Kasuistik

Long-Term Continuous Spinal Anesthesia in Severe Tetanus with Autonomic Disturbance

H. Sugimoto, M. Shibuya, M. Uenishi, J. Yokota, C. Terai, T. Shimazu, T. Megawa, T. Yoshioka, and T. Sugimoto

Department of Traumatology, Osaka University School of Medicine

Summary. The mortality rate from tetanus is still high if the disease is accomapanied by signs of autonomic nervous system dysfunction. We treated a 75-year-old woman with tetanus and autonomic dysfunction with continuous high spinal anesthesia for 23 days. She recovered. Spinal anesthesia may be a useful adjunct for the treatment of severe tetanus.

Key words: Spinal anesthesia – Tetanus – Autonomic disturbance

Severe tetanus may be complicated by a syndrome of "sympathetic overactivity" manifested by excessive sweating and salivation and by abrupt major fluctuations in the arterial blood pressure. The mortality rate is unexpectedly high [1, 22, 31, 32]. This report describes the use of continuous spinal anesthesia in such a patient, in addition to established therapeutic modalities for tetanus including mechanical ventilation, sedation, and neuromuscular blockade with curare.

Case Report

A 75-year-old woman sustained a minor laceration of the great toe. Eight days later, she complained of dysphagia, trismus, and stiffness around the shoulder girdle. She was hospitalized with a diagnosis of tetanus and was given tetanus hyperimmune globulin and tetanus toxoid. Within 24 h, generalized muscle spasms were present; the following day, apnea occurred, followed by cardiac arrest. She ws successfully resuscitated and then transferred to our institution. She had previously been in good health, but had never received tetanus toxoid.

On admittance, she was breathing spontaneously through an endotracheal tube at a rate of 28 breaths/min. Her blood pressure was 154/100 mm Hg, heart rate 100 beats/min, sinus rhythm normal. She was alert. She had muscular rigidity, most prominently affecting the jaw, neck, and torso. The deep tendon reflexes were greatly hyperactive. Minor stimuli resulted in frequent generalized muscle spasms. The toe laceration appeared clean and dry. The cerebrospinal fluid and arterial blood gas analysis were both normal.

Tetanus hyperimmune globulin was given intramuscularly (3,000 U), intrathecally (250 U) and into the wound (250 U). She was given additional tetanus toxoid and a 7-day course of penicillin (10,000,000 U i.v. every 12 h) was begun. Intravenous diazepam did not reduce the frequency of the opisthotonic attacks. They were treated with pancuronium bromide and continuous positive pressure ventilation with a volume-controlled ventilator. Other supportive measures included digitalization and intravenous hyperalimentation. Tracheostomy was performed on the third hospital day because of profuse tracheal secretions.

Serum catecholamines were determined daily (9:00 a.m.) throughout the hospital course. Catecholamines were also determined daily on an aliquot of a 24-h urine collection.

