the peritoneal cavity of the other either directly or after previous defibrination, the quantities injected at one time varying from 32 to as much as 92 per cent. of the total quantity of blood estimated to be in the animal's own body. (In rabbits I found the quantity of blood on an average one-eighteenth of the body weight.)

The following are some of the figures:⁵

³ I am indebted to Mr. Richardson, of the Chemical Laboratory of Charing Cross Hospital, for kindly undertaking these analyses for me.

⁴ A woman, also under Dr. Abercrombie's care, who presented during life various motor and sensory disturbances in the lower limbs, and died with cystitis and acute bedsores.

⁵ Intraperitoneal Transfusion, *Jl. Anat. and Physiol.*, 1887.

200 per cent. (Experiment 1),⁶ and gained throughout steadily in weight.

61	"	(Experiment 2).
92	"	(Experiment 3), followed later by 54 per cent.
66	"	(Experiment 4).
70	"	(Experiment 5).
50	"	(Experiment 7).
54	"	(Experiment 8).
50	"	(Experiment 9).
50	"	(Experiment 10).

In the last 4 cases the blood injected had been previously defibrinated, and the absorption of corpuscles thus facilitated. In Experiment 10 the excess of corpuscles in the circulation after the transfusion amounted to as much as 38 per cent. of the normal number; and it took three weeks before this excess was steadily day by day got rid of.

In most of the experiments the animals remained in perfectly good health from the very beginning, usually, indeed, adding considerably to their body weight. Thus in Experiment 1 the increase in body weight in 4 weeks was 12 per cent.; in Experiment 3, where 92 per cent. of blood was injected at one time, the increase was even greater, namely 19 per cent. in 3 weeks; in Experiment 5 it was 13 per cent. in 3 weeks. Judging by this, perhaps the most reliable standard, the health of the animal remained good, and the conditions produced in these experiments might be regarded as those aimed at, namely an excessive destruction of blood in a healthy animal.

RESULTS.

The result as regards the distribution of pigment in the various organs concerned were not as I had expected. I thought in this way to produce a large excess of pigment in the liver. On the contrary, the increase was never more than slight, and not even constant, even in the cases in which such enormous quantities of blood had been injected as 200 per cent. in three months (Experiment 1); or 92 per cent., causing an increase of 28 per cent. of red corpuscles in the circulation, followed by a subsequent injection (Experiment 3); or of 54 per cent. of defibrinated blood (Experiment 8); or 50 per cent. of defibrinated blood, causing an increase of 38 per cent. of the corpuscles per unit volume of blood in the circulating blood (Experiment 10). In the last case, indeed, there was no increase at all; and in none of the experiments did the appearances presented by the liver differ in the slightest from those found in health. Nor was the result affected by the length of time after the transfusion. The animals were killed at varying intervals—2, 7, 10, 21, 30 days up to 3 months after the injection.

As regards the distribution of pigment between liver and spleen, even more notable if possible as it appeared to me, was the difference between the condition produced in these experiments and that found in pernicious anæmia. For while, as I have said, the liver contained little or no increase of pigment, the spleen was in all cases packed with it—to a degree, indeed, more striking than I ever was able to produce by any other method of inducing excessive blood destruction.

I do not think it would be possible to test the influence of extravasation more severely than was done in these experiments. The quantities of blood to be disposed of at one time by absorption amounted usually to half the animal's own blood, and sometimes equalled or exceeded that amount.

As a sample experiment I may record Experiment 10. Rabbit, weight 4 lb. 2 oz.; 50 c.cm. of defibrinated blood injected into peritoneal cavity (equivalent to about 50 per cent. of the total quantity of the animal's own blood). Temperature before operation 37.2° C. Highest increase of red corpuscles in blood (per unit volume) reached on third day, namely, 38 per cent. Gradual fall in their number till the normal was reached on the twenty-third day. Temperature on day after injection, 37.2° C. On following day, 37.6° C., by which time animal seemed in every way well; eating as usual. On fourth day, 37.2° C. After death (killed on thirtieth day) no trace of peritonitis. Liver absolutely normal, showing not the slightest increase of pigment, not sufficient even to give any darkening with sulphide of ammonium. Spleen, on the other hand, packed with pigment, becoming coal black in that reagent (iron reaction).

In another relation a conclusion of some importance appears to me deducible from the above facts. As I have

stated, the health of the animal, as best evidenced by the increase in body weight, was unaffected by the transfusion. The excess of corpuscles was not immediately but gradually got rid of, without incommencing the animal, without fever, without hæmoglobinuria—presumably, therefore, by agencies similar to those operating in health. The destruction of the large excess of blood and the subsequent disposal of the hæmoglobin and blood pigment were presumably effected in the same way as in health.

Further, the distribution of pigment between spleen and liver was the same as that found in health and the reverse of that obtaining in pernicious anæmia—in the former the spleen containing the largest excess, in pernicious anæmia the liver. This result seems to me to denote a difference in the character of the blood destruction in the two cases.

