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Technique and Indications of the Therapeutic Intramedullar Transfusion of the Bone Marrow in Children.

By JAN RASZEK-ROSENBUSCH.

Among various, mainly, but not exclusively haemopoietic organs, which are responsible for the cellular and biochemical structure of the blood, the bone-marrow plays one of the leading roles as the site of production and ripening of a great many blood elements.

It meant, therefore, a very great achievement for the study of biology of blood as well as for the pathology, diagnostics and

prognostics of the disorders of the blood, when the bone-marrow has been made accessible to bioptic examination.

The first studies of marrow were made on samples from the tibia and the femur (*Pianese* 1903, *Ghedini* 1908). These bones, however, are of the later ones to react to haemopoietic disorders and are rather difficult to puncture or to trephine. *Seyfarth* was the first who 1923 obtained intravitally specimens of bone-marrow from the sternum by trephine. This method has been then developed as a diagnostic procedure by *Custer* (1933), *Dameshek, Henstell,* and *Valentine* (1937), and very many others.

The introduction of the biopsy of the bone-marrow on a larger scale, as a routine method of clinical investigation has only been made possible, however, since a much simpler procedure of an intravital access to the bone-marrow, by means of the *sternal puncture,* has been devised by *Arinkin* in 1929. A flood of publications has since revealed the utmost diagnostic and prognostic value of the biopsy of the marrow in all kinds of disorders of the blood and also in infectious diseases.

The discovery of an easy access to the bone-marrow has, on the other hand, opened quite new possibilities, also for *therapeutic* methods. The direct application of the therapeutic agent to the diseased organ intensifies obviously its activity and permits to attain locally much higher concentrations of active substance than is possible by other means of administration. The most striking example for the importance of the local application of drugs and biologically active substances, made possible thanks to the discovery of a simple method of access to the diseased organ for primarily only diagnostic purposes, is the *intralumbar* therapy. Since the introduction of the *lumbar puncture* by *Quincke,* not only diagnostics, but also the treatment of many diseases of the central nervous system underwent a thorough and extremely beneficial change. The analogy to the *sternal puncture* is obvious. And, as a matter of fact, already *Arinkin* himself endeavoured to use his method for the introduction of drugs (Calciumsalts), *Markoff* tried next the introduction of liver extracts by the same method. And in the last years the administration of transfusion fluids into bone-marrow cavities has been advocated by *Henning* (1940), *Tocantins* et al. (1941), *Gimson* (1944), and many others. Specially designed needles have been devised by several authors for this purpose and even a special pattern of such a needle for "intramedullary transfusion" has been approved by the Medical Research Council in Great Britain.

My own investigations on this subject started independently from the above mentioned, as far back as 1938, at the Children's

Hospital of the Pediatric Department of the Medical College in the John Casimir University in Lvov, from two theoretical points of view:

1. I was interested in the direct accessibility of the bone-marrow for the therapeutic agents in general, as a method of treatment.

2. I suspected, together with Professor *Groër,* that the bone-marrow either produces, or stores some yet unknown, but necessary biological factors, which may be responsible for the normal structure and functioning of the haemopoietic system.

From the point of view of this working hypothesis the problem of a possible substitutional therapy by means of a *direct transfer of bone-marrow from healthy donors into the bone-marrow cavity of diseased receivers* acquires quite an outstanding importance.

I decided thus to work out a method of direct transfusion of the fully active and healthy bone-marrow into the marrow cavity of diseased children and to study the effects of such transfusions in cases, in which disturbances of biological activity of the bone-marrow could be suspected.

The technique of this procedure has been devised after extensive preliminary studies on bodies of deceased children of different age. Its practicability has been since proved on many cases and never presented greater difficulties.

Technique.