On the 4th hospital day, dramatic abrupt fluctuations in blood pressure within the range of 230 to 90 mm Hg (in systolic pressure) appeared (Fig. 1), accompanied by profuse salivation and excessive sweating. On the 5th hospital day, the blood pressure fell to 60/40 mm Hg and the heart rate fell from 120 to 70 beats/min. Dopamine (5 µg/kg·min) restored the blood pressure, but it still fluctuated erratically, a pulmonary artery catheter was inserted to permit more precise monitoring of the hemodynamic status.
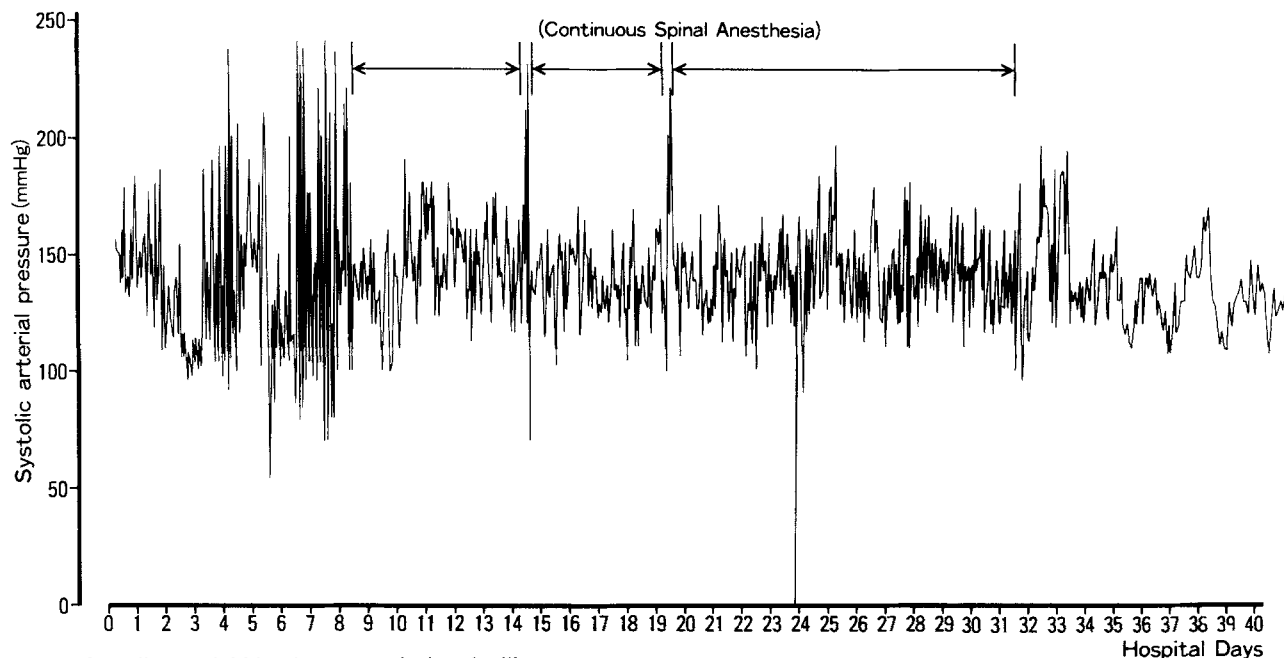
Fig. 1. Systolic arterial blood pressure during the illness

In view of the increased hemodynamic instability, a trial of spinal anesthesia was instituted. An intrathecal catheter was inserted through the L3–L4 interspace and directed cephalad for 20 cm. A test dose of 1 ml of 1% lidocaine intrathecally resulted in an immediate fall in blood pressure from 168/71 to 97/44 mm Hg, accompanied by decrease in total peripheral resistance (TPR), central venous pressure (CVP), and pulmonary wedge pressure (PWP) as shown in Fig. 2. The blood pressure still tended to elevate when the tracheostomy was suctioned, but this response was eliminated following an additional intrathecal administration of 2 ml lidocaine. Intravenous epinephrine was used to titrate cardiac output, TPR, CVP, and PWP to within acceptable ranges. The excessive salivation and sweating ceased. Because of the favorable response, it was decided to maintain the spinal anesthesia by continuously infusing isotonic 0.5% bupivacaine. Epinephrine infusions in the range of 0.02 to 0.18 µg/kg·min maintained the systolic blood pressure above 100 mm Hg. The changes of systemic blood pressure, oxygen consumption, and carbon dioxide production before and after the introduction of spinal anesthesia are shown in Fig. 3.

