

when these wet shafts were pumped out on their advice the incidence markedly decreased. They also suggested that possibly the entry of the organisms might be through the skin—a guinea-pig can be infected through the skin—but they were of the opinion, after a general review, that the mode of entry was through the alimentary canal. A point of interest is, though it is complicated by the contemporary onset of colder weather, that the incidence of the disease in our area had practically ceased, and that the troops were issued with high "gum" boots a week before we saw the last case of jaundice. Since writing the last sentence two cases have been noted.

In the proofs of a forthcoming paper by the Japanese workers which was sent to us by Dr. Flexner it is stated that they have succeeded in finding the spirochætae of jaundice in the kidneys and urine of 33 per cent. of ordinary field-rats in the infected areas in Japan. They suggest that the infection may be conveyed by the rats' urine, either directly or indirectly. We have not yet had time to confirm these findings, but hope soon to be able to do so.

Cases have occurred in the Allied troops in different parts of the front. Dr. L. Martin has published an account of some cases investigated by him in the French Army, and we also know of other cases which have occurred among the troops in Flanders which have also been proved experimentally. Whatever be the portal of entry of the spirochæta it would appear that wet and muddy trenches are a predisposing factor. If the infection had been water-borne there would have been a more widespread epidemic. If vermin or mosquitoes had been the infecting agents the epidemic could hardly have been so localised, and the experiments which we have performed, such as they are, would seem to exonerate them. We would also add that there have been up to now no ward or laboratory infections. The patients have been cared for in a general ward with no further precautions than would be carried out if they were enteric cases.

#### Conclusion.

The clinical and experimental examination of about 100 cases of Weil's disease which we have been in a position to investigate during the last six months justifies, we think, the conclusion that the disease, as it has been observed among British troops in Flanders, is identical with that described by Inada and his collaborators in Japan.

The virulence of the infection in the cases seen here is much less than that described in Japan, which is well shown by the comparatively low mortality. All the essential findings of the Japanese authors have been confirmed, save that our cultural attempts have so far failed.

In addition we have noted the occurrence of cases of spirochætosis which have not shown any external jaundice.

The success of our work is to a great extent due to the efficiency and zeal of our laboratory attendant, Sergeant B. Baker, R.A.M.C. (T.F.).

*After-note.*—Since writing the paper we have been able to confirm the statement of the Japanese workers mentioned in the paper with regard to the finding of the spirochætae in the kidneys of field-rats. Of 9 rats taken from the right part of Segment 1 in the chart in the paper, 5 proved infective to guinea-pigs. Of 6 rats from the left end of Segment 1 one communicated the disease. The kidney of the rat was crushed and emulsified, and injected intraperitoneally into the guinea pig. The disease in the infected animal was typical, and we have found the typical *S. ictero hæmorrhagica* in the organs of the guinea-pig. Levaditi preparations of the rat kidney have shown the spirochætae, and we have also found them in films made from an emulsion of the kidney stained by Fontana's stain.

**MEDICAL SICKNESS, ANNUITY, AND LIFE ASSURANCE FRIENDLY SOCIETY.**—The usual monthly meeting of the committee was held at 300, High Holborn, on Jan. 19th, Dr. F. J. Allan being in the chair. The reports submitted showed the epidemic of influenza which has been universal throughout the country to have affected the medical profession. It was decided to apply for a further £15,000 in the new 5 per cent. War Loan, and to convert the society's existing holdings, amounting to £25,500, also in the new 5 per cent. War Loan. This transaction, when complete, will give the society a total of £40,500. The important question of the depreciation of stock values was considered and a further £6000 added to the investment reserve, which now stands at £10,000.

## TOXIC JAUNDICE IN MUNITION WORKERS.<sup>1</sup>

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THE aspects of the subject dealt with in this contribution are: (I.) the morphological changes in the blood occurring in a series of 14 clinical cases of toxic jaundice from trinitrotoluene poisoning; and (II.) certain points in the morbid anatomy of the disease as observed in a series of seven fatal cases.

### I.—Changes in the Blood.

The 14 cases here recorded are those of munition workers who were admitted to hospital during the months August to December, 1916. Most of them have been under observation for weeks or months, and as many of them are still coming up regularly for examination these results must be regarded as partial and preliminary. Sufficient has already been made out, however, to show that very profound changes in the composition of the blood may occur as a result of trinitrotoluene poisoning; indeed, it might be said that such changes are the rule in cases where pronounced clinical symptoms, and especially jaundice, have manifested themselves. One case only out of the 14 examined, a man who, clinically, was never seriously ill, showed no blood changes. All the others had definite deviations from the normal of some sort or another.