Choice of site. First the source of the bone-marrow designated for the transfusion and also the site of the transfusion itself had to be carefully decided upon. According to the findings collected by *Custer* and *Ahlfeld* and also *Jaffe* on many sectional cases, the distribution of the red, active marrow varies in an adult in different bones. It is contained in bones of the skull and thorax (sternum, ribs, scapulae and claviculae), in the vertebrae and the os innominatum, in small quantities also in the upper ends of the femur and humerus. This distribution of the red marrow is the result of the physiological decrease of its activity, which is a function of age, for at birth and for the first 3-4 years of life all the bones of the body contain only red, haemopoietic marrow. This process, caused by a progressive change of the red into the much less active yellow marrow, occurs in distal parts of the bones earlier than in the proximal ones: first in the shafts of the long bones, then in the bones of the thorax and finally in the vertebrae. When on the contrary, the inactive, yellow marrow regenerates into the red, the turn order is the reverse: The regeneration takes place first in the vertebrae and last in the distal ends of the long bones. It can be thus concluded that the sternum should be considered as the site of choice both for obtaining the marrow from

the donor and its administration into the receiver. The donor being always an adult, his most important reservoir of red, active marrow is the *sternum*. The same bone is again predisposed to serve as a receptaculum for the transfused marrow in the receiver, as one of the most active centres of regeneration. Finally the sternum lies almost directly under the skin and, as it has been shown by *Arinkin*, easily accessible. Only in cases in which, as in very small children, we have to deal with an insufficiently developed sternal cavity, we are compelled to transfuse into the tibia cavity, which in young children still contains red, regenerable marrow. Also after repeated transfusions into the sternal cavity a local thickening of the periost and some obstructions in the spongiosa, owing to reactive and scarring processes, may hinder the further introduction of the transfused matter into the sternum. In such cases we are once more compelled to change the classical site of the transfusion and to transfuse, even in elder children, into the tibia cavity. The results are, however, much less effective, especially in elder individuals.

Regarding the question as to which part of the sternum should be punctured in order to assure the best results, both in obtaining sufficient quantities of an active marrow from the donor, as in attaining the roomiest cavity for the transfusion in the receiver, it must be first of all emphasized that we should always endeavour to perform the puncture in the mid-line of the sternum. The best place for the operation is the sector between the 3rd and 4th rib. Lower introduction of the needle may meet with bone fissures. According to *Pässler* such fissures occur in about 20 % of cases in the lower parts of the sternum. We may be, however, compelled, for instance after repeated transfusions, to enlarge the site of the operation to the space between the 2nd and the 4th rib.

There are sometimes solid bony trabecula running across, between the outer bony plate and the hind one. They may also hinder the puncture and the infusion. They are most frequently found at the level of the border-line between corpus and manubrium sterni. Sometimes, however, they are also met with, if much less frequently, in the lower parts of the sternum. If one happens to hit such a trabeculum with the needle, the aspiration of bone-marrow is impossible and one is compelled to withdraw the needle and to repeat the puncture at some other point.

The choice of the donor. The donor must be an adult, in perfect health and condition, not too old—between 20 and 40—obviously tested against syphilis and tuberculosis, as also all kinds of latent infections (tonsils, teeth, urogenital tract, etc.). The necessity of the serological control of the blood must be stressed. The donor must obviously belong to the same blood group as the patient, or to the zero group. Besides this precaution, however, direct tests for compatibility should never be omitted and the occur-

rence of Rh antibodies taken into consideration. In one word, all the precautionary measures, which are obligatory in relation to the transfusion of blood, should be taken. Strong, healthy donors get over the loss of 10-15 c.c. of their bone-marrow without any noticeable symptoms within 3-4 days. We had donors, who without any inconvenience supplied us within 4-6 weeks (twice a week) with 80-100 c.c. of bone-marrow in all. From this one sees how rapidly the loss of these quantities of bone-marrow is replaced in healthy individuals. Nevertheless the donor should always remain under clinical control and his blood should always be tested before each intervention, if he is used repeatedly.