The spinal anesthesia was administered continuously from the 8th to the 31st hospital days. Clinically, the level of spinal anesthetic for motor nerve system was approximately C6. She retained movement of the upper limbs. However, the level for the autonomic nervous system was thought to be higher because excessive sweating, including on her
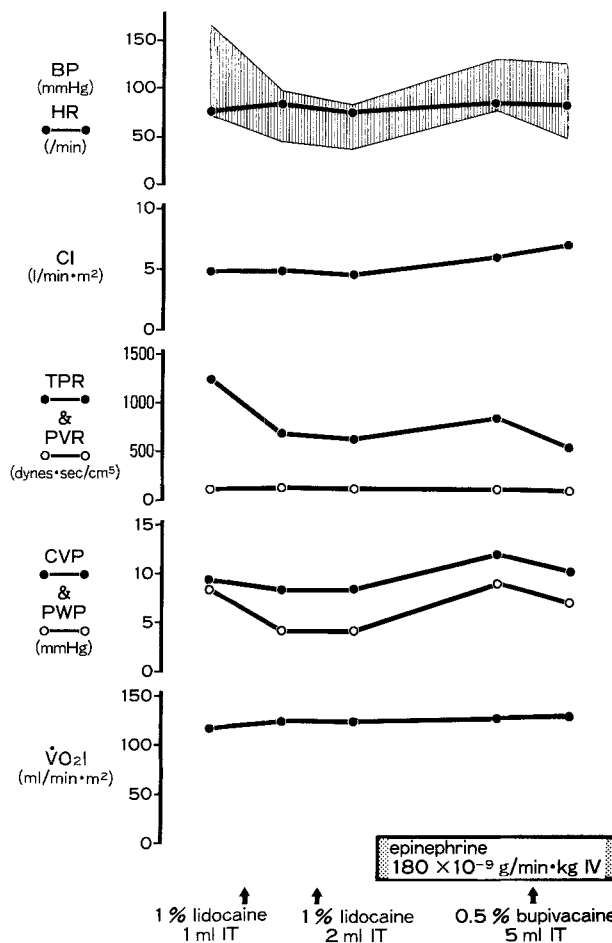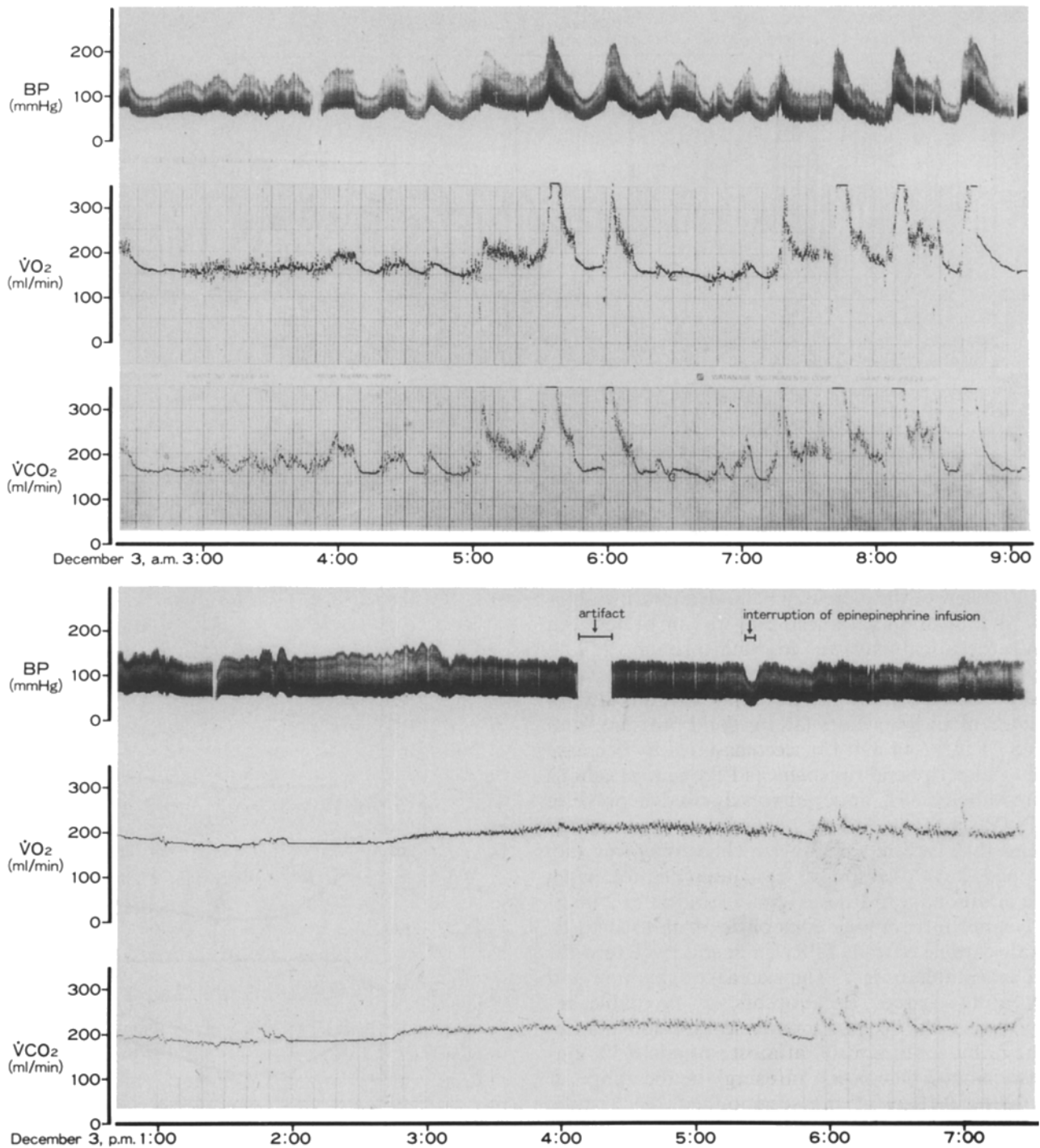

