suprarenal medulla. Since it is in this tissue that the production of adrenaline takes place, it seems not unlikely that hyperadrenalism may be an associated factor in hypertension, and that its existence may be reflected in the high amino-acid content. This relationship is to be the subject of further investigation.

Associated with the increase in amino-acids in this present series of cases, it was noted that there is also a very marked increase in the blood purins⁷ (estimated as uric acid); values varying between 4.0 and 13.3 mg. per 100 c.cm., instead of the normal 1.0 to 3.0 mg. per 100 c.cm., were obtained. The significance of this finding is not clear, because it is known that uric acid of itself has no influence upon blood pressure; in gout, for example, there is an increase in blood uric acid without any accompanying increase in blood pressure.

There is also to be noted the question of the markedly raised cholesterol content of the blood in hypertension recorded by various observers.⁸ That cholesterol in itself is not responsible for this pathological condition is at once obvious when the large number of patients suffering from hypercholesterolaemia, following upon biliary obstruction, pernicious anaemia, diabetes mellitus, and pregnancy, without concomitant affection of the blood pressure, is taken into consideration. However, it is said that repeated injections of cholesterol into experimental rabbits results in arterio-sclerosis.⁹

The source of the increased cholesterol content of the blood is probably referable to an alteration in the cholesterol metabolism taking place in the liver, and it may be said, therefore, that the hypercholesterolaemia is primarily a liver condition. The cholesterol normally excreted by the liver, together with the bile pigments, bile salts, and other biliary constituents, is derived partially exogenously and partially endogenously; that is to say, partly from sterols ingested as food, and partly from the fatty constituents derived from the breakdown of red blood corpuscles, which is said to occur in the Kupffer cells of the liver. The sterols are converted by the liver, partly into cholesterol, and partly into bile salts,¹⁰ and it may well be that owing to the action of some toxic body upon the liver cells the normal course of metabolism is modified in favour of a production of cholesterol at the expense of bile salts. Such an altered course of metabolism is known to occur, and, indeed, is held to be a factor in the causation of gall-stones.¹¹ Hypercholesterolaemia is therefore probably an associated factor in, rather than a cause of, high blood pressure; but this also is to be the subject of further investigation.

That some toxic factor is concerned is strongly suggested by the work of Gheorghian,¹² who found that the injection of blood from patients with high blood pressure caused a rise in blood pressure in experimental animals. It seems probable that the toxic factor is a normal product of metabolism, since it has been observed by O'Connor¹³ that a high blood pressure resultant upon urinary obstruction in cases of enlarged prostate yields to suprapubic drainage. Retention of this specific toxic body in renal disease, therefore, satisfactorily explains hyperpiesis in this condition. It is to be inferred that the toxin is present only in small amount from the fact that there is no very marked difference between the blood urea and blood non-protein nitrogen figures; indeed, the non-protein nitrogen values, as already pointed out, are remarkably low. The series of blood urea determinations in cases other than nephritis suggested that there is some slight impairment of renal function, but not enough in itself to lead to such a degree of retention of this toxic factor as to cause an increase in blood pressure such as may reasonably be supposed to occur with gross damage to the kidney.

This toxic body may conceivably be present in excess as a result of overproduction. This possibility is suggested by the work of Nuzum, Seegal, Garland, and Osborne,¹⁴ who showed that the blood pressure of a rabbit can be raised and nodular sclerosis produced by feeding on a high protein diet for two years.

The conclusion to be drawn tentatively, therefore, from this present investigation is that hypertension is due to

the presence in excess of a specific amino-acid. This excess may be due to retention resulting from renal disease, to overproduction, or more probably to some impairment of hepatic function whereby this body is not efficiently destroyed.

Finally, I wish to record my thanks to the trustees of the John Burford Carhill Endowment for a grant which has enabled me to carry out this work; to Dr. J. A. Braxton Hicks, director of the John Burford Carhill Laboratories; and to Dr. F. D. M. Hocking, assistant pathologist to Westminster Hospital, for their helpful advice; to Sir James Purves-Stewart, Dr. de Souza, and Dr. Hildred Carhill, for permission to make use of cases in their wards at Westminster Hospital.