Necessary implements. The implements necessary for the bone-marrow transfusion are the following:

1. A 2-5 c.c. syringe for anaesthesia of the skin and the periost.

2. A set of closely fitting injection needles (No. 10-12) for the above syringe, with short, but very sharp ends.

3. Two special needles for sternal puncture, one for the donor and one for the receiver.

As the best needle for the intramedullar transfusion I consider the pattern devised by *Klima* and *Rosegger*, or by *Rohr*. The *Salah* needle, commonly used in England, especially the M. R. C. pattern for intramedullary transfusion, can also be used. Independently of the pattern all such instruments must answer to the following claims:

a) They must be of the best make and of best material, so as to prevent breaking, bending and splintering into the bone.

b) They should be provided with a short but very sharp end, so as to easily penetrate the outer bony plate of the sternum, without damaging the hind plate.

c) The length of the needle should not exceed 2-5 cm. Longer needles are not handy and break easily. Shorter ones may not reach the cavity in cases of adiposity.

d) The tubular lumen of the needle should not exceed 1-2 mm. The styletto must be of closest fitting, in order to prevent the bone splinters from falling into the tubule.

e) The fitting for a Record syringe must guarantee absolute tightness, otherwise the aspiration of the marrow will be impossible.

f) The needle must be fitted with a scutiform screw, which permits to adjust the length of the point of the needle, so as to prevent the needle from piercing the hind bony plate of the sternum and from falling into the cavity of the thorax. This gadget has been introduced by *Arieff*.

4. A 2-5 c.c. record syringe for extracting a sample of the marrow from the receiver. This syringe must be completely dry. If the dry sterilisation of the syringe is impossible it should be washed out with saline as to prevent the lysis of the marrow cells.

5. A 10-20 c.c. first rate record syringe for the transfusion. It should be

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All syringes and needles should be in first rate condition, closely fitting and absolutely tight, as they are supposed to work under considerable pressure.

6. Iodine for skin desinfection, 2 % Novocaine solution for anaesthesia and 2 % natrium citrate solution for rinsing of the syringe for the transfusion.

7. Dressing material.

The performance of the transfusion. The donor and the receiver are placed in a lying position on two parallel tables, with uncovered sternal region. After a careful desinfection of the skin, the skin and the periost are anaesthetized first in the donor, then in the receiver with 2 % novocaine solution. For this purpose the syringe should carry the needle mounted with the opening of its end looking downwards, to the opposite side of the graduated scale of the cylinder. The needle should be inserted a little lower down from the point we want to anaesthetize, with the opening upwards and the scale of the cylinder downwards. A small amount of the novocaine solution is then injected in the skin and under the skin. Now the position of the syringe is altered: It must be turned in order to bring the scale of the cylinder upwards. The opening of the needle is then turned downwards. By means of a slantwise push the periost is then pierced and the needle is slowly driven under the periost as far as possible. 0.2-0.3 c.c. of the novocaine solution are then injected under considerable pressure. The needle is then drawn back and the procedure repeated in 2-3 neighbouring places. It is very important to anaesthetize the whole field of operation. The operation begins after some 10-12 min. necessary to attain full anaesthesia:

First the length of the needle is adjusted—with help of the scutiform screw—according to the thickness of the subcutaneous fat layer. The needle with the stiletto is then inserted at a previously selected point of the sternum of the *receiver*. The needle is driven slantwise, so as to lengthen its way through the spongious stratum. The moment of the entrance into the sternal cavity is felt as a slight, but distinct crackling and is signalled by a slight short pain, felt by the patient. The needle sticks then firmly in the bone. If the needle is sharp enough and the procedure is carried out as described above, no hammering of the needle is ever necessary, to make it penetrate the outer bony plate.

Next the stiletto is removed and a 2-5 c.c. record syringe is inserted. The piston is then slowly withdrawn and a very small

amount of marrow (0.2-0.3 c.c.) aspirated. This is necessary to be sure that the needle is correctly *in situ* and also to collect a sample of the marrow for investigation. This accomplished, and the syringe removed, the stiletto is reinserted and the whole instrument left firmly sticking in the bone.