Fig. 2. Hemodynamic changes following the trial application of spinal anesthesia on the 8th hospital day. IT, intrathecal infusion; IV, intravenous infusion

Fig. 3a, b. Effects of spinal anesthesia combined with exogenous epinephrine infusion on blood pressure (BP), oxygen consumption ($\dot{V}O_2$) and carbon dioxide production ($\dot{V}CO_2$). (a) The 8th hospital day, before spinal anesthesia (b) The 8th hospital day, during spinal anesthesia (0.5% bupivacain 2 ml/h IT & epinephrine 90×10^{-9} g/min·kg IV)

face, and salivation ceased after the introduction of spinal anesthesia. Trial interruptions of the spinal anesthesia on the 14th and 19th hospital days were promptly followed by dramatic fluctuations in blood pressure (Fig. 1), accompanied by excessive sweating and salivation. The hemodynamic changes are presented in Table 1. On the 23rd hospital day, cardiac arrest occurred without obvious cause. The patient was easily resuscitated by external cardiac massage. On the 31st day, the spinal

Table 1. Hemodynamic changes during interruption of total spinal anesthesia and exogenous epinephrine administration on the 19th hospital day

		During infusion[a]	During interruption[b]
BP	(mm Hg)	164/77	226/96
PAP	(mm Hg)	31/15	43/20
PWP	(mm Hg)	13	19
CVP	(mm Hg)	10	12
HR	(/min)	90	90
CI	$(l/min \cdot m^2)$	5.0	6.1
TPR	$(dynes\ s/cm^5)$	1,297	1,434
PVR	$(dynes\ s/cm^5)$	124	128
LVSWI	$(g \cdot m/m^2)$	75.1	117.5
RVSWI	$(g \cdot m/m^2)$	6.8	17.6
$\dot{V}O_2$	$(ml/min \cdot m^2)$	128	189

[a] Continuous infusions of epinephrine $(27 \times 10^{-9}\ g/min \cdot kg$, IV) and 0.5% bupivacaine (2 ml/h, IT)

[b] 1 h after interruption of the infusions BP, blood pressure; PAP, pulmonary arterial pressure; PWP, pulmonary wedge pressure; CVP, central venous pressure; HR, heart rate; CI, cardiac index; TPR, total peripheral resistance; PVR, pulmonary vascular pressure; LVSWI, left ventricular stroke work index; RVSWI, right ventricular stroke work index; $\dot{V}O_2$, oxygen consumption

anesthesia was discontinued without reappearance of the profuse salivation or sweating. The muscular spasms had completely disappeared. There was some persistent fluctuation in the blood pressure, but this was less pronounced than it had been previously. By the 41st day, she had been weaned from the ventilator. The patient was discharged fully recovered on the 64th day.