It is on these experiments, and for the above reason that I base my conclusion that blood destruction in pernicious anæmia is not simply an exaggeration of that which occurs in health. The interpretation I have put upon these results in this relation may, of course, be incorrect. But as regards the question whether the excessive pigment accumulation in the liver cells which one finds in pernicious anæmia, unaccompanied, be it noted, by any corresponding increase in the spleen, and accompanied by a large deposit of pigment in the cells of the convoluted tubules of the kidney, can be brought about by absorption of extravasated blood, the results of these experiments give only one possible answer, and that is in the negative.

SUMMARY.

1. Extravasations are not of the frequency or the magnitude in pernicious anæmia to be themselves the cause of this variety of anæmia. They are not infrequently entirely absent.

2. No evidence of such extravasations are to be found in the lymphatic glands through which the blood must necessarily have been absorbed.

3. The characteristic pigment changes in liver, kidney, and spleen in pernicious anæmia, and the no less characteristic distribution of pigment between these organs cannot be produced by absorption of extravasated blood however large in quantity.

I think the conclusion must be permitted that this form of anæmia does not owe its peculiar pathological features to the occurrence of extravasation. If, then, I fail for the present to be converted to the view so strongly advocated by Dr. Stockman, I trust that it will not be ascribed to any partiality on my part for any different view, but rather to the circumstance that in my experience both pathological data and those derived from experimental results are quite opposed to his view.

PERNICIOUS ANÆMIA A SPECIFIC FORM OF "INTESTINAL" ANÆMIA.

Perhaps a word may be permitted me in criticism of the views which I have myself presented, namely, that pernicious anæmia is a specific form of gastro-intestinal anæmia.

The first remark I would make is that the conclusions I have enunciated seem to carry us both rapidly and far from the starting point from which we set out. They answer the question whether pernicious anæmia is a special form of anæmia in the affirmative, if only on the ground that the pathological changes found in connection are constant and distinctive. They go further. On the basis of data derived from experiment they localise the chief seat of blood change to the portal area, and the organs in relation to it. On the ground of experiment they, moreover, likewise assert that the increased blood destruction which characterises the disease differs in important respects from that occurring in health and resembles rather that caused by certain poisons possessing special destructive properties on the blood. So far, then the conclusions come to are based either on pathological observation or physiological experiment.

I do not consider that (a) beyond establishing the hæmolytic nature of this form of anæmia; (b) establishing further from experiment that in health blood destruction is confined to the portal area; (c) tracing back the blood destruction in pernicious anæmia to this same area; (d) and lastly in establishing that, so far as my experiments show the peculiar

⁶ In four transfusions in the course of three months this animal had to dispose of twice its own quantity of blood.

distribution of blood pigment in pernicious anæmia, cannot be produced experimentally otherwise than by special agents, and especially not by any simple exaggerated blood destruction such as follows transfusion; beyond these points I do not consider that my results go. Therefore in deducing from the foregoing facts that the blood destruction in pernicious anæmia is probably due to the action of some special poison; and inasmuch as it occurs in the portal area, that this poison reaches the blood from the gastro-intestinal canal, one goes further than the facts appear to justify. If these deductions be taken alone apart from their context—the context in this case being the pathological and physiological data above described—they are naturally open to such a criticism.

I do not consider, however, that it is right to consider these deductions apart from their context. The whole view as to pernicious anæmia being a special form of anæmia is based on facts which establish that an excessive blood destruction, initiated within the portal area, is the characteristic feature of this disease; and that this destruction differs from that in health, from other forms of excessive blood destruction, and notably from anything met with in the anæmia of wasting and malignant disease where no increased destruction at all occurs.

DIFFERENCE BETWEEN PERNICIOUS ANÆMIA AND CHLOROSIS: REGARDED BOTH AS VARIETIES OF INTESTINAL ANÆMIA.

I think that the above point is one of some importance in considering the true relationship of pernicious anæmia to other forms of anæmia. For if attention be confined exclusively to the final deduction that pernicious anæmia is the result of the absorption of poisons from the intestinal tract, the disease might erroneously be grouped in the same category as chlorosis and other forms of what might for convenience be termed "intestinal" anæmias, which, if we accept Sir Andrew Clark's view, are also the result of absorption of poisonous substances from the intestine. Both varieties of anæmia—pernicious anæmia and chlorosis or the anæmia of adolescence associated with constipation—would be referred to the absorption of poisons from the intestinal canal.

And yet no greater contrast could exist between two diseases than, in my opinion, exists between pernicious anæmia and chlorosis—chlorosis being the result of defective blood formation (that is, hæmogenic), pernicious anæmia being the result of excessive blood destruction (that is, hæmolytic).