The same operation is then repeated with help of another similar needle in the *donor*. After the removal of the stiletto a bigger record syringe (10-20 c.c.) is inserted and the marrow slowly aspirated. It is quite easy to withdraw 10-12 c.c. of the marrow substance. This is not only our own experience. *Arinkin* and also *Reich* never had any difficulty in obtaining such quantities of the marrow substance from their patients, under normal conditions and with help of the sternal puncture. The withdrawal of such comparatively large quantities of bone-marrow is against the assertion of some authors not very much more painful than the withdrawal of the classic sample. The sensation felt during this procedure is described by the intelligent donors as a feeling of intense suction rather than of a real pain. Nevertheless such quantities are not to be avoided, should the transfusion be effective. The bone-marrow substance is of course diluted with blood, but this is not only inevitable but also without greater importance, in view of the fact, that this blood comes from the network of bone-marrow vessels and is undoubtedly carrying all the biologically active substances of the marrow.

When the necessary quantity of the marrow has been withdrawn, the syringe and the needle are removed together and the wound is dressed by an assistant. Now the stiletto of the needle, sticking in the receiver, is removed, the donor's needle put away and the syringe with donor's marrow inserted on the receiver's needle. The contains of the syringe are then slowly injected into the cavity of the receiver under considerable pressure. This procedure is slightly painful. Sometimes a slight and transitional swelling of the bone is observed. After the transfusion has been accomplished the syringe is removed together with the needle and the wound is dressed under compression.

It is obvious that the whole procedure must be carried out under conditions of maximally attainable asepsis. One must be further very cautious not to withdraw the needle unprovided with the stiletto or the syringe, in order to avoid a subcutaneous emphysema.

The remains of the transfused matter should be controlled microscopically regarding the normal character of the marrow of the doner and whether its dilution with blood was not too great.

Indications.

Generally speaking the transfusion of bone-marrow may be indicated:

1. Where it can be suspected that the bone-marrow from a healthy donor may contain substances necessary for the normal haemopoiesis, but lacking or inactive in the organism of the patient.

2. When the normal activity of the bone-marrow of the patient is supposedly overburdened by the pathologically heightened requirements.

From these points of view one could expect some positive results from our method in the following disorders:

1. Pernicious anaemia.
2. Leukaemias.
3. Agranulaemia.
4. Infections.

1. *Pernicious Anaemia.* There are no data about a possible storage of the *haemopoietic principle* in the marrow. It can be assumed, however, that as one of the most important working points of the haematopoietic principle, the bone-marrow contains probably more of it than it actually requires. If this is so, then the haematopoietic principle of the marrow is assuredly more complete and more active than the same principle originated from other sources. Its direct application into the organ of the erythropoiesis should be all that the more efficient.

These were the points of view, which led us to apply the bone-marrow transfusion in cases of megaloblastic, hyperchromaemic anaemia.

Here an example of the results:

Case No. 3/39. N. C., a 13-year-old girl. Family history of no importance. Whooping cough and measles at the beginning of the school age. Actual symptoms began almost a year ago with pains in the epigastrium immediately after meals. Since 3 weeks fever (39-40 C.), which after a few days descended to subfebrile temperatures (37.5-38 C.). Pains in the lumbar region, headaches, vertigo, faints, singing in the ears, nausea and in the last days—vomits. Received to the Hospital on Febr. 16, 1939.

Status at the reception (16.-19. 2.). Normally developed girl. Extreme pallor of the skin, with a yellowish hue. Pallor of the mucous membranes.