Discussion

There are two main causes of death related to the cardiovascular disturbance in severe tetanus. One of them is unexpected cardiac arrest [6, 7, 13, 15, 30, 32] which typically occurs in the midcourse of the disease, sometimes after tracheal suction or other physical stimuli, but most often without obvious cause. When beta-adrenergic blocking agents have not been used, resuscitation is usually possible and the blood pressure quickly recovers. The mechanism is unclear, but the abrupt occurrence of the arrest and its good response to resuscitation suggest that it is most likely due to cardiac parasympathetic nervous stimulation. There is evidence that the parasympathetic nervous system and particularly the vagal nuclei are affected by tetanus toxin [2, 16]. Furthermore, it has been proposed that neutral integration of cardiovascular control and baroreceptor reflexes are impaired in severe tetanus [9, 11]. It could be possible therefore to

prevent cardiac arrest by vagal cardiac nerve blockade [7].

The other cardiac cause of death is myocardial degeneration [7, 16, 20] with persisting hypotension in the preterminal phase of the disease. This is not specific to severe tetanus, but is common, especially in conditions in which endogenous catecholamines are released in large quantities [20]. Serum catecholamine levels are known to be elevated in severe tetanus [3, 10, 17–20, 29]. Local release of norepinephrine from cardiac sympathetic nerve endings may have a more and direct effect on the myocardium than the circulating catecholamines [25].

Various drugs have been used in severe tetanus [4, 5, 8, 11, 12, 14, 15, 17, 18, 21, 23, 24, 26–28, 32, 33] especially propranolol and labetalol [12, 15, 18, 23, 24]. However, these agents are not uniformly effective [4, 8, 11, 12, 32] and hypotension [5, 8, 33] induced by them may result in serious consequences. Beta-blockade also may make resuscitation difficult when arrest occurs [32].

In order to prevent cardiac arrest and myocardial degeneration, it is necessary to block not only the sympathetic but also parasympathetic nervous systems. Circulatory support then becomes mandatory, especially to prevent hypotension. The hemodynamic depression of total spinal anesthesia can be readily controlled by small amounts of catecholamines. The serum concentrations of exogenous epinephrine required to maintain hemodynamic variables at an appropriate level appear to have no appreciable adverse cardiac effects [25]. The concept that locally released catecholamines play a primary role in myocardial degeneration is in part supported by the low serum and urine catecholamine values that we measured during total spinal anesthesia (Fig. 4). Both the serum and urinary norepinephrine levels were decreased, probably reflecting a decline in norepinephrine release from sympathetic nerve endings. The high serum and urinary epinephrine levels were due to exogenous administration.

Contrary to our expectations, sudden cardiac arrest occurred once during the administration of total spinal anesthesia. However, resuscitation was readily possible – in contrast to the reported experience when beta-blockers are used. The dose of bupivacaine we used was not sufficient for obtaining perfect total spinal anesthesia; it probably resulted in incomplete parasympathetic blockade. Cardiac arrest may have been prevented by larger doses of bupivacaine.