*A. Changes in the leucocytes.*—These were worked out on a basis of the absolute number per cubic millimetre of each variety of leucocyte, and the following fairly elastic figures were taken as the limits of the normal:—

Neutrophil polymorphs	...	3600–6750	per c.mm.
Lymphocytes	...	1200–2700	"
Eosinophils	...	30–360	"

The leucocytic changes as calculated on this basis may be given as: (a) Neutrophil leucopenia, (b) neutrophil leucocytosis, (c) lymphocytosis, and (d) eosinophilia.

(a) *Neutrophil leucopenia.*—This, the most striking of the leucocytic changes, was present at some stage of the disease in 9 out of 14 cases (Nos. 1, 2, 4, 8, 9, 10, 12, 13, and 14). In 4 of these (Nos. 1, 2, 10, and 12), 2 of them fatal, the leucopenia was extreme, under 1100 per c.mm.; of the other 5 affected, the highest neutrophil count was 3175. In the 2 fatal cases (Nos. 1 and 2) the leucopenia was progressive and terminal, the final counts being 120 and 636 respectively. One case (No. 10) illustrates very well the polymorphonuclear recovery which accompanied clinical improvement in the condition of the patient. While the patient was seriously ill the neutrophils numbered only 1080 and 1092. A fortnight after her discharge from hospital they were 6280. In 3 cases (Nos. 2, 8, and 10), one of them fatal (No. 2), neutrophil leucopenia was associated with an anæmia of pernicious type (*vide infra*).

A progressive failure of the leucoblastic function of the bone marrow is therefore to be regarded as one of the most common manifestations of severe trinitrotoluene poisoning, but that it is not a constant feature in fatal cases is shown by Case 3, details of which are given below. It may be mentioned also that in another fatal case, which was not investigated during life, the bone marrow showed evidence of great leucoblastic, as well as erythroblastic, activity. Here the whole duration of illness was only one month, yet the liver changes were extreme, and it seems reasonable to suppose that there had not been time for the development of the full toxic action on the marrow. Whether this neutrophilic failure is due to a direct action of the poison on the leucoblastic tissue one cannot say with certainty, inasmuch as all the cases in which it occurred presented clinical evidence of an antecedent or accompanying hepatic lesion (jaundice, &c.), while both the fatal cases showed a typical advanced trinitrotoluene cirrhosis of the liver post mortem.

(b) *Neutrophil leucocytosis.*—This change was present in a notable degree in one (fatal) case only (No. 3). Here, at the first examination, the total leucocyte count was 14,200,

<sup>1</sup> A contribution to the discussion on the subject at the Royal Society of Medicine on Tuesday, Jan. 23rd.

of which 10,000, or 70.5 per cent., were polymorphonuclears, while a month later, on the day before the patient's death, the figures were 22,000 and 19,200 (87.25 per cent.) respectively. This change was unassociated with any variation in the lymphocytes or in the red cells or hæmoglobin, but at the first count there was an eosinophilia of 1000 per c.mm. Post-mortem examination showed the bone marrow in the shaft of the femur to be largely fatty, with a narrow peripheral zone of red. Microscopically there were found small foci of very active leucoblastic proliferation. The inspection,

Table giving a Summary of Blood Changes in 14 Cases of Trinitrotoluene Poisoning.

Case.	Age.	Lymphocy- tosis.	Polymorpho- nuclear.		Anæmia of pernicious type.	Eosinophilia.
			Leuco- cytosis.	Leuco- penia.		
1	30	—	+sl.	++	—	—
2	35	—	—	++	—	—
3*	52	—	++	—	+	+ <sup>1</sup>
4	24	+	—	+	—	—
5	28	+	—	—	—	+ <sup>2</sup>
6	20	+	—	—	—	—
7	40	++	—	—	—	—
8	19	++	—	+	+	—
9	22	+	+sl.	++	—	—
10	49	+	—	++	+sl.	—
11*	31	—	—	—	—	—
12	34	—	—	++	—	—
13	18	+	+sl.	+	—	+ <sup>1</sup>
14	17	—	—	+sl.	—	—
—	—	+, above 3000, ++, above 4100 per c.mm.	+, over 6800, ++, over 19,000 per c.mm.	+, under 3200, ++, under 1100 per c.mm.	+, Erythro- cytes under 1,600,000, +sl., under 3,000,000, per c.mm.	+ <sup>1</sup> , over 1000, + <sup>2</sup> , over 400 per c.mm.
—	—	Upper limit of normal, 2700 per c.mm.	Normal limits, 3600-6750 per c.mm.		In each case colour index above 1.	Upper limit of normal, 360 per c.mm.