No clinical findings in the chest and the abdominal organs, besides a slightly painful right subcostal region. Liver and spleen not palpable. Nervous system and urogenital tract in order. Temp. 37.6 C. *Wassermann* and *Meinicke* tests: negative. *Mantoux* tuberculine test strongly *positive*. No blood and no parasites in stools. Stools contain many undigested particles. Urine: Traces of albumine, sugar and acetone: absent; urobiline and urobilinogene: increased; diazo test: negative; indican and bile pigments: absent. In the sediment some urates and very few leucocytes: *Blood findings* (B. F.) on Febr. 16: Haemoglobin: 22 %, red cells: 760,000, white cells: 3200. *Schilling* count (Sch. c.): Myelocytes: 1 %, juveniles: 1 %, stab cells: 6 %, segmented cells (hypersegmentation) 51 %, eosinophiles: 5 %, monocytes: 1 %, lymphocytes: 35 %. Anisocytosis, poikilocytosis, polychromasia. 2 normoblasts, blood group B.—Febr. 19: Haemogl.: 19 %, r.c.: 744,000, Index: 1.27. Wh. c.: 4200, platletts: 54,000. Sch. c.: Myelocytes: 2 %, metamyelocytes: 1 %, stab: 18 %, segm.: 58 %, eosin.: 0, basoph.: 0, lymph.: 19%. Pronounced anisocytosis, polychromasia, basophile granulation of the red cells. *Achlorhydria,* even after the histamine stimulation. Total acidity 7.

Course. From Febr. 16 till Febr. 24: Iron, as ferrum reductum in large doses, hydrochlorid acid. No response. From Febr. 24 till April 28; liver orally and parenterally. Slowly progressing recovery, but persistent anchlorhydria. On April 6: pleuritis exsudativa dextra tb. till May 3. Good recovery. B. F.: Haemogl.: 88 %, r. c. 4,090,000, Index 1, wh. c.: 3500, Sch. c.: Stab 9 %, segm.: 47 %, eosinoph.: 6 %, basophiles: 3 %, lymph.: 29 %, monocytes: 6 %. Anchlorhydria. Total acidity: 7. The patient is doing very well, has gained in weight and leaves the hospital on May 17, 1939, with an adequate prescription for maintenance.

6 months later, on Nov. 30, 1939, the patient suffers from a relapse and must be hospitalized. Extreme pallor of the skin with yellowish hue. The organs of the chest without findings. X-ray examination: negative. Spleen hard and palpable under the costal arc. Elargement of the liver. B. F.: Haemogl.: 25 %, r. c.: 1,100,000, index 1,1, wh. c.: 3000. Sch. c.: Myelocytes: 5 %, stab: 5 %, segm.: 40 %, eosin.: 2 %, lymph.: 43 %, nonoc.: 7 %. Anisocytosis, polychromasia, granulated erythrocytes, macroblasts, normoblasts, megalocytes. *Bone-marrow biopsy:* Myeloblasts: 12 %, myelocytes: 20 %, juveniles: 17 %, stab: 12 %, segm.: 13 %, eosin.: 8 %, lymph.: 10 %. Nuclei: 7 %, proerythrocytes: 10 %, megaloblasts: 2 %, macroblasts: 72 %, 43 normoblasts, mitotic forms: 1,7 %. Urine: negative. Ekg.: negative. Achlorhydria also after histamine stimulation. Liver treatment orally and parenterally, iron and hydrochloric acid till Jan. 31, 1940. Rapid recovery B. F.: on Jan. 31: Haemoglobin: 70 %, r. c.: 3,648,000, index: 0,9, wh. c.: 6100. Sch. c.: Stab: 6 %, segm. 42 %, eosin.: 10 %, basoph.: 0, lymph.: 39 %, monoc.: 3 %. The patient leaves the hospital.