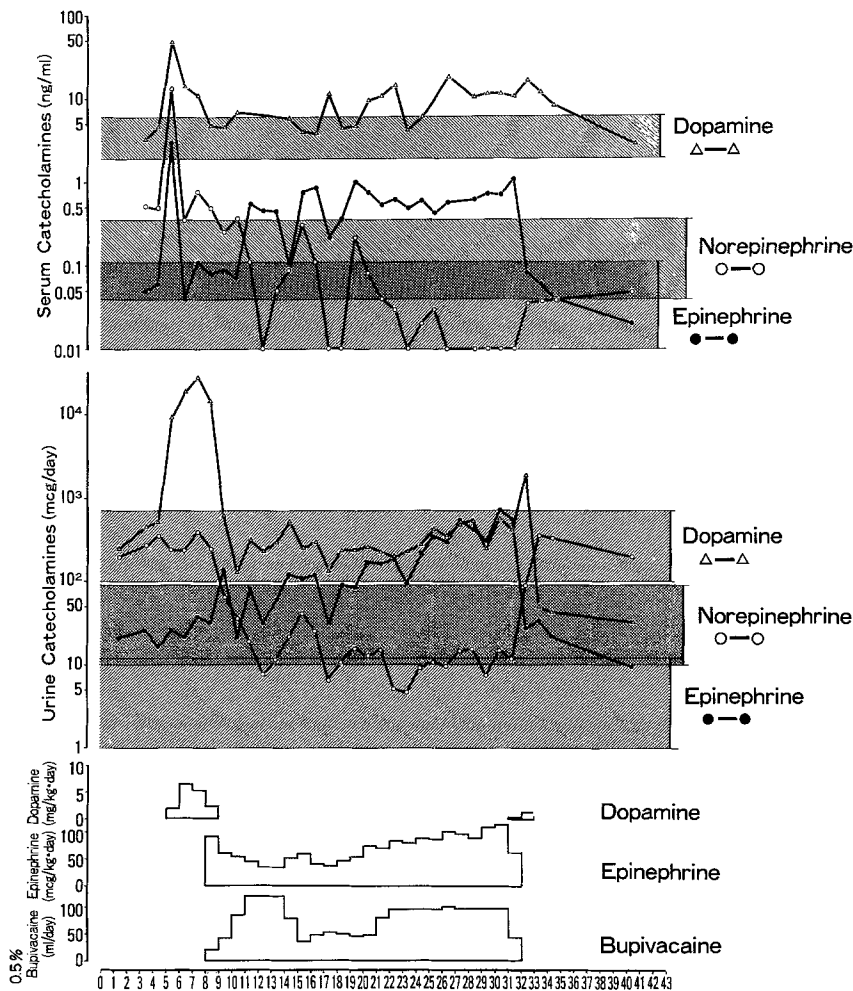In addition to hemodynamic stabilization, total spinal anesthesia depresses salivation and sweating

Fig. 4. Serum and urinary catecholamine levels

and may lower respiratory complications. Reduced requirements of sedatives and muscle relaxants could reduce the frequency of drug-induced organ dysfunction.

The complications of long-term spinal anesthesia are usually minimal, although meningitis is of course of potential hazard.

We conclude that total spinal anesthesia may have an important role in the treatment of patients with severe tetanus.

References

1. Armitage P, Clifford R (1978) Prognosis in tetanus: use of data from therapeutic trials. J Infect Dis 138:1–8
2. Baker AB (1942) The central nervous system in tetanus. J Neuropathol Exp Neurol 1:394–405
3. Benedict CR, Kerr JH (1977) Assessment of sympathetic overactivity in tetanus. Br Med J 2:806
4. Buchanan N, Cane G, De Andrade M (1979) Autonomic dysfunction in tetanus: the effects of a variety of therapeutic agents, with special reference to morphine. Intens Care Med 5:65–68
5. Buchanan N, Smith L, Cane RD, et al. (1978) Sympathetic overactivity in tetanus: fatality associated with propranolol. Br Med J 2:254–255
6. Tsueda K, Oliver PB, Richter RW (1974) Cardiovascular manifestations of tetanus. Anesthesiology 40:588–592
7. Clifton B (1964) Hypotension associated with tetanus. Lancet I:785–788
8. Connor H, Hine IP, Hart DC (1979) Labetalol in severe tetanus. Br Med J 2:502
9. Corbett JL, Spalding JMK, Harris PJ (1977) Hypotension in tetanus. Br Med J 3:423–428
10. Dastur FD, Bhat GJ, Nair KG (1975) Autonomic dysfunction as a problem in the treatment of tetanus. Prog Drug Res 19:245–251
11. De Michele DJ, Da Silva AMT (1983) Cardiovascular findings in a patient with severe tetanus. Crit Care Med 11:828–829
12. Dundee JW, Morrow WFK (1979) Labetalol in severe tetanus. Br Med J 1:1121–1122
13. Edmonson RS, Flowers MW (1979) Intensive care in tetanus: management, complications, and mortality in 100 cases. Br Med J 1:1401–1404
14. Gullo A, Romano E, Mocavero G (1983) Continuous epidural block in tetanus. Anaesthesia 38:817–818
15. Hanna W, Grell AC (1980) Oral labetalol in the manage-