\* Male.

however, failed to reveal any inflammatory cause for the persistent leucocytosis, which stands out in striking contrast to the other fatal and clinically serious cases. In three other cases (Nos. 1, 9, and 13) an early and slight neutrophilia was present, but was speedily followed in each instance by a pronounced leucopenia.

(c) *Lymphocytosis*.—This was one of the most commonly observed changes; it occurred at some time or other in 9 out of 14 cases (Nos. 2, 4, 5, 6, 7, 8, 9, 10, and 13), and varied in different patients from 3150 to 5100 per c.mm. Considerable variations were often seen from time to time in the same patient, but the fluctuations were irregular and did not appear to have much, if any, significance. In the remaining 5 cases the lymphocytes ranged within normal limits, except that in two cases (Nos. 8 and 10) there was a single temporary drop to 1040 and 1160 respectively. The chief point to be observed is that even in fatal cases and in those showing profound polymorphonuclear or erythrocytic failure the lymphocytes were maintained at or above the normal level. In two cases a lymphocytosis was the only change noted.

(d) *Eosinophilia*.—This was observed in three cases (Nos. 3, 5, and 13), and in two of these it was well marked, once (No. 3) accompanying a marked neutrophil leucocytosis, once (No. 13) with a slight neutrophilia. It appears to be of doubtful significance, but it may be noted that in no case did an excess of eosinophils coexist with a neutrophil leucopenia. Altogether the number of eosinophils was found to be a very variable quantity in these cases.

B. *Changes in the erythrocytes and hæmoglobin*.—These have been much less conspicuous than the leucocytic changes. A serious degree of anæmia was observed in 3 cases only, all the others, including 2 of the fatal cases, had red cell counts of over 4,000,000, but a slight grade of chlorotic anæmia was present in several. In the 3 serious cases the anæmia was of the "pernicious" type, with a colour index over 1, but very varying degrees of severity were presented. In the most extreme case there was a fall in the red cells to well under 1,000,000, and as the hæmoglobin was not reduced to anything like the same extent (25-30 per cent.) a high colour index (1.5 to 1.8)

presented itself. The erythrocytes in this case were greatly altered qualitatively, anisocytosis was well marked, with many megalocytes. During the worst phase numerous erythroblasts made their appearance, and polychromatophilia was present. In the other 2 cases the red cells fell to 1,500,000 and 2,900,000 respectively, with colour indices of 1.4 and 1.1. Qualitative changes in the red cells were not striking, some anisocytosis with many megalocytes, and in one case slight polychromatophilia. It is to be noted that punctate basophilia was not seen in any case, which is in striking contrast to the findings of Malden in workers in dinitrobenzene and anilin.

## II.—Some Points in the Morbid Anatomy.

One of the chief problems here is the nature of the liver changes. The lesion appears to lie somewhere between a subacute yellow atrophy and an ordinary multilobular cirrhosis of irregular distribution. The action of the poison on the hepatic cells is probably slow and insidious, and the degenerative changes are speedily followed, if not actually accompanied, by leucocytic infiltration and fibroblastic overgrowth. The degenerative and other processes, once set going, are progressive, even when the patient has been removed from the influence of the poison, and in a certain proportion of cases a fatal termination ensues in from 4 to 12 weeks after the first symptoms. Certain portions of liver tissue escape complete destruction, and these show evidence of more or less regenerative hyperplasia. It may be assumed that in some cases this persistent and regenerated hepatic tissue will be sufficient to maintain the life of the individual for a considerably longer period than three months, but what the ultimate fate of such persons will be time alone can show. The after-history of surviving cases of trinitrotoluene poisoning will require to be carefully investigated, not only on account of their great intrinsic interest, but also for the light they may throw on cirrhosis of the liver in general.

I have recently had the opportunity of examining, post mortem, 12 cases of accidental death in workers at a munition factory. In one of these, a woman aged 38, distinct liver changes were discovered—namely, an early but definite round-cell infiltration of the portal tracts and numerous discrete (? regenerative) nodules of varying size scattered throughout the organ.