8 months later, on Sept. 1, 1940, she returned to the hospital with a third relapse. Since a few months she left off taking liver. Since 3 weeks she complains of pains in the epigastrium after meals. Has lost 6 kg. of body weight. The skin is again yellowish and very pale. No findings in the lungs, but a systolic murmur over the apex of the heart. Liver and spleen distinctly

enlarged. B. F.: Haemogl.: 41 %, r. c.: 2,260,000, index: 1,2, wh. c.: 3600, Sch. c.: Stab: 5 %, segm.: 26 %, eosin.: 1 %, basoph.: 0, lymph.: 38 %. Numerous megaloblasts, granulated erythrocytes. Since Sept. 1 till Oct. 22: Campolon parenterally. B. F.: Haemogl.: 49 %, r. c.: 2,390,000, index: 1, wh.c.: 5300, Sch. c.: Stab: 3 %, segm.: 55 %, eosinophiles: 6 %, lymph.: 30 %, monoc.: 6 %. The general condition unchanged. *In view of the lack of response to the classical treatment,* which has proved itself so efficient previously, *we decided to try the bone-marrow transfusion.* On Oct. 30, 1940, 10 c.c. of bone-marrow from a healthy donor of the blood group B are transfused into sternal cavity of our patient. B. F.: on Oct. 31 (24 h. *after the transfusion):* Haemogl.: 65 %, r. c.: 3,120,000, index: 1, Sch. c.: Juveniles: 1 %, stab: 3 %, segm.: 49 %, eosin.. 1 %, lymph.: 42 %, monoc.: 4 %. The patient looks almost normal, the pallor has disappeared, is euphoristic. On Nov. 6: Haemogl.: 64 %, r. c.: 3,020,000, index: 1, wh. c.: 4500, Sch. c.: Stab: 3 %, segm.: 35 %, eosin.: 1 %, lymph.: 56 %, monoc.: 5 %.On Nov.7, *the II.bone-marrow transfusion,*from the same donor. B. F. on Nov. 11: Haemogl.: 72 %, r. c.: 3,500,000, wh. c.: 7800, index: 1. Sch. c.: Stab: 2 %, segm. 46 %, eosin.: 2 %, basoph.: 1 %, lymph.: 43 %, monoc.: 6 %. Nov. 18: Haemogl.: 80 %, r. c.: 4,020,000, index: 1, wh. c.: 4600. Sch. c.: Stab: 2 %, segm.: 61 %, eosin.: 2 %, lymph.: 30 %, monoc.: 5 %. The patient leaves the hospital in excellent condition, has gained again on body weight.

This case is remarkable, first, because it was impossible to obtain during the third relapse the hitherto usual response by means of the classical treatment, as if the haemopoietic principle by some obstacle would be hindered to reach its working point. Secondly, because of the startling and *immediate* response to the bone-marrow transfusion. The recovery lasted this time at least 10 months, as long as the child had been in contact with the hospital. Similar effects could be observed in several other cases of a similar clinical behaviour. *It appears therefore that the bone-marrow can as a matter of fact be considered as another reservoir of the haemopoietic principle so potently active, that its application into the bone-marrow of the diseased person is followed by an immediate response within 24 hours.*

2. *Leukaemias.* There are three different theories of the aetiology of leukaemia: The infective, the neoplastic and the theory of specific factors. This last one, proposed by *Ziegler,* modified by *Naegeli,* and lately supported by the experiments of *Miller* and *Turner,* and *Turner* and *Miller,* comes very near to our own ideas about the presumed role of the healthy bone-marrow, as a reservoir of optimally balanced factors, necessary for the normal leukopoiesis.

I am perfectly aware, however, that my experiments, concerning the bone-marrow transfusion into leukaemic patients are

only of empiric value and that their results may have many meanings. Nevertheless I had some very startling and promising results in several cases especially of lymphatic leukaemia.