ment of the sympathetic overactivity of severe tetanus. South Med J 73:653–654

16. Hörtnagl H, Brücke Th, Hackl JM (1979) The involvement of the sympathetic nervous system in tetanus. Klin Wochenschr 57:383–389

17. Hörtnagl H, Brücke Th, Hackl JM (1979) Dysfunction of the sympathetic nervous system in tetanus. A study of 3 cases. Klin Wochenschr 57:391–395

18. Kanarek DJ, Kaufman B, Zwi S (1973) Severe sympathetic hyperactivity associated with tetanus. Arch Intern Med 132:602–604

19. Keilty SR, Gray RC, Dundee JW, et al. (1968) Catecholamine levels in severe tetanus. Lancet II:195

20. Kerr JH, Corbett JL, Prys-Roberts C, et al. (1968) Involvement of the sympathetic nervous system in tetanus. Studies on 82 cases. Lancet II:236–241

21. Miller MT (1983) Epidural morphine in treatment of tetanus. S Afr Med J 63:31

22. Nicholson D (1976) Tetanus – still a therapeutic challenge. Heart Lung 5:226–227

23. Omar MAK, Wesley AG, Pather M (1979) Labetalol in severe tetanus. Br Med J 2:274

24. Prys-Roberts C, Corbett JL, Kerr JH, et al. (1969) Treatment of sympathetic overactivity in tetanus. Lancet I:542–546

25. Reichenbach DD, Benditt EP (1970) Catecholamines and cardiomyopathy: the pathogenesis and potential importance of myofibrillar degeneration. Hum Pathol 1:125–150

26. Rie MA, Wilson RS (1978) Morphine therapy controls autonomic hyperactivity in tetanus. Ann Intern Med 88:653–654

27. Sainani GS, Deshpande VRD, Balsara AB, et al. (1975) Role of beta-adrenergic blocking drug propranolol in severe tetanus. Prog Drug Res 19:361–366

28. Sun S, Dolar D, Özenç E (1982) Intrathecal morphine in tetanus. Br J Anaesth 54:699

29. Toothill C, Dykes JRW, Ablett JJL (1970) Urinary catecholamine metabolite concentrations in tetanus. Br J Anaesth 42:524–530

30. Trujillo M, Castillo A, Espana JV, et al. (1980) Tetanus in the adult: intensive care and management experience with 233 cases. Crit Care Med 8:419–423

31. Vaishnava H, Bhawal C, Munjal YP (1975) Mode of death in tetanus. Prog Drug Res 19:439–442

32. Wesley AG, Hariparsad D, Pather M, et al. (1983) Labetalol in tetanus. The treatment of sympathetic nervous system overactivity. Anaesthesia 38:243–249

33. Woods KL (1978) Hypotensive effect of propranolol and phenoperidine in tetanus. Br Med J 2:1164

Hisashi Sugimoto, M.D., Ph.D.
Department of Traumatology
Osaka University School of Medicine
1-1-50 Fukushima, Fukushima-ku, Osaka 553, Japan