With regard to the series of 7 post-mortem examinations on which these remarks are based a few points of outstanding interest may briefly be referred to.

The weight of the liver varied from 20 to 32 ounces, the average being 27 ounces. The degenerative cirrhotic process, as evidenced by the dark-red contracted areas, was always most advanced in the left lobe and inferior marginal region of the right lobe. Often these two portions of the organ were composed almost entirely of red tissue. Another striking feature was the frequency with which large rounded yellow nodules projected from the under surface of the right lobe on each side of the gall-bladder, less often from the Spigelian and quadrate lobes.

The bone marrow of the femur was examined in 6 cases. In 5 of these the red marrow was in excess, extending well down the shaft of the bone, but on microscopic examination a definitely erythroblastic reaction was found in one case only. Here the yellow marrow of the shaft was completely replaced by a cellular red marrow, the appearance being comparable to that seen in pernicious anæmia. Evidence of considerable leucoblastic activity was also present. Unfortunately, there had been no opportunity to examine the blood during life. In Case 3, the patient with neutrophil leucocytosis, the shaft marrow was fatty, with a narrow red layer next the bone. Microscopically some small foci of active leucoblastic proliferation were seen.

The spleen was never appreciably enlarged, the weight varying from 4 to 7 ounces in different cases.

Ascites to the extent of five or six pints was present in 3 cases. Clinical examination of the fluid in one case showed a very scanty cellular deposit with a preponderance of leucocytes. A very few red blood corpuscles and endothelial cells were also present.

Hæmorrhages in various situations were present in 5 cases, most frequently in the peritoneum and pericardium, less frequently in the stomach, lungs, pleuræ, endocardium, and skin. In one case there was very extensive hæmorrhage into the peritoneum and subperitoneal cellular tissue, especially

of the omenta, mesocolon, mesentery, and appendices epiploicæ. In the same case there was profuse terminal oozing into the stomach. In the other 4 cases the hæmorrhages were mainly petechial.

Perhaps the most interesting single case was that of a man, aged 52, where the lesions of trinitrotoluene poisoning were associated with a well-marked hæmochromatosis affecting especially the liver, pancreas, and abdominal lymph glands. Unfortunately, the urine had not been examined during life, and at the post-mortem examination the bladder was empty. The hæmosiderin granules, which gave a bright blue colour when treated with potassium ferrocyanide and hot hydrochloric acid, but a green colour with cold hydrochloric, were most abundant in the lymph glands. It is fairly certain that we are here dealing with two independent affections, inasmuch as it has been shown that a very long time, a year or more, is required for the deposition of such large amounts of iron-containing pigment, while the illness due to trinitrotoluene was in this man's case only of 10 weeks' duration. It is possible, however, that the pre-existing hepatic lesion may have made that organ unduly susceptible to the action of the poison.

Leeds.

## Reviews and Notices of Books.

### Gynecology.

By WILLIAM P. GRAVES, A.B., M.D., Professor of Gynecology at Harvard Medical School. With 303 half-tone and pen drawings by the Author and 122 microscopic drawings by MARGARET CONGEE and RUTH HESTIS; 66 of the illustrations in colours. London and Philadelphia: W. B. Saunders Company. 1916. Pp. 777. Price 30s.

THIS is designed both as a text-book and a general reference work. It is divided into three parts; the first deals with the physiology of the pelvic organs and the relation of gynecology to the general organism, the second is intended primarily for the undergraduate and deals with gynecological diseases, and the third is devoted exclusively to the technique of gynecological surgery, and is written for the assistance of the advanced student and practitioner. The section dealing with the relationship of gynecology to the general organism forms a most interesting and instructive review of our knowledge on these points and will prove extremely useful to the student in view of the increasing importance at the present time of the internal secreting glands. It includes an account of hypo-function of the ovaries and its relation to infantilism and a useful résumé of Schickele and Keller's views on chronic metritis and cystic degeneration of the ovaries and their relation to uterine hæmorrhage. Our knowledge, scanty as it is, of the relations to gynecological diseases of the thyroid, the parathyroid, the adrenals, and the hypophysis is also excellently summarised. As the author points out, the subject is a comparatively new one, and he is anxious to impress upon the student the importance of the correlation of all the branches of medicine and surgery. The completeness with which the author treats these subjects is exemplified by the fact that he includes in his review such conditions as the nervous system, the peritoneum and omentum, the bones and joints, the gall-bladder, and the acute infectious diseases.