This is the history of one of such cases:

Case No. 8/41. N. L., a 5-year-old girl. Family history of no importance. Has always been well until September 1940, when she fell ill with high temperature, abdominal pains and vomiting. Received to the hospital on Jan. 2, 1941, *Status at the reception* (Jan. 2-4): Pronounced pallor of the covers. Foetid odor from the mouth. On the left tonsil a thick, white-yellowish membrane. Lungs without findings. The left cardiac border extended about 1 cm. to the left of mamilla. Over the apex a systolic, anaemic murmur. Abdomen in the niveau of the chest. Liver about 1 cm. under the costal arc. Spleen not palpable. Urine: no changes. X-ray examination of the chest: negative. *Wassermann* and *Mantoux* tests: negative. B. F.: Haemogl. 27 %, r. c. 928,000, index: 1,04, wh. c.: 3500. Sch. c.: Myelocytes: 3 %, juvenile: 3 %, stab: 8 %, segm.: 4 %, lymph.: 82 %. Blood group A. Bone-marrow biopsy: 96 %, lymphocytes: 4 %, segmented cells. Temp.: 38,2 C. General condition: serious. As diphtheria could not be clinically excluded and it was not advisable to wait for the bacteriological diagnosis, 15,000 units of antitoxic serum have been injected (at the reception). The bacteriological findings proved, as a matter of fact, negative. Until Jan. 6: only general care and analeptics. On Jan. 6: I. *bone-marrow transfusion* (10 c.c.). B. F. on Jan. 7: Haemogl.: 49 %, r. c.: 2,000,000, index: 1.2, wh. c.: 2000, Sch. c.: Stab: 12 %, segm. 3 %, lymph.: 85 %. Jan. 10: On the right thigh a large inflammatory infiltrate. Temp.: 39.5. Better appetite and condition. II. bone-marrow transfusion (10 c.c.). Jan. 11: Temp. 38.5. B. F.: Haemogl.: 40 %, r. c.: 2,050,000, index: 1, wh. c.: 3500. Sch. c.: Stab: 11 %, segm.: 12 %, lymph.: 77 %. Blood transfusion (380 c.c.). Ferrum red. Jan. 12: B. F.: Haemogl.: 59 %, r. c.: 2,940,000, index: 1, wh. c.: 2150. Sch. c.: Juven.: 2 %, stab: 6 %, segm.: 23 %, lymph.: 69 %. Temp. 38.8 C. Incision of the phlegmona on the right thigh. Jan. 18: B. F.: Haemogl.: 52 %, r. c.: 2,216,000, index: 1.2, wh. c.: 3200. Sch. c.: Stab: 33 %, segm.: 14 %, eosin.:1 %, lymph.: 52 %. Jan. 23: Temp.: 36 C. Throat since a week cleaned. B. F.: Haemogl.: 60 %, r. c.: 2,916,000, index: 1.04, wh. c.: 2200. Sch. c.: Stab: 15 %, seg.: 6 %, eosin.: 1 %, lymph.: 76 %. III. bone-marrow transfusion (10 c.c.). Jan. 24: Temp. 37.6. B. F.: Haemogl.: 62 %, r. c.: 3,080,000, index: 1, wh. c.: 3200. Sch. c.: Stab: 7 %, segm. 4 %, eosin.: 1 %, lymph.: 88 %. Jan. 25: Very good appetite, has gained 1600 gm. on body weight. II. blood transfusion (250 c.c.). Jan. 27: B. F.: Haemogl. 75 %, r. c.: 3,320,000, index: 1.1, wh.c.: 3200. Sch. c.: Stab: 18 %, segm. 22 %, lymph.: 60 %. Jan. 28: IV. bone-marrow transfusion (10 c.c.). Jan. 30: B. F.: Haemogl. 75 %, r. c.: 3,200,000, index: 1.15, wh. c.: 4200. Sch. c. Stab: 14 %, segm. 7 %, lymph.: 77 %, monocytes: 2 %. Bone-marrow biopsy: Myelocytes: 2 %, metamyelocytes: 2 %, stab: 2 %, segm.: 1 %, lymph.: 93 %, 10 erythroblasts to 100 white cells. Febr. 4: V. bone-marrow transfusion (10 c.c.). Febr. 5: B. F.: Haemogl.: 80 %, r. c.: 3,920,000, index: 0.9, wh. c.: 4300, Sch. c.: Stab: 12 %, segm.: 5 %, lymph.: 81 %, monoc.: 2 %. Febr. 7: VI. bone-marrow transfusion. Bone-marrow biopsy: Myelocytes: 1 %,