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PREVENTION OF TUBERCULOSIS BY MEANS OF TUBERCULIN.

BY

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THERE is general agreement that the subcutaneous tuberculin test is a reliable test of tuberculous infection. Can anyone afford to ignore the warning furnished by such an indication, with knowledge of all the numerous minor manifestations and risks of latent tuberculosis, and of such incidents as the occurrence of tuberculous meningitis, for example, in apparently healthy children? Will any thoughtful and informed individual to-day rest completely satisfied with anything short of guaranteed absence of infection in this disease? Were infection not merely frequent and inevitable, as it appears to be, but irremediable, as seems to be generally assumed, less might be said; and it is probable that a feeling of inevitability is the explanation of the calmness with which wholesale tuberculous infection is regarded, or disregarded, both by the medical profession and by the community at large. "We have all got it," they say, quite pleasantly. But such was not Koch's view, and such is not the view of those who have proved for themselves, or who accept the truth of his assertions, that his specific method of diagnosis is almost uniformly reliable, and that, in addition, incipient tuberculosis can be cured with certainty. Even if his specific methods of treatment be regarded as merely ancillary to the ordinary hygienic methods of cure, the contention that nothing short of complete eradication is a satisfactory standard would still hold force. But some of us regard specific immunization not as ancillary merely, but as a prime factor in curative and preventive treatment, though experience is required to settle the important question of exactly how far we can depend upon its help alone.

The above general argument was more or less embodied in a short paper, with three illustrative cases, published by me in the *Journal* four years ago (October 16th, 1926, p. 682), but since then it has become more clearly envisaged, and the following example was entered upon largely from the theoretical point of view, that in the matter of tuberculosis nothing will be completely satisfactory in the medical history of children but definite, ascertained freedom from infection, indicated by a negative tuberculin test, as is the common practice in veterinary work.

The two girls, A and B, who are the subjects of the following report, were, at the time this record opens, 13 and 14½ years

of age respectively and in good, ordinary health. On being submitted to the tuberculin test, however, the following results were obtained.

B was negative to all five test injections (Chart II), and the Koch phenomenon was absent also. In A, however (Chart I), the first (reduced) test dose produced a negligible effect, but the second injection, two days later, with twice the amount (0.0007 c.cm.), produced a distinct, though atypical, reaction,

CHART I (A).

CHART II (B).

and both injection sites showed marked areas of inflammation. This result in the case of A might not by itself have been accepted as conclusive, but upon proceeding with a series of immunizing injections numerous slight typical reactions were soon forthcoming, including one or two of a more pronounced character, illustrated in Chart III.

There was therefore no doubt as to the positive reactivity of this case.

There was no evidence of focal reaction anywhere; a few minute cervical glands, such as are common in children, may have harboured a trace of infection, or this may have existed in bronchial, mediastinal, or mesenteric glands, but there was no evidence. Nor was there anything suggestive in the medical history. She had had a severe attack of broncho-pneumonia when a few weeks old. There was a liability to colds in the head, which often went down into the chest, but were apparently of an ordinary type, a tendency to get hot and perspire at night, and a tendency to occasional slight marginal blepharitis.

CHART III (A).

Otherwise her general health was very good, though she was considered not quite so hardy as her sister. Subsequent x-ray examination agreed with the stethoscopic findings in being negative.

I proceeded at once with an effort to exterminate the infection. Following Koch, who still remains the most illuminating authority on method in the employment of his preparations, a course of immunization by bacillary emulsion was carried out. Beginning with a dose of 0.0005 c.cm. B.E., and rapidly increasing during the first week, a steady progression of inoculations was carried out at intervals of two, three, or five days, with a proportionate increase of dose of, at first, one-fifth, then one-sixth, ending in the course of three months with 0.5 c.cm. B.E. (2½ mg. bacillary substance). Throughout the course there were frequent mild reactions which, though distinct, caused little or no subjective disturbance. On two occasions the temperature rose, following an injection, to 101.7° and 103.2° respectively, but even on those occasions the disturbance did not amount to more than that of a moderate and temporary febrile attack. This procedure had as its objective attainment of a progressive immunity to B.E., and on reaching the dose of 0.5 c.cm., it was considered that the child's endurance had been sufficiently taxed, and it was decided to leave an interval and

note the result. The general effect of this course of treatment was actually beneficial, apart from the temporary disturbance following each injection, though what was being aimed at was not so much the immediate establishment of an obvious high standard of health as extinction of infection, to be gauged by a future test.