Part II. contains a very good account of the common gynecological affections. We notice that the author does not distinguish between kraurosis and leucoplakia vulvæ, and the statement that the main symptom of kraurosis is itching is not quite correct. Professor Graves correctly points out that the subject of endometritis is in a state of considerable confusion, yet he does not do much to simplify matters, as he still describes gland hypertrophy resulting from circulatory changes under the heading of endometritis. The section on cystitis and pyelitis is good. There is an interesting description of the radiation treatment of cancer and of Percy's heat treatment. The excellent results obtained by Howard Kelly in the treatment of fibroid tumours by radium are also alluded to—a mode of treatment of much promise for the future. It is surprising to find in so excellent a book a recommendation of the use of intra-uterine pessaries in the treatment of antelexion of the uterus.

In the section dealing with the amenorrhœa of youth, Professor Graves also quotes Rieck's treatment of amenorrhœa and oligomenorrhœa by the intra-uterine stem pessary only to condemn it. Would it not have been better to have omitted it altogether?

The various gynecological operations are well and clearly described in Part III., and the value of the book is greatly enhanced by the very numerous and good illustrations, mainly drawn by the author himself. The drawings of the microscopic sections are also good, and the index is a complete one.

### *Raymond, or Life and Death.*

By Sir OLIVER J. LODGE. London: Methuen and Co., Limited. 1916. Pp. 404. Price 10s. 6d. net.

MORE than three years ago, in his presidential address before the British Association, Sir Oliver Lodge stated his conviction that memory and affection are not limited to that association with matter by which alone they can manifest themselves here and now, and that—as a corollary of this persistence—personality itself persists beyond bodily death. He had been led to this conclusion, not by such things as intuition and revelation, but by the careful and systematic examination of occurrences still regarded as occult, and by the reduction of these to order through the methods of science. The book before us records a further examination of the evidence for the survival of personality in a particular case, and as the case is the writer's youngest son, who met his death during the attack on Hooze Hill in September, 1915, it has a special and poignant interest.

Sir Oliver Lodge deals with his subject in three parts. The first, described as the "Normal Portion," gives a short biographical sketch of Raymond Lodge as he was in life, with his letters from the front and others from brother officers about him. The second part is entitled "Super-normal Portion," and deals with the messages received from Raymond Lodge after his death—"communications," as the author describes them, "from which sentiment is not excluded, though still they appear to be guided and managed with intelligent and on the whole evidential purpose." In the third part, with the heading "Life and Death," the author defines the part which he takes in the great controversy and his view of "the real existence of some kind of vital essence or vivifying principle as a controlling and guiding entity."

With the first and third parts criticism has little place. For the intimate glimpse into a strenuous young life lamentably cut short nothing but gratitude can be felt, and this part alone makes the book worth reading. The equally intimate glimpse into the author's own philosophy—the result of a lifetime of steady patient work and thought—is a second gift of no mean value. The value of the "communications" is much more difficult to appraise. The obvious criticism must indeed arise in every mind: how trivial and indeed almost contemptible are the communications themselves. And the author has done well to devote a chapter to precisely this criticism, explaining that the demand for a proof of the identity of a departed friend is best achieved by the recalling of trifling reminiscences. Affection and lofty sentiment must be the common attributes of the spirit world, but particular little jokes and morsels of fun give away the identity of the "communicator." Let us grant this as reasonable, and let us accept the possibility of communications by this means through a sensitive control, we believe, for our part, that intercourse between spirit and spirit, when any occurs, occurs without the medium of a control. Sir Oliver Lodge appears to have reached by a system of wiring and motor-transformers what may conceivably be freely accessible in wireless telegraphy—if such a simile can be justified.

### LIBRARY TABLE.

*Text-book of Nervous Diseases for the Use of Students and Practitioners of Medicine.* By CHARLES L. DANA, A.M., M.D., LL.D., Professor of Nervous Diseases in Cornell University Medical College. Eighth edition. Bristol: John Wright and Sons. 1916. Pp. 632. Price 21s. net.—Dr. C. L. Dana's well-known text-book of nervous diseases has reached an eighth edition. The previous one was reviewed by us in 1910, but such are the advances in the study of diseases of the nervous system that text-books rather rapidly become