stab: 9 %, segm.: 3 %, lymph.: 87 %, single normoblasts. Febr. 8: B. F.: Haemogl.: 75 %, r. c.: 3,680,000, index: 1.04, wh. c.: 5600. Sch. c.: Stab: 20 %, segm.: 10 %, lymph.: 69 %, monoc.: 1 %. Febr. 10: Temp. 37.4 C. VII. bone-marrow transfusion (7 c.c.). Febr. 12: B. F.: Haemogl.: 56 %, r. c.: 3,740,000, index: 0.8, wh. c.: 5400. Febr. 14: VIII. bone-marrow transfusion (10 c.c.). Febr. 15: B. F.: Haemogl.: 65 %, r. c.: 3,840,000, wh. c.: 4200. Febr. 17: IX. bone-marrow transfusion. Febr. 19: B. F.: Haemogl.: 79 %, r. c.: 3,920,000, index: 1, wh. c. 3920. Febr. 24: B. F.: Haemogl.: 67 %, r. c.: 3,420,000, index: 0.99, wh. c.: 4000. Febr. 25: X. bone-marrow transfusion (10 c.c.). Febr. 27: B. F.: Haemogl.: 73 %, r. c.: 3,410,000, index: 1.06, wh. c.: 6200. Excellent condition, has gained 2200 in weight. Leaves the hospital.

In this case, therefore, a 5-year-old girl with symptoms of *lymphadenosis aleukaemica,* necrosis of the right tonsil and in a very poor general condition has received within nearly 2 months 10 bone-marrow and 2 blood transfusions. The general condition of the patient has been strikingly improved, she has gained in weight, lost her pallor, anorexia, apathy, temperatures and improved her blood picture. The necrosis disappeared during the treatment. The marked improvement of the white cell count after each transfusion was the most remarkable feature of the treatment. The blood transfusions were applied in order to improve acutely the general condition. This procedure was always repeated in the first stages of the treatment of leukaemias by means of bone-marrow transfusions.

In another case of a 14-year-old boy with familiary aleukaemic lymphadenosis and haemorrhagic symptoms we obtained by means of 20 bone-marrow transfusions a lasting remission and a complete return of the blood picture to the norm, in May and June 1939. This boy, who is now (1947) 22 years of age and recently graduated from Cambridge, is still in perfect health. Unfortunately the notes concerning his history have been lost owing to war conditions.

Not all cases of leukaemia, however, did respond so successfully to the bone-marrow transfusions. We had best results in aleukaemic lymphadenosis. All advanced cases with necrotic processes were refractory. But already the results obtained until now encourage us to carry on with our research also from experimental point of view. We expect to be able to say more about it in the near future.

3, 4. Our results in cases of *Agranulocytosis* and various *infections* will also be published in a special paper.

Summary.

The author has devised a method of bone marrow transfusion from a healthy donor into the sternal bone-marrow cavity of a diseased child, by which 10 c.c. of bone marrow can easily be transfused. The method is fully described and also some results are communicated concerning the treatment of pernicious anaemia and aleucaemic lymphadenosis.

Zusammenfassung.

Der Autor berichtet über eine Methode zur Transfusion des Knochenmarkes eines gesunden Spenders in die Markhöhle eines erkrankten Kindes, durch die leicht 10 ccm transfundiert werden können. Mitteilung von Befunden bei perniziöser Anämie und aleukämischer Lymphadenose.

Résumé.

Les auteurs décrivent une méthode de transfusion de moelle osseuse d'un donneur sain dans la cavité médullaire sternale d'un enfant malade selon laquelle on peut facilement transfuser 10 cm^3 de moelle osseuse. Ils font part de leurs résultats dans l'anémie pernicieuse et la lymphadénose aleucémique.

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