After an interval of six and a half months the test was repeated in both cases, with the results charted below.

CHART IV (A).

CHART V (B).

The previous non-reactor B was again negative (Chart V). The previous reactor A tolerated the former reacting dose of 0.0007 c.cm., and also a dose of twice this amount, with only a trace of temperature disturbance and no clinical symptoms, but reacted typically to the third test dose of 0.0035 c.cm. (Chart IV). On the whole she exhibited some diminution of reactivity, and seemed to be maintaining a more settled type of temperature. The injection site reaction was again decidedly positive, contrasting markedly with that of the negative case. Focal reaction was not observed.

A second series of injections was begun five weeks later with a dose of 0.000005 c.cm., and was carried out rapidly. The dose was doubled with seven out of the first ten injections, the proportionate increase being then gradually reduced in the course of the next ten days to one and one-sixth, which rate of increase—one and one-sixth of each preceding dose—was consistently maintained throughout the remainder of the series, with the exception of the final injection of 1 c.cm. B.E.

CHART VI (A).

CHART VII (B).

(5 mg. solid substance), which was one and one-seventh. During the first forty-nine days forty-two injections were given. The interval between the next six doses was two days, and between the last three doses, three days. The total number of injections was fifty, and the time occupied sixty-six days. The inoculations were very well borne; there was less temperature disturbance than during the previous series, and little or no inconvenience was experienced. The general condition was well maintained throughout, and the weight at the end was slightly more than at the beginning.

The next tuberculin test, carried out seven and a half months later, was interesting, inasmuch as, in the case of A, contrary to expectation, it turned out to be completely negative. The record, together with that of the control case B, also negative as before, is shown above (Charts VI and VII).

With this satisfactory evidence in hand nothing further was done in the way of treatment; there had been no particular

alteration of the general mode of life throughout. According to Koch, we were now "entitled to assume that no fresh or progressive tuberculosis was present which required specific treatment."

After an interval of just over seven months the tests were again repeated, and were again both completely negative.

CHART VIII (A).

CHART IX (B).

There was no restriction of activity during any of the reported tests, so that the influence of exercise upon these temperature records is not excluded.

A few words may be added concerning the findings at the sites of injection. There was in general distinct evidence in the reactor, during the reactive period, of the incidence of the Koch phenomenon—increased inflammatory reaction at the injection site—in striking contrast with

the entirely negative, or quite trifling, effect in the case of B; but it is of interest to note that even after A's temperature test record had become entirely negative there was still a distinctly greater degree of local sensitiveness in her case than in the case of B. This is believed to be due to a corresponding inherited difference in the quality of the tissues, A's skin being soft and fair and easily reddened by the sun, while B's skin is firmer, darker, and less sensitive. It should be noted, however, that there was a relative diminution in sensitiveness in the case of the reactor, as, during the phase of positive general reactivity, her injection site reactivity was also distinctly greater than it became subsequently, at the time of the two negative general tests.

These results are a source of legitimate satisfaction, as both individuals can now be placed in the tuberculin-tested negative group, and guaranteed, so far, free from tuberculosis. The details of the testing process have been completely mastered by the patients themselves, and entail no inconvenience and no trouble beyond the taking of the temperature record. It is purposed to repeat this test annually in future, at all events for a time.

Can this be taken as an example? I believe it can to some extent; for it is the actual accomplishment of a result which was deliberately aimed at beforehand, and which, on theoretical grounds, has much to support it. The subcutaneous tuberculin reaction is generally accepted as definite proof of infection, and there has now accumulated a large body of evidence in support of the curative efficacy of tuberculin treatment. If this be accepted the conclusion is clear. We have here a method of elimination worthy of close attention and elaboration. In a search for other preparations and other procedures have we not strayed from the path clearly pointed out by Koch so many years ago?

FORTY CASES OF HYDATID DISEASE.

