7731 P

An Experimental Study of the So-Called Liver Death Syndrome in Biliary Surgery.

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A series of experiments was undertaken with the idea of reproducing in experimental animals the clinical and postmortem findings observed in so-called "liver deaths" after biliary surgery, to which Heyd[1] first called attention. Such deaths fall into 2 distinct groups. In the first group death occurs shortly after operation, hyperpyrexia is the outstanding symptom, and degenerative liver changes are the only notable autopsy finding. In the second group death is deferred for 10 to 14 days, uremic symptoms predominate, and autopsy reveals the liver changes just described, plus similar degenerative changes in the convoluted tubules of the kidney. None of the usual surgical causes of death is apparent.

Ten sets of experiments were performed upon dogs whose renal competency was assured by detailed preoperative studies. The following experiments failed to reproduce the clinical and postmortem pictures desired:

1. Traumatic necrosis of the liver by various manual and instrumental methods. Eight dogs.
2. Various types of interference with the hepatic and portal circulation.* Sixteen dogs.
3. Obstruction of the biliary tree by ligation and division of the common duct, with or without cholecystectomy. Twelve dogs.
4. Intraperitoneal implantation of normal liver, as done by Andrews and Hrdina[2] and previous workers. Approximately 150 gm. of liver was implanted in each of 5 dogs.
5. Intraperitoneal injection of normal liver, as described by the same authors, who were able by this method to cause an autolytic peritonitis as in experiment 4, a finding which we could not confirm. Three dogs were used. Three hundred grams ground liver was extracted in 3,000 cc. of warm sterile water and concentrated to 17, 18.5 and 25 cc. respectively.
6. Intravenous injection of 20 cc. of extract of normal liver, extracted and concentrated in the proportion and by the method just described. One dog.

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[1] Heyd, C. G., *Ann. Surg.*, 1924, **79**, 55.

* A detailed study of this group of experiments will shortly be published.

[2] Andrews, E., and Hrdina, L., *Surg. Gynec. Obst.*, 1931, **52**, 61.

The following experiments were wholly or partially successful:

7. Obstruction of the biliary tree, as described in experiment 3 was continued 12 to 20 days and then released in 8 of the dogs which survived the first operation. The clinical picture of the second group of liver-kidney deaths was reproduced in all cases. Urinalysis and blood chemistry showed the changes characteristic of an acute renal condition, the blood nonprotein-nitrogen rising in 5 cases to 72, 81, 93, 105, and 171 mg. per 100 cc. All the animals died in uremic coma or were sacrificed when their condition was terminal and all the autopsies revealed degenerative changes in the liver and kidney corresponding to the histologic picture seen in human patients.

8. Intravenous and intraperitoneal extracts of the livers of the dogs in experiment 7 were injected in 10 other dogs, but did not reproduce the desired changes. One hundred thirty grams of liver was extracted in 130 cc. of sterile water, normal saline solution and 95% alcohol respectively, the alcoholic extract being concentrated to 13 cc.

9. Intravenous and intraperitoneal injection of saline and water extracts made by the above method in 6 dogs in which an attempt had been made to produce liver necrosis by chemical methods (the use of a carbon tetrachloride mixture). This experiment was likewise unsuccessful, but in the light of our other studies it now seems highly probable that experiment 8 failed because the extracts were not sufficiently concentrated, and that experiment 9 failed for the same reason, and because so long a time elapsed between production of the liver damage and injection that regeneration could have occurred.

10. Intraperitoneal injection with the water and saline extract of the liver of a patient who died a typical hyperpyrexia death after cholecystectomy produced the clinical and histologic picture characteristic of the liver-kidney syndrome in human patients, the degenerative changes in the liver and in the convoluted tubules of the kidneys being very marked. Similar injections with alcoholic extract of the same liver did not reproduce these changes. Three dogs. All the extracts were made in the same proportion, 130 gm. of liver to 150 cc. of sterile water, normal saline solution, and 95% alcohol respectively, and 30, 50, and 75 cc. of the extract were injected on successive days in each dog.

From these experiments and in the light of clinical studies elsewhere reported,[3] it is concluded: 1. The release of biliary obstruc-

[3] Boyce, F. F., and McFetridge, E. M., *Arch. Surg.*, in press.

tion rather than the obstruction itself is responsible for the fatal outcome in some cases of biliary surgery. 2. The hepatic changes always present in biliary disease are aggravated in some cases by the surgery instituted to relieve it, which imposes upon an already damaged liver an intolerable burden. As a result of the degenerative hepatic changes, there is released into the circulation a toxic substance which is presumed to be a water-soluble foreign protein. 3. When, after liver function fails, the kidney takes up the function of detoxification, there is resulting damage to its convoluted tubules, through which foreign proteins are excreted. 4. The liver-kidney syndrome is a single pathologic process, of which the kidney pathology represents the second stage.

Further experiments are at present being undertaken to support the hypothesis herein set forth.

7732 P

Precipitation and Complement-Fixation Reactions with Pneumococcus Soluble Specific Substance.

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The following observations, while but part of a broader investigation of the complement-fixation test with specific bacterial antigens in the diagnosis of infection,[1-4] have, nevertheless, a special significance in that they indicate the relative sensitivity of precipitation and of complement fixation with a highly purified bacterial antigen. The reports of other observers have been based upon studies with more complex antigens.[5-7]

[1] Wadsworth, Augustus, Maltaner, Frank, and Maltaner, Elizabeth, *J. Immunol.*, 1925, **10**, 241.

[2] Wadsworth, Augustus. In: The Newer Knowledge of Bacteriology and Immunology, Jordan and Falk, editors, Chicago, University of Chicago Press, 1928, p. 831.

[3] Wadsworth, A. B., van Amstel, J. E., and Brigham, M. W., *J. Immunol.*, 1930, **19**, 289.

[4] Rice, C. E., *J. Immunol.*, 1932, **22**, 67.

[5] Dean, H. R., *Z. f. Immunitäts.*, 1912, **13**, 84.

[6] Parker, J. T., *J. Immunol.*, 1923, **8**, 223.

[7] Goldsworthy, N. E., *J. Path. and Bact.*, 1928, **31**, 220.