Buchbesprechungen

Tumor Aneuploidy. (Editors: Büchner T, Bloomfield CD, Hiddemann W, Hossfeld DK, Schumann J) With contributions by Andreeff M, Barlogie B, Bassewitz DB von, Becher R, Bloomfield CD, Büchner T, Carbonell F, Eagle B, Fliedner TM, Ganser A, Göhde W, Grundmann E, Hauss J, Heimpel H, Henze G, Hiddemann W, Hoelzer D, Hossfeld DK, Kaufmann U, Kleinemeier HJ, Klinnert V, Langermann H-J, Melamed MR, Miller D, Müller K-M, Redner A, Rees JKH, Riehm H, Ritter J, Roessner A, Schellong G, Schumann J, Steinherz P, Thongprasert S, Weh H-J, Wörmann B. Springer, Berlin Heidelberg New York Tokyo 1985. VIII, 141 pp., 49 figs., 56 tabs. Soft cover DM 48,—.

Das vorliegende Buch über die Tumor-Aneuploidie ist eine Zusammenstellung der in europäischen und amerikanischen Forschungsgruppen untersuchten, verschiedenen Teilaspekte von DNA-Veränderungen in Neoplasien. Es sind die bisher vorliegenden Erkenntnisse über Chromosomenanalysen und quantitative durchflußzytophotometrische DNA-Messungen bei Leukämien und soliden Tumoren dargestellt. Neben Aspekten der Zytogenetik und der Tumorheterogenität werden die jeweilige Inzidenz der Aneuploidie sowie ihre Bedeutung für die Prognose und Therapieplanung erörtert. – Die einzelnen Teilaspekte der Tumor-Aneuploidie sind jeweils klar dargestellt. Der Leser wird in komprimierter und dennoch detaillierter Weise über den aktuellen Wissensstand informiert. Darüber hinaus wird eine Reihe noch offener Fragen aufgeworfen, die erst in zukünftigen und interdisziplinären Untersuchungen beantwortet werden können. – Das Buch bietet die Möglichkeit, sich in kurzer Zeit und zu einem angemessenen Preis mit der Problematik der Tumor-Aneuploidie vertraut zu machen.

W. Mellin (Münster)

Praktikum der Genetik. (Herausgeber: Winkler U). **Band 3: Humangenetik.** (Herausgeber: Wolf U, Mitherausgeber: Winkler U). Mit Beiträgen von Bender K, Bissbort S, Günther E, Mayerová A, Müller CR, Speit G, Vogel W, Wieacker P, Wienker TF. Springer, Berlin Heidelberg New York Tokyo 1985. XIV, 214 S., 38 Abb. Brosch. DM 29,80.

Praktikum der Genetik Band 3: Humangenetik ist ,das‘ Buch für wissenschaftliche Assistenten, die mit der Planung und Durchführung von Praktikumsversuchen beauftragt sind. In übersichtlicher, praxisbezogener Gliederung werden exemplarisch wichtige biochemische Methoden dargestellt. – Die Versuche sind nach zytogenetischen, biochemischen, immunologischen und molekularbiologischen Themen zusammengestellt und decken damit die derzeit wichtigsten Arbeitsmethoden der Humangenetik ab. Biologische Grundlagenforschung ist ebenso berücksichtigt wie praktische Medizin. So ist der vorliegende Band gleichermaßen geeignet für Biologen, Biotechniker und Mediziner. – Die einzelnen Versuche sind entsprechend praktikumsgerecht gegliedert. Einer kurzen theoretischen Einführung zur jeweiligen Fragestellung folgt ein detaillierter Zeitplan zur Versuchsdurchführung. Eine Liste über benötigte Materialien erleichtert die Organisation auch bei größerer Teilnehmerzahlen. – Die Versuchsabläufe sind vorbildlich beschrieben. Reichliche Illustrationen, Schemazeichnungen und schrittweise Anweisungen machen auch dem Neuling verständlich, was wie zu tun ist. – Aufgrund der außergewöhnlichen Anschaulichkeit scheint dieses Buch auch lohnenswert für den, der nicht selbst experimentell arbeitet, sondern Einblick in Methoden praxisbezogener Humangenetik erwerben will.

H. Schuster (München)