BY

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HYDATID disease in Europe is sufficiently uncommon to warrant occasional reports on series of cases, with special reference to treatment and results. The etiology of the disease is too well known to require special comment here. Suffice it to say that in primitive agricultural countries where sheep and dogs abound and proper slaughterhouses are rare the echinococcus finds its ideal home.

Propagation is effected either by direct contact with dogs or by the use of contaminated feeding utensils. There appear to be no special symptoms characteristic of hydatid disease, those produced originating from the presence of a tumour causing pressure upon, or destruction of, adjacent structures. These secondary symptoms vary considerably, depending upon the site of the cyst and its size; typical examples are jaundice, pruritus, ascites, haemoptysis, etc.

Rupture is uncommon, though one of my patients (No. 35) was admitted as suffering from a perforated gastric ulcer of which he showed many classical signs. Laparotomy, however, revealed rupture of a hydatid cyst close to the portal fissure. Suppuration occurs occasionally, and may give rise to all the symptoms of an acute cholecystitis (No. 40). Gall-stones and chronic cholecystitis have been noted in two patients (Nos. 16 and 20), both of whom were subjected to cholecystectomy.

From Table I it will be seen that in this series the incidence of the disease among males and females is equal, and that the majority of cases have been of the liver. The exact figures are: cysts of the liver 31, other sites 9. As ascertained up to June 30th, 1930, the results of treatment were as follows: cured 29, relieved 6, died 5. Considering the poor physique of many of the patients, a number of whom were also suffering from chronic malaria, these results may be regarded as quite satisfactory. The period covered by the series is from September, 1926, to April, 1930; the cases in Table I, which are in chronological order, show a remarkable sequence of male and female patients.

TABLE I.

No.	Sex and Age.	Site.	Treat-ment.	Result.	No.	Sex and Age.	Site.	Treat-ment.	Result.
1	F., 53	Liver	Exsection	C	21	M., 30	Liver	Drainage & obliteration	R
2	F., 50	Liver	Drainage	C	22	F., 50	Liver	Exsection	C
3	M., 25	Liver	Exsection	C	23	M., 46	Liver	Drainage	R
4	F., 30	Thigh	Drainage	C	24	M., 18	Ischio-rectal	Drainage	C
5	M., 61	Liver	Exsection	C	25	F., 38	Omentum	Removal	C
6	M., 12	Lung	Resection & drainage	C	26	F., 25	Liver	Drainage	R
7	F., 16	Liver	Drainage & obliteration	C	27	F., 25	Liver	Exsection	C
8	F., 24	Omentum	Removed	C	28	F., 12	Liver	Drainage	D
9	M., 40	Liver	Drainage	D	29	M., 30	Liver	Drainage	R
10	M., 43	Lung	Paracentesis	R	30	F., 55	Uterus	Curettage	D
11	F., 55	Liver	Drainage	C	31	F., 21	Liver	Exsection	C
12	M., 26	Omentum	Removed	C	32	F., 20	Liver	Drainage	C
13	F., 45	Liver	Drainage	R	33	F., 40	Liver	Drainage	C
14	M., 40	Liver	Drainage	D	34	M., 64	Liver	Exsection	C
15	M., 25	Liver	Exsection	C	35	M., 3	Liver	Exsection	C
16	F., 34	Liver	Drainage	C	36	M., 31	Liver	Drainage	C
17	F., 25	Liver	Drainage & obliteration	C	37	M., 10	Liver	Drainage	D
18	M., 20	Liver	Drainage	R	38	F., 30	Liver	Drainage	R
19	F., 40	Liver	Drainage	C	39	M., 47	Lung	Resection & drainage	C
20	F., 70	Liver	Exsection	C	40	M., 25	Liver	Drainage	C

Notes.—In Case No. 5 an operation was recently performed for another cyst; Nos. 16 and 18 were associated with gall-stones; No. 36 ruptured into peritoneal cavity; and No. 40 had acute suppuration. C=cured; R=relieved; D=died.

OPERATIVE TREATMENT.

Cysts of the Liver.

The methods adopted in the case of liver cysts are three in number: (1) drainage; (2) drainage with partial obliteration of the cavity; (3) complete removal. In the present series 18 cases were treated by drainage, 3 by partial obliteration, and 10 by complete removal.