I express no opinion as to the correctness or otherwise of the above view of chlorosis being an intestinal anæmia due to the absorption of deleterious substances. I would merely point out that the view that chlorosis is an intestinal anæmia is in my opinion a purely clinical view. It is devoid of the slightest pathological basis. The blood change is a fact; the constipation may or may not exist. But even if both co-exist, the relationship between the two is as dark as ever. There is no evidence whatever to connect the deficient formation of hæmoglobin with the absorption of poisonous products from the intestine.

In the case of pernicious anæmia, on the other hand, the matter stands as I think very differently. The facts denoting excessive destruction are, I think, indubitable, and are easily demonstrable, whether regard be had to the blood pigment in liver and kidney, to the increased excretion of urinary pigment increased excretion of iron in the urine, to occasional presence of blood-pigment granules in urine. Hardly less conclusive, in my opinion, are the experimental data which appear to indicate: (1) That this destruction occurs in the portal circulation, especially within the spleen; and (2) that it is not simply an exaggeration of that which occurs in health, but resembles rather that produced by special poisons.

To deduce, then, from these data that the blood destruction in pernicious anæmia has special characters of its own, and, inasmuch as it occurs within the portal area, that the agent or agents that affect the blood injuriously reach it from the intestine—such a conclusion, I venture to think, is not so much a hypothesis—in the sense that the view regarding chlorosis is a hypothesis—as a legitimate interpretation of the data, both pathological and physiological, which we have as yet to hand. So far as the available data go, the position I would venture to take up is that the facts in favour of per-

niciouæmansia being a special variety of anæmia are more numerous and more firmly based than those in favour of it being merely an extreme form of ordinary anæmia.

It still remains to be ascertained what the nature of the special intestinal factor is underlying the disease. I have shown in a former paper that it is not any excess of ordinary putrefactive processes. The alternative appears to be the view I then expressed, that the special factor underlying that form of anæmia termed pernicious, "is the presence, under certain favourable conditions, of organisms of specific nature within the gastro-intestinal tract."² It is, in short, a specific form of gastro-intestinal infection.

Moreover, the view that there is something special in pernicious anæmia seems to me not only based on physiological and pathological data, but to accord most fully with the clinical facts. For it serves most simply, in my opinion, to account for the comparative rarity of the disease, a fact, as it appears to me, difficult to explain on the view that it is only an extreme condition, the product of many morbid conditions.

Cancer, elsewhere than in the gastro-intestinal tract, never causes the distinctive features of this variety of anæmia. Moreover, it is only exceptionally that cancer, even in that tract, does so.

Moreover, as I pointed out in my first work, and as Dr. Hale White has very fully shown from a careful study of all the *post-mortem* records of Guy's Hospital, it is mostly in connection with the gastro-intestinal tract that lesions and morbid conditions are found, whether malignant disease, or inflammatory affections, or worms, etc.

The rôle of these various conditions in causing the disease is only a favouring one, and not the chief one. If without the intervention of some special factor they could cause this variety of anæmia, then pernicious anæmia would not be the comparatively rare disease it is. Both clinical and pathological facts appear to me, therefore, to point to something special as the occasion of the destruction which marks this form of anæmia, and the gastro-intestinal tract as the seat of origin of the disease.

Dr. GIBSON observed that he had personally received much benefit from the work of Dr. Hunter, more particularly in regard to the question of treatment by intestinal antiseptics. With reference to the pathological side of the disease he would only remark that in the *post-mortem* examinations he had seen there had often been few, if any, hæmorrhages. The last case under his own care, for example, was one in which by means of treatment the patient had temporarily recovered; his hæmocytes had risen from 500,000 or 600,000 to over 5,000,000; and he had been discharged from hospital in a condition which seemed to be one of health. He returned, however, in a few weeks to tell that he had begun to feel unwell, and within a week he died. After death there was not a trace of hæmorrhage, not even in the retina. The speaker's own opinion was strongly in favour of the views of Dr. Hunter.

A CASE OF PULMONARY HYPERTROPHIC OSTEO-ARTHROPATHY.¹

By F. RUFENACHT WALTERS, M.D., M.R.C.P.,
Physician to the North London Hospital for Consumption.

THE case which I am bringing before you to-day illustrates a condition at first confounded with acromegaly, but subsequently shown by Marie to be quite distinct. It is of interest from its comparative rarity, as only seven other cases have been described as such in English medical papers, and two of these are doubtful, while a third is an Australian case. Taking the whole literature of the subject, I have been able to discover altogether thirty-one cases which have been recognised by their reporters and which appear to be typical, and twenty-eight more which may belong to the same group but are either disputed, insufficiently reported, otherwise described, or not quite typical.

J. M., umbrella maker, aged 34, came under my care on April 1st, 1895, as an out-patient of the North London Consumption Hospital. His

² *Trans. Med. Soc.*, vol. xiii, 1890.

¹ Read in the Section of Pathology at the Annual Meeting of the British Medical Association, held in London July-August